THE PREVALENCE AND RISK FACTORS OF CHRONIC NON-COMMUNICABLE LUNG DISEASES IN ADULTS IN RURAL AND URBAN SUDAN

'Thesis submitted in accordance with the requirements of the Liverpool School of Tropical Medicine for the degree of Doctor in Philosophy by Rana Ahmed'

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Abstract

The burden of chronic non-communicable lung disease in adults in rural and urban Sudan

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Non-communicable diseases (NCDs) are a major and increasing global health issue. They represent 71% (41million) of all global deaths including 3.9 million due to chronic respiratory diseases (CRDs) and chronic obstructive pulmonary disease (COPD) in particular. COPD is now the third most common cause of death globally; 90% of COPD deaths occur in Low and Middle-Income Countries (LMICs). Sub-Saharan Africa (SSA) and Middle East and North Africa (MENA) countries report similar mortality rates from COPD of 18 per 100,000 population. However, the burden of COPD SSA is disputed and reports offer variable prevalence estimates, ranging from 4.1% to 22.2%. The work in this thesis set out to contribute new knowledge to this area by conducting a review of the literature about non-communicable lung disease in SSA and MENA and through population-based cross-sectional studies (one urban and one rural) of the burden of non-communicable lung disease in adults in Sudan.

For the literature review, a broad review was undertaken to capture the breadth of work on non-communicable lung disease in SSA and MENA. The two cross-sectional studies were done to the same core Burden of Obstructive Lung Diseases (BOLD) protocol. The urban study was done in Khartoum state and sampled from the non-institutionalised population aged 40 years and above; the rural study was done in Gezira state and used the same sampling approach but with an extended age range – 18 and above. Alongside the rural study the potential role for digital data was explored for future studies of this nature.

Review of the literature found that whilst research has been done in this area, it is limited in breadth and depth. The prevalence of chronic respiratory symptoms (mainly shortness of breath was 10.9% and 18.7% in the urban and rural study participants, respectively). The prevalence of post bronchodilator airflow obstruction was 10.3% and 14.8% in urban Sudan and 5.5% and 7.7% in rural Sudan using Lower Limit of Normal (LLN) and Global Initiative for Chronic Obstructive Lung Disease (GOLD) definitions respectively. Older age was the main factor associated with airflow obstruction in both populations and helps to explain the difference in prevalence between the urban and rural studies as the latter included younger participants. Low Forced Vital Capacity (FVC) prevalence estimates were similar in the urban and rural studies - 58.1% vs 58% (Third National Health and Nutrition Examination Survey (NHANES) reference values), respectively. Pilot testing of digital compared to paper-based data capture found high levels of agreement between the two approaches suggesting that the former could be adopted in future work of this nature.

Taken together, the work presented in this thesis highlights the limited breadth and depth of research on non-communicable lung disease in SSA and MENA to date and identifies a high burden of chronic respiratory symptoms and spirometric abnormalities (mainly low FVC) in adults in urban and rural Sudan. These findings suggest there is a substantial but under-recognised burden of non-communicable lung disease in Sudan and elsewhere in SSA and MENA that calls for greater attention from the research community alongside public health and health system strengthening for the prevention and control of these problems.

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Dedication

To my Mother and Father who taught me to work hard for the things that I aspire to achieve, loved and supported me unconditionally…
To my other half, Mohamed, who has been a constant source of support and encouragement…
To my two little stars Mustafa and Minna…

Declaration

I declare this thesis is the result of my own work and has not been presented previously, except where stated below. The contributions of others are listed here and described below. The work was conducted at the Epidemiological Laboratory, Sudan and Liverpool School of Tropical Medicine, UK. My supervisors, Professor Kevin Mortimer (LSTM, UK), Professor Bertie Squire (LSTM, UK), Professor Asma El Sony (Epi-lab, Sudan) and Ms Rachael Thomson(LSTM, UK) advised on design, conduct, analysis and reporting for all research presented here.

The two BOLD studies presented in chapter 3 and 4 of this thesis were projects run by the Epidemiological Laboratory (Epi-lab) organisation in Sudan. Both projects had teams of data collectors, spirometry technicians, and project coordinators. The field work and data collection for the urban study led by Dr Nada Bakri and Dr Bandar Noory, however I led the rural study along with Dr Rashid Osman. I undertook all data management of both studies as well as design sampling and analysis plan of the rural study with the assistance of Professor Kevin Mortimer.

In the study presented in chapter 5, I did design, program, collect and analyse all study data. Ryan Robison proof read and edited the manuscript, Rasmus Malmborg edited the paper as consultant and funder while Professor Burney edited the manuscript.

The work within this thesis reflects work completed during my PhD study conducted in Sudan and funded by the Norwegian Heart and Lung Patient Organisation (LHL International Tuberculosis Foundation), The ATLAS Alliance and NORAD, Norway.

Individuals	Contribution	Chapter
Ryan Robinson (Liverpool School of Tropical of Medicine, UK)	Editing and review Editing and review	2 5
Professor Asma El Sony (Epi-Lab, Sudan)	Funding acquisition and editing	5
Rasmus Malmborg (LHL's International Tuberculosis Foundation, Oslo, Norway)	Funding acquisition and editing	5
Professor Peter Burney (Imperial College, London, United Kingdom)	Review and editing	5

List of abbreviations

AFO	Airflow Obstruction
ARIA	Allergic Rhinitis and its Impact on Asthma
ATS	American Thoracic Society
BOLD	Burden of Obstructive Lung Disease
BTS	British Thoracic Society
COPD	Chronic obstructive pulmonary disease
DALYs	Disability Adjusted life Years
Epi-Lab	The Epidemiological Laboratory
ERS	European Respiratory Society
FEV1	Forced Expiratory Volume in 1 second
FVC	Forced Volume Capacity
GBD	Global Burden of Diseases
GINA	Global Initiative for Asthma
GOLD	Global Initiative for Chronic Obstructive Lung Disease
HIV	Human Immunodeficiency Virus
ISAAC	International Study of Asthma and Allergies in Childhood
LLN	Lower limit of normal
LSTM	Liverpool School of Tropical Medicine
MENA	Middle East and North Africa
NCDA	East African Non Communicable Disease Alliance
NCDs	Non-communicable diseases
NGO	Non-governmental Organisation
NHANES III	Third National Health and Nutrition Examination Survey
PHC	Primary Health Centre
PLATINO	Chronic obstructive pulmonary disease in five Latin American cities study
PDA	Personal Digital Assistant
PTB	Pulmonary treated Tuberculosis
SSA	Sub-Saharan Africa
TB	Tuberculosis
The Union	International Union Against Tuberculosis and Lung Disease
UNDP	United Nation Development Program
WHO	World Health Organization

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Chapter 1 General introduction

1.1 Global burden of NCDs

Non-communicable diseases (NCDs), including cardiovascular diseases, diabetes, cancer and chronic respiratory diseases (primarily asthma and chronic obstructive pulmonary disease (COPD)), caused about 41 million deaths worldwide, representing 71% of all deaths (1). According to the latest WHO estimates, 15 million people aged between 30 and 69 die from NCDs annually (1). Eighty five percent of these deaths occurred in low and middle-income countries (1,2). The WHO NCDs status report of 2014 highlights that the number of deaths due to NCDs increased from 35 to 38 million in 2012 (3). NCDs are considered a major cause of deaths in LMICs, excluding those in sub-Saharan Africa(SSA)(4) as HIV/AIDS, pregnancy-related conditions, hypertension and injuries are the leading causes of death among adults in SSA(5). However, the projected data suggest a rapid increase in NCDs in SSA over the coming years which will have a significant economic impact, with the disease burden disproportionately affecting working-age-adults (4). NCDs have been identified by the WHO as a barrier to personal, community and national development, and as such addressing these diseases is an urgent development issue (4).

The WHO world health report in 2000 stated that lower respiratory tract infections, COPD, tuberculosis (TB) and lung cancer are amongst the top 10 causes of death worldwide. Respiratory diseases represent 17.4% of all deaths and 13.3% of all Disability-Adjusted Life Years (DALYs) (6). According to the report, the burden of chronic respiratory diseases (CRDs) including asthma, COPD, and lung cancer will increase as a result of tobacco usage and population ageing (6). However, CRDs are given limited attention, given their public health importance (7). The WHO strategy for prevention and management of CRDs was developed in 2001(6) but as stated by D Enarson and Aït-khaled et al, this strategy was only followed lately in 2005 and highlighted the need to integrate CRD prevention and control programs into health systems worldwide (7). COPD, asthma, occupational lung diseases, post-TB and post-pneumonia CRDs have been declared as emerging public health problem in developed regions of Low- and middle-income countries (LMICs) (8).

1.2 Africa/MENA Region

The Middle East and North African (MENA) region is located between Asia, Africa, and Europe, extending from Morocco to Pakistan, and is known as the Greater Middle East. Based on the United Nations agencies categorisation (9), the region includes 23 countries (Figure 1.1). Countries are sometimes omitted from MENA depending on organizational definitions, such as that of the World Bank (10), and are instead considered part of North Africa or Asia. These countries include Sudan, Somalia, Afghanistan, and Pakistan. In Sudan, as in the region, Islam is the predominant religion and Arabic is the most commonly spoken language.

Figure 1.1 Middle East and North African region as defined by the United Nation agencies.[1]

SSA is the region on the continent located south of the Sahara. The area is divided into sub-regions: West, East, Middle and South Africa. All African countries included in this region are either fully or partially located south of the Sahara. Sudan is often geographically located in SSA but is also considered part of North Africa and Arab world (11) (Figure 1.2).

[1] Figure Source: HIV and other sexually transmitted infections research in the Middle East and North Africa: Promising progress?, http://sti.bmj.com/content/89/Suppl_3/iii1.abstract

Figure 1.2 Sub-Saharan Africa as defined by the United Nations agencies (in colour) [2]

The Eastern Mediterranean Region Office (EMRO) is a regional office established by the WHO to support health and provide health statistics from most MENA countries, including Sudan. The EMRO reported that tackling NCDs in MENA is crucial as there is a growing burden of NCDs in the region where the reported number of deaths was 2.2 million in 2012, representing 53% of all deaths and an alarming rise of NCD prevalence is expected to result in 2.4 million deaths per year in the region by 2025 (12). Regional data on CRDs mostly concern asthma and COPD and suggests that about 8% of the population in the EMRO have asthma and the number of deaths due to asthma expected in the region for 2030 is 27,000. There is substantial variation in premature mortalities resulting from NCDs in the region, varying from

[2] Figure source : https://diningforwomen.org/sub-saharan-africa-and-the-sustainable-development-goals/

24% in Tunisia to 63% in Afghanistan (13). Available data for mortality due to CRD in the region ranges from 2% to 4% (13).

In Africa as a whole, the WHO predicts an increase of 27% in NCD deaths by 2030. While the burden of communicable diseases has been the primary concern, this is changing rapidly; by 2030 the number of deaths due to NCDs is expected to outstrip the number of deaths due to communicable, maternal perinatal and nutritional diseases combined (14). In addition, there is a projected increase of 50% in number of deaths due to NCDs in LMIC by 2030 (15). The expectation that NCDs will become the leading cause of ill health, premature death and disability in Africa means their burden will increasingly negatively affect socio-economic development on the continent (14,15). Premature deaths due to NCDs was 43% in 2011 as reported by WHO, higher than in EMRO (13). However, SSA is expected to have a considerable change in NCDs mortality and deaths due to NCDs is projected to account for 46% of all deaths by 2030 (15).

Despite the epidemiological transition from communicable to non-communicable diseases, research has focused on the former to date (16). Organisations like the WHO have identified the need for research including basic burden of disease data about NCDs as a priority and have created a global action plan for the prevention and control of NCDs as well as region-specific plans of action, as in EMRO (12,17). In addition, the East African NCD Alliance (NCDA) recently led the creation of a continent-wide NCD Research Group to aid NCD research in a comprehensive, multi-sectoral and harmonised methodology by including a region-wide group of multi-disciplinary teams (18).

1.3 Sudan

Sudan is in North East Africa, bordered by 7 countries (Fig. 1.3). Sudan, now known as North Sudan, is the third largest country in Africa and the sixteenth largest in the world with a population of 41,511,526 (19,20). Sudan is a rich country in terms of natural resources and population but has been affected by war for most of its independent history since 1955 with most conflict occurring in the South, in Southern Kordufan and Blue Nile states. In 2011, its southern states seceded, forming the Republic of South Sudan causing considerable economic instability. Loss of oil

income was the most significant issue as this represented over half of the government's income and 95% of its exports. This has resulted in much decreased economic growth (21) as well as the unequal distribution of economic resources and reduced access to natural resources. The government's failure to overcome these challenges were cited by the World Bank as a major determinant of poverty in Sudan (21).

Civil conflicts have also recently spread to other parts of northern Sudan in the Darfur states. Health, population, and nutrition have been significantly affected by these conflicts. WHO reported that more than 2 million people have died, and more than 4 million are currently internally displaced or have become refugees because of these conflicts and their related impacts. Health services have been extremely negatively impacted during the two decades of conflicts, despite not being well-established beforehand (22).

Figure 1.3 Sudan, country map and neighbouring countries.[3]

[3] Map source: https://www.thinglink.com/scene/885206811320254465

As reported by WHO, the total deaths from NCDs in Sudan were estimated to be 297,000 in 2012 which accounts for 34% of the total deaths in the country that year. Lower respiratory infections were the leading cause of death, killing 37.8 thousand people in 2012 (23). WHO reported that CRDs accounted for 2% of the total deaths from NCDs, though they highlighted that these estimates have a high degree of uncertainty because they are not based on national NCD mortality data (24). Nevertheless, in 2016 reports by the Federal Ministry of health in Sudan showed that NCDs represented 87% of the patients attending outpatient clinics in hospitals, while respiratory diseases were the fourth highest cause of death in Sudan, accounting for 3.9% of the total number of the deaths in hospitals and 10.3% of the total number of child deaths. The prevalence of respiratory disease is 36 people per 1000, ranking second highest after Malaria. Additionally, deaths due to respiratory disease represent 5.5% and 3.2% of the total number of deaths in Khartoum and Gezira state respectively (25). On the other hand, according to El Sony *et al,* asthma ranked the third most common cause of hospitalization following pneumonia and malaria in 2004 (26).

COPD, amongst other CRDs, has been inadequately investigated in Sudan and studies regarding disease prevalence and their main determinants are scarce, being conducted only in specific populations such miners and coronary artery disease patients (27,28).

1.4 Khartoum and Gezira state

Khartoum State is located in the heart of Sudan and is bordered by 7 other states (River Nile, Northern State, Kassala, Gadaref, Gezira, White Nile and North Kordofan). It is the most populated and urbanized state in Sudan consisting of urban, semi-urban, rural, and internally displaced populations from different conflict areas with a total population of 5,274,321. Respiratory diseases were listed as one of the most common causes of death in hospitals in Khartoum state in 2016; contributing 5.5% of the total deaths in Sudan due to respiratory diseases.

Gezira state is in the eastern central region of Sudan, lies south of Khartoum state and is bordered by 4 localities (Khartoum, Gadaref, White Nile and Sinnar). It has a population of 3,780,915. The population of the state is rural, with 80% of its people living in rural areas and 19.1% urban according to the 2008 national census(20).

Respiratory diseases were again listed as one of the most common causes of death in hospitals in Gezira state in 2016; contributing 3.2% of the total deaths in Sudan due to respiratory disease.

1.5 The health system in Sudan

The Sudanese health policy aims at assuring an equitable access to preventive, promotive and curative health services to the population. The country follows a three-tier health-care delivery system: (A) Federal level, which is mainly responsible for the formulation of national policies, plans and strategies: resource mobilization, overall monitoring and evaluation, coordination, supervision, training and external relations; (B) State level, which is responsible for the formulation of State policies, plans and strategies, according to federal guidelines, funding and implementation of plans; and (C) Local/district level, which is mainly responsible for the implementation of national/state policies and service delivery based on the primary health care approach. Hospitals in Khartoum and Gezira States vary from state to local level, and are categorized into general, specialized, and rural hospitals. In addition, there are sector hospitals which belong to specific sectors such as the military, the police, or the Ministry of education. Since 1976, primary health care has been adopted as a key strategy for healthcare provision in Sudan and this has been further emphasized in the national comprehensive strategy for health (1992-2002) and in the 25-year strategic health plan (2003-2027) - see Figure 1.4 (22). Private for-profit and non-government organization sectors are supplementing the health service coverage at various states (22).

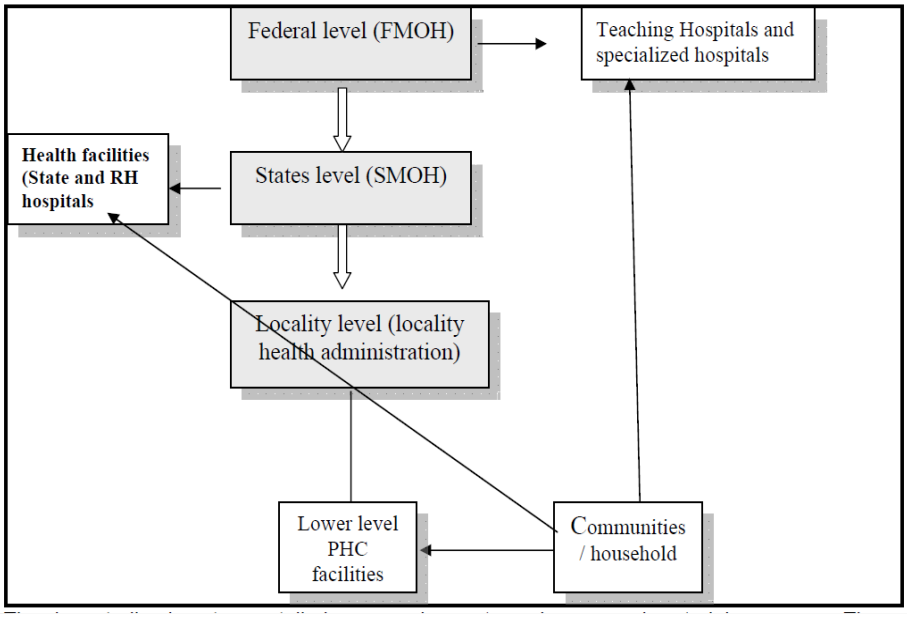


Figure 1.4 The health-care system organization of Sudan[4]

1.6 Asthma and COPD services in Sudan

Sudan's Asthma Guidelines were developed in 2002 (29) and built on the International Union Against Tuberculosis and Lung disease (The Union) model while adapted for the Sudanese context. These guidelines made the use of essential medicines mandatory due to limited resources (30). Nevertheless, these guidelines have not yet been widely adopted in the country. Peak flow meters are not used effectively for diagnosis and staff remain unable to carry out the long-term management of asthma patients (26). Asthma services are normally provided in emergency rooms in Sudan as a first referral point. Hospitalised patients are asked to attend follow-up appointments in specialised outpatient clinics. Unlike asthma, there are no management guidelines for COPD in Sudan and the use of spirometry devices for diagnosis is confined to particular specialised hospitals. Additionally, COPD is poorly understood by both the general public and some physicians in Sudan.

1.7 Smartphone data collection

Smartphones have been described as the combination of the traditional Personal Digital Assistant (PDA) and mobile phone, with an improved focus on the mobile phone part. These handheld devices incorporate mobile phone capabilities with the

[4] Sudan Federal Ministry of Health (www.fmoh.gov.sd)

more common features of a handheld computer or PDA. As information communication technologies grow, with software supporting 'Android' platforms and the development of many open-source applications, researchers in the health sector have begun using smartphones as a tool in patient data collection, disease surveillance, clinical research and national surveys (31,32). However, paper-based questionnaires continue to be the main data collection tool in many countries, especially in SSA (32).

1.8 The Epidemiological laboratory

The Epidemiological Laboratory (Epi-Lab) is a public health services research centre, situated in a non-governmental, non-profit organization based in Khartoum, Sudan (33). It has been designated as a collaborative Centre of the WHO and the International Union against Tuberculosis and Lung Disease (The Union) and WHO. The University of Oslo and the International Cooperation, International Tuberculosis Foundation (LHLI) are co-founders.

In order to assess the burden of chronic NCDs in Sudan (especially COPD) Epi-Lab has been involved in implementing two Burden of Obstructive Pulmonary Lung Disease (BOLD) studies in Sudan in collaboration with Imperial college, London. Fieldwork for the first study was done between 2012 and 2014 in Khartoum State and for the second study between 2015 and 2016 in Gezira State. Epi-lab has hosted all studies presented in this thesis.

1.9 Objectives

Overall:

- To improve our understanding of chronic non-communicable lung disease in Sudan.

Specific:

- To measure the prevalence and investigate the main risk factors of airflow obstruction and chronic obstructive pulmonary disease in Khartoum State.
- To measure the prevalence and investigate the main risk factors of non-communicable chronic lung diseases in adults in Gezira State.

- To study the variation in the prevalence of airflow obstruction and other chronic lung disease between rural and urban populations in Sudan.
- To compare prevalence findings from Sudan with global findings in BOLD studies.
- To study the applicability of using smartphones in the data collection of BOLD studies.
- To compare smartphone data collection methods with paper-based methods in BOLD studies with respect to accuracy, completeness, and the quality of data in Gezira State, Sudan.

1.10 This thesis

The thesis consists of six chapters. Chapter 1 (this chapter) has presented is a general introduction to the topics and objectives of the study. Chapter 2 is an overview of the literature on the epidemiology of non-communicable lung disease in SSA and MENA with a focus on asthma and COPD. Chapter three describes a study of the burden, prevalence, and main determinants of CRD in urban Sudan. Chapter four describes a study of the burden, prevalence, and main determinants of CRD in rural Sudan. Chapter 5 describes a study of the use of automated data collection in comparison to traditional paper-based collection done as part of the rural survey conducted in Gezira state. Chapter 6 concludes the thesis with a summary and discussion of the findings of these studies and identifies areas for further research. A schematic presentation of the relationships of the studies with chapters has been illustrated in Figure 1.5.

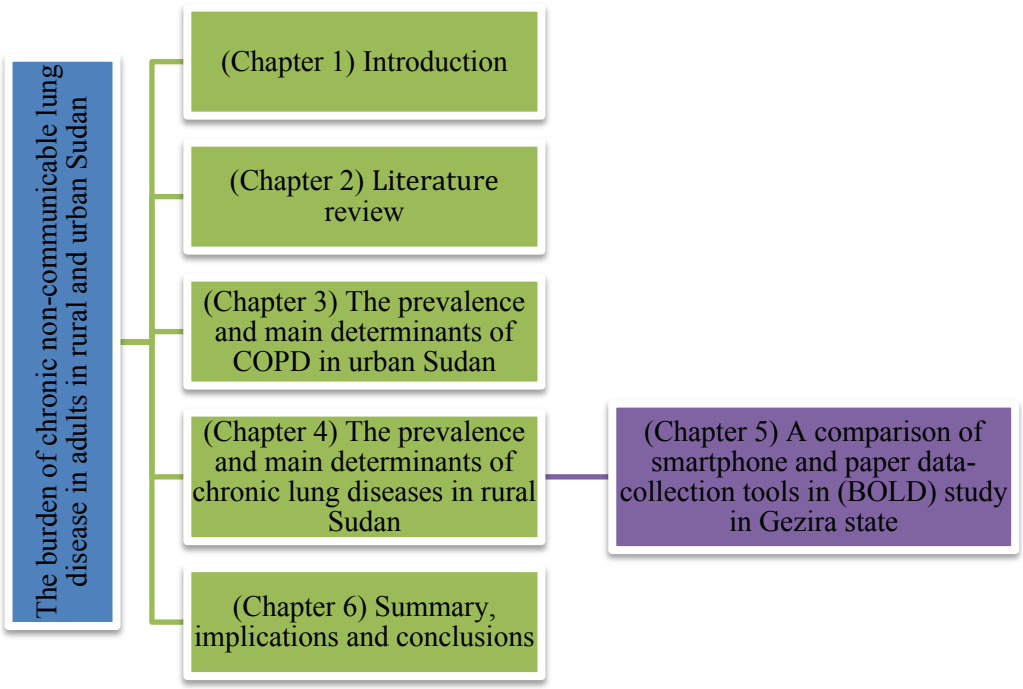


Figure 1.5 Study conceptual framework of the burden of non-communicable lung diseases in rural and urban Sudan.

Chapter 2 The epidemiology of Chronic Obstructive Pulmonary Disease and asthma in SSA and MENA regions

2.1 Search strategy

A detailed search strategy was developed and revised appropriately for the following electronic databases: PubMed, Science direct, Global health, Medline, Google Scholar, and BOLD website, using English only text from established peer- reviewed journals with no time limits, however most recent publications were included. Due to the lack of academic articles in the area of the epidemiology of chronic non communicable lung diseases in SSA and MENA regions wider search strategy was undertaken using more general terms to identify studies for inclusion in this review. The search strategy combinations of key terms and inclusion criteria are stated in Appendix (1). The researcher also reviewed relevant academic books, organisational publications and grey literature.

2.2 Introduction

Non-communicable diseases (NCDs) are a major and increasing global health issue. Annually, death from the main four categories of NCDs represents 71% of the global death (2). Of these, 3.9 million were due to CRDs. WHO estimated that over the following decade respiratory diseases would be responsible for the largest increase in global mortality (17,34). LMICs are responsible for 80% of the NCD deaths, of which an estimated 12% are due to respiratory problems, particularly asthma and COPD (2,34). Respiratory diseases also have significant economic impacts, causing 4.7% of global DALYs, two-thirds of which are due to COPD and one-fifth due to asthma (2). Much of the details has already been given in the preceding chapter.

The impact of CRDs in the developing world is a growing problem. COPD rose from the fourth to the third most common cause of death between 1990 and 2010 (35–37). Ninety per cent of COPD deaths now occur in LMICs (38–41). However, in many of these countries, governments and medical professionals have historically not given CRDs commensurate attention. This study set out to review the literature on the epidemiology of CRDs in sub-Saharan Africa (SSA) and the Middle East and North Africa (MENA) with a focus on asthma and COPD.

2.3 Airflow Obstruction

Airflow obstruction indicates predominant spirometric findings of a reduced expiratory airflow compared to the total amount of air exhaled. Its defined as a reduction in the ratio of forced expiratory volume in 1 second (FEV_1) to forced vital capacity(FVC). Its considered as the central feature of chronic obstructive pulmonary disease (COPD) and primarily associated with smoking(42–44).

2.4 COPD

In the previous decade, airflow obstruction has frequently been defined as a functional disorder, which is the result of different diseases such as chronic bronchitis or emphysema, bronchiectasis, bronchiolitis obliterans, chronic post-tuberculosis lung disease and smoking-related airway disease (45–47).

Four professional boards defined COPD and adopted the same key points in the definition for COPD as the European Respiratory Society (ERS) in 1995, the American Thoracic Society (ATS) in 1995, the British Thoracic Society (BTS) in 1997 and the Global Initiative for Chronic Obstructive Lung Disease (GOLD) in 1998 (47).

The ATS and ERS define COPD as a "preventable and treatable disease state characterised by airflow limitation that is not fully reversible" (48,49). GOLD standardised the definition of COPD to a "preventable and treatable disease categorised by persistent airflow limitations which is mostly increasingly related and enhanced by chronic inflammatory responses of the airways and lung to harmful elements or smokes" (49). Despite this, varying definitions of COPD are used globally (50). COPD is mainly caused by cigarette smoking and leads to symptoms of cough, excessive sputum production, and breathlessness, causing considerable disability as the illness progresses (51).

2.5 Asthma

The Global Initiative for Asthma (GINA) defines asthma as a "heterogeneous disease, usually characterised by chronic airway inflammation. It is characterised by a history of respiratory symptoms such as wheeze, shortness of breath, chest tightness and cough that vary in intensity and over time, together with expiratory airflow limitation" (52). However, asthma lacks a gold standard definition with other

definitions also in use. Nevertheless, bronchial hyper-responsiveness, airway inflammation, and obstruction which may be reduced spontaneously or with medication are widely accepted features (53). There can be a chronic reduction in FEV_1 and peak expiratory flow (PEF), with the degree of reduction being one marker of disease severity (54).

In epidemiological settings, methods of identifying asthma mainly depend on airway reversibility, however a study by Albert *et al* reported a limitation of using bronchodilator reversibility as an indication for asthma as the study concluded that reversibility status on one occasion is an unreliable basis for concluding clinical decisions(55).

2.6 Disease management and global initiatives

Several guidelines, such as GOLD, GINA, and the 'Allergic Rhinitis and its Impact on Asthma' (ARIA) guidelines were developed to improve the management of CRDs.

2.6.1 CRDs initiatives

In 2002, the WHO developed 'The Global Strategy for the Prevention and Control of NCDs'. Clear objectives were drawn to provide better surveillance and monitor NCLD trends and lower the level of exposure to recognised risk factors. Moreover, it aimed to strengthen the available health care systems (6). In addition to general guidelines for NCLDs, asthma and COPD action plans for 2013 up to 2020 were developed to follow the WHO treatment guidelines and provide influenza vaccination for patients with COPD (17,56). In 2002 and 2003, the WHO conducted the World Health Survey as a standardised survey tool to allow comparisons between diseases findings, including asthma within and between countries to inform policy in a wide range of countries (57,58).

2.6.2 COPD initiatives

Consistent across different guidelines, such as GOLD, the ERS and ATS, is the need for spirometry to diagnose COPD (48,59–62). GOLD requires the diagnosis of COPD to be based on spirometric testing, specifically the documentation of a post-bronchodilator 'forced expiratory volume in one second' (FEV1) to 'forced vital capacity' (FVC) ratio (FEV1/FVC) of <0.7 (61,63). In addition to spirometry, COPD

is also diagnosed based on the level of patient symptoms and potential risk of exacerbations (59,61,64) . In contrast, the American Thoracic Society (ATS) and European Respiratory Society (ERS) defines COPD as FEV1/FVC ratio below the lower limit of normal (LLN) (46,65).

In 2015, the ERS/ATS published an official statement evaluating recognised COPD diagnostic standards and recommending further study to evaluate the long-term prognosis of diagnosed patients based on different COPD definitions (48). The guidelines highlighted that the confirmation of diagnosis can be ascertained by observing airflow limitation, defined by a low post-bronchodilator FEV1/FVC ratio. However, exposure to potential causative factors, such as smoking, and present symptoms should be taken into consideration. Additionally, the statement highlighted that using a fixed cut-off point can potentially overestimate COPD in elderly populations while underestimating the disease among populations younger than 45, when compared to the use of LLN (48). This was also discussed in GOLD 2014 and 2016 annual reports, where it was asserted that more frequent diagnoses of mild COPD in adults above 45 might be due to the use of fixed ratio FEV1/FVC (59,64). In addition GOLD reported that the use of staging based on FEV1 only was insufficient and there is a lack of proof for different staging classifications and therefore the GOLD staging system has been modified (59,64).

2.6.2.1 BOLD Initiative

The BOLD initiative was established to further develop international standardised methods for estimating COPD prevalence and associated risk factors in populations who are 40 and older (66,67). It has been designed to provide consistent methods with which to compare COPD burden within and between countries, as well as to study the variations, where they exist (68,69). Additionally, it aims to measure the influence of COPD on quality of life, activity limitation, respiratory symptoms and usage of healthcare services (67,70). BOLD studies have provided a framework for assessing the economic burden of COPD by developing the 'BOLD Health Economic Model' (66,70) and the distribution of the disease in relation to age, sex, and smoking status across a range of countries and settings (67,69). BOLD studies have also helped to describe the clinical symptoms reported by subjects diagnosed with COPD (67), provided a comparison of the effect of using different definitions such as

ATS/ERS and GOLD on COPD prevalence and explored the variation of risk factors and their impact on the variation of COPD prevalence (67,68).

In all BOLD studies implemented worldwide, the BOLD Operations Centre provides training for local study staff, materials to be used for questionnaires and data collection forms, in addition to quality control tools for collected spirometry data as well as for questionnaire data at each stage of the collection process (68). This includes a revision of the pre- and post-bronchodilator spirometry test, as well as the questionnaire data. A web platform for electronic data entry in all BOLD studies has also been developed by the BOLD Operation Centre with all paper questionnaires collected in the field being entered electronically (68).

2.6.3 Asthma initiatives

In the 1990s, GINA proposed strategies and guidelines for asthma management, and standardised the definition so it could be clearly distinguished from other respiratory diseases (71). In 1996, the International Union Against Tuberculosis and Lung Disease adopted these guidelines to control asthma in developing countries (72). However, as demonstrated by Aït-Khaled *et al*, there is a need to effectively utilise these guidelines, especially in rural areas in Africa (73).

2.7 Global COPD and asthma disease burden

The Global Burden of Disease study estimated that COPD affected almost 251 million people globally in 2016 and resulted in 3.17 million deaths (5% of all global deaths in 2016) (74). However, it is poorly recognised and undertreated in most populations (74,75). Asthma is estimated to affect 235 million people, and the WHO reported that 383,000 deaths in 2015 were due to asthma (76). Furthermore, 635 million people are reported to be living with some level of asthma-like symptoms (57).

Worldwide, males and females are affected by COPD to a similar extent (4.9% and 4.7%, respectively) (77). The gender distribution of asthma varies with age: in childhood males are more frequently affected, but after adolescence prevalence is higher among females (78). Overall, asthma is estimated to affect slightly more females than males (5.1% and 4.6%, respectively) (77).

WHO estimates that 65 million people have moderate to severe COPD and three million people die as a direct cause of it annually. This corresponds to 5% of all global deaths, the majority of which occur in LMICs. Deaths from COPD show an upward trajectory (79,80). The number of individuals affected by asthma is predicted to increase to 400 million by 2025 (57,81).

In Africa, mortality from COPD was estimated to be 18.1 per 100,000 in 2001 with a similar rate, 18.3 per 100,000, seen in Eastern Mediterranean countries (47). While deaths less frequently result from asthma than COPD, WHO estimates that there are 250,000 deaths per year from asthma, mainly in LMICs (82). Asthma is in the top twenty causes of disability in children globally (73).

2.8 Burden of COPD in United States, Europe and Asia and Pacific

Different studies are currently being conducted across the world to estimate the prevalence of COPD. NHANES III (Third National Health and Nutrition Survey) was the most important study in COPD prevalence in US from 1988 to 1994. It highlighted many challenges and limitations in previous studies regarding COPD and unexpectedly estimated high levels of COPD prevalence in adult populations (83). The study reported a prevalence of 13.9% with approximately 10% of these classified as a disease stage of severe or very severe (83).

According to the most recent published data from NHANES III the prevalence of respiratory symptoms, COPD and asthma that was medically diagnosed in US populations aged 25 and older was 15.1% based on spirometric lung function testing and 5.2% based on medical diagnosis of COPD (chronic bronchitis, emphysema, or both) (84). In contrast, a recent study from Canada illustrated that estimations of worldwide COPD prevalence range from 5% to 10% (85).

One popular COPD study was the PLATINO study (Chronic Obstructive Pulmonary Disease in five Latin American cities study). It was designed to follow a two-stage sampling approach to obtain probability samples of adults aged 40 or older. The study prevalence ranged from 7.8% (78/1000) in Mexico City to almost 20% (174/885) in

Montevideo. Prevalence was higher in men and older people, and those with a lower education level, lower BMI and greater exposure to smoking (86).

Estimates regarding COPD prevalence have shown notable variation around the world where different methodologies have been used. A systematic review that included thirty two prevalence estimates from 17 countries and eight WHO classified regions, and aimed to understand the true burden of COPD and interpret worldwide prevalence findings, argued that several factors complicated the estimation of the true burden of COPD (46). Their findings addressed the variability in methods used in conducting COPD studies, whether based on spirometry, assessment of respiratory symptoms, patient-reported disease or expert opinion. The findings included inconsistencies in COPD definitions and reported figures that included asthmatic patients (46). As shown in the same systematic review, prevalence estimates varied from 0.23% to 18.3% while most well designed studies reported a prevalence between 4% and 10% in adult populations (46).

The first quantitative worldwide summary of COPD prevalence literature was reported in a systematic review and meta-analysis conducted in 2006 aiming to quantify the global burden and prevalence of COPD from population-based studies published from 1990 to 2004 (87). This study illustrated the notable variation in estimates and heterogeneity of methodologies and definitions used (87). This was consistent with the previous stated review (46). It demonstrates that for key regions outside Europe and North America high quality estimates for COPD prevalence are lacking, and while there are some spirometry studies in American, South-East Asian and Western Pacific regions, there were none in Africa or the Eastern Mediterranean during the review period (87).

Other studies confirmed these previous study findings and reiterated that many factors can influence the prevalence estimations and therefore it is crucial to note the country, methods used and base population for reported prevalence (46,69,87). A systematic review aimed at understanding the variability of chronic obstructive pulmonary disease data in Europe repeated these assertions (45). This review included 21 countries and prevalence ranged from 2.1% to 26.1%, while COPD mortality rates ranged from 7.2 to 36.1 per 105 population, differing based on

country, age group and methods used. In six of the nine papers that used the GOLD definition of COPD included in this review, the prevalence findings varied from 10.2% in Spain to 26.1% in Austria (45).

The International BOLD study of 12 BOLD sites found higher prevalence variation, from 13.3% in Germany to 26.1% in Austria (45,69). In addition, prevalence of COPD Stage II or higher was 10% in the overall population. This was higher in men than in women (11.8% and 8.5% respectively) (69).

In the Asia and Pacific region, COPD was considered a high-burden disease at all levels. It was highly associated with mortality and morbidity as shown by most of the studies in the region. Different studies from Singapore, Japan, Taiwan and Hong Kong reported that 7% to 10% of middle-aged and elderly populations had an airflow obstruction and nearly half of them had moderate to severe COPD (88). Recent findings from northern Thailand were consistent with the Asia and Pacific region as the reported prevalence was estimated to be about 1% across all ages and increasing sharply to 8–10% or higher in individuals aged 40 or older (87,89).

2.9 COPD burden in SSA

The burden of COPD in SSA is disputed and reports offer variable prevalence estimates (90,91). Finney *et al* conducted a systematic review of nine cross-sectional studies (five from South Africa, two from Nigeria, one from Malawi and one from Cape Verde) reporting a prevalence ranging from 4.1% to 24.8% based on the diagnostic method used (92). Chan-Yeung *et al* estimate a prevalence of 179 per 100,000 in Africa and 301 per 100,000 in Eastern Mediterranean countries, less than that of America and Europe (38,93). However, a recent systematic analysis by Adeolaye *et al* reported the estimated median prevalence of COPD in people aged 40 or older as 13.4% (range 9.4% to 22.1%), translating to 26.3 million (18.5 to 43.4 million) cases of COPD in SSA (94). In SSA, Cape Town in South Africa had the highest prevalence estimates published in the international BOLD study, where GOLD stage II prevalence was 22.2% in men older than 40 (38,79,95).

There are several possible explanations for the variation in COPD prevalence estimates. Firstly, relevant epidemiological data is lacking because of a paucity of

data from representative samples (27). Secondly, the studies that do exist are limited by the lack of a standardised definition of COPD with marked variation in the diagnostic methods used (33). In particular, there is a widespread shortage of good quality post-bronchodilator spirometry (90,96). Diagnosis frequently depends on clinical judgment, and knowledge about COPD is often limited. Many people, including health workers, are not well informed about the effects of cigarette smoking and exposure to smoke from the burning of biomass fuels on their respiratory health (97).

2.10 Asthma burden in SSA

There is similarly large variation in reported asthma prevalence in Africa. Available published data gives estimates of asthma prevalence in SSA between 6% and 20% (98). The International Study of Asthma and Allergies in Childhood (ISAAC) has been the most widely used prevalence research methodology in Africa (82), as its diagnostic criteria have been shown to be reproducible and able to differentiate between children with allergic diseases in different areas of the world (99). Another review reported that prevalence rates in Africa varied according to the ISSAC study results (Ethiopia 9.1%, Kenya 15.8%, Nigeria 13.0% and South Africa 20.3%) while rural areas reported lower prevalence than urban areas (38,100). In 2011, Musafiri *et al* reported an increase in asthma prevalence in Africa over the past two decades, with 50 million people currently living with asthma (101). In 2013, a systematic review by Adeloye *et al* reported a similar prevalence to that of high-income countries. In 1997, the aggregated prevalence was highest in South Africa (53% of 5-12 year olds) and lowest in The Gambia (1.9% of >15 years) (73). Adeloye *et al* estimated that asthma increased in prevalence from 11.7% in 1990 to 12.8% in 2010 in the general population. Evidence of this rise is also provided by the Global Burden of Asthma Report, which asserts that the highest levels of asthma are in South Africa (54). ISAAC phase three reported that Africa, the Indian sub-continent and the Eastern Mediterranean had the highest proportion of severe asthmatics (102).

2.11 COPD burden in MENA countries

As in SSA, the burden of COPD is increasing in MENA countries. Although there is a paucity of good epidemiological data, there appear to be substantial differences in prevalence estimates between countries in the region (93,96). Tunisia reportedly has

a prevalence of 4.2% - 4.7% compared to 125 per 100,000 people in Algeria and 5.6% in Lebanon (93,103,104). A recent study from Saudi Arabia estimated COPD prevalence to be 2.4% in the general population and 14.2% among smokers (105). Prevalence of 3.7% in 40 to 80 year olds was reported in Abu Dhabi, United Arab Emirates (106). The BREATHE study, a large observational population-based survey, completed in ten countries in MENA and Pakistan, reports that the available data from the region does not represent national COPD prevalence accurately as community-based prevalence surveys in the region are infrequent and available epidemiological data are either incomplete or restricted to a small area (93,96,107). The estimated overall COPD adjusted prevalence according to symptoms or diagnosis and 10-pack/year smoking was 3.6%, and is higher in men than in women (5.2% and 1.8%, respectively) (108).

2.12 Asthma burden in MENA countries

There is substantial variability in the reported prevalence of asthma in the MENA region. In 1998 the ISAAC study reported an overall prevalence of 16.5% in North Africa and 10.7% in the Eastern Mediterranean (93). The study showed prevalence in children at 5% and 12% in rural and urban Sudan respectively (109), and ranging from 8.8% to 9.5% in rural and urban Jordan respectively (93). The World Health Survey published the global asthma prevalence from 70 countries in 2012. The overall prevalence in the Eastern Mediterranean region was 2.9%, 3.0% and 7.9% for 'doctor diagnosed', 'clinical', and 'wheezing symptoms asthma' respectively (57). In contrast, the 'Asthma Insights and Reality in the Maghreb' (AIRMAG) study reported an overall prevalence of 3.6% in the general population of Maghreb, with no significant disparity between the three countries (Algeria, Morocco, and Tunisia) (73,93,110). Egypt reported a prevalence of 14.7% for wheezing in that year and 9.4% of medically diagnosed asthma (111). There was varying prevalence in Saudi Arabia, ranging from 8% to 25% in children, with 19.6% of adolescents having medically diagnosed asthma (112) and 4.1% of adults self-reporting asthma (113). Results from Iran showed a similarly varying prevalence ranging from 1.4% to 5.9% in the adult population (114).

2.13 COPD studies focused on rural and urban populations

Studies around the world have studied differences in COPD prevalence between rural and urban populations. Others have studied only rural or urban populations.

A study from two areas in Sweden reported COPD prevalence among never-smokers was 2.0% for GOLD1, 1.4% GOLD2 and 1.3% for GOLD3. Occupational exposure to gas, dust or fumes in never-smokers was significantly associated with both COPD and GOLD grades. There was no significant difference in prevalence between the two studied areas or sex and prevalence increased significantly with age (35).

In two areas in China, a study was conducted in populations aged 40 and older in urban (Liwang) and rural (Yunyan) areas in Guangdong. The study reported overall COPD prevalence of 9.4% and a significant association between COPD and living in rural areas. The overall prevalence was significantly higher in non-smoking women living in the rural study area (7.2% vs. 2.5% for non-smoking women and 12.0% vs. 7.4% for overall prevalence). Use of biomass fuels and indoor pollution was significantly associated with COPD as use of biomass fuel was found to be higher in rural areas (88.1% vs. 0.7% in urban areas) (115). Systematic review findings were consistent with the above study and confirmed that prevalence of COPD was significantly higher in rural Chinese populations (80). In the same study, the overall prevalence of COPD in seven provinces in China was found to be 8.4% (men 12.4%, women 5.1%), which was significantly higher for rural residents (79,80,116).

A population based cross-sectional study targeting people aged 40 and older in one province in in Northern Thailand assessed the differences in COPD prevalence in rural and urban communities. The study assessment, based on the GOLD criteria, found that both rural and urban communities were equally under-diagnosed and undertreated. COPD prevalence was higher in rural populations (6.8% compared to 3.7% in urban group). Females had the highest prevalence in the general population with more severe disease in rural communities (4.4% in rural vs. 0.9% in urban group). These findings were explained as the result of the higher levels of smoking among females in rural communities. Other than smoking status and aging, especially in urban men, no risk factors were associated with a significant difference in prevalence calculations (89).

In Turkey (83), a BOLD study on COPD prevalence was conducted in different rural and urban areas. The study recruited adults aged >18. In the group aged 40 and older, COPD prevalence was 9.1%, while in younger adults it was 2.9%. The overall prevalence was 6.9%, and 18.1% in both current smokers and those aged 40 and older. In the younger age group of smokers, the prevalence was 4.5%. Cigarette smoke was the greatest cause of COPD in all subgroups except for in females in rural areas. Similar to findings from other studies in developing countries and Africa (89,97,117), this study found 54.5% of females with COPD living in rural areas were exposed to smoke from biomass fuels. Smoking was responsible for COPD in 40% of females and 91% in males in the urban region and 26% in the rural region. Eighty per cent of COPD patients in rural regions had COPD due to exposure at work (83). This finding was replicated in a study from India which asserted that the COPD burden among rural women in developing countries was largely a consequence of chronic exposure to biomass fuels smoke (118).

In Tunisia, a survey was conducted on the general population living in the urban area of Sousse. Two areas were surveyed and participants were aged 40 and older. The prevalence, according to GOLD, of stage 1 COPD was 7.8% and of stage 2 COPD was 4.2%. COPD was more prevalent in participants with BMI<20kg/m (low) and in participants aged 70 and older. In smokers who smoked <10 packs per year, the COPD prevalence was 2.3%, while it was 16.1% in smokers of ≥20 packs per year (104).

FRESH AIR Uganda is one of the first studies in SSA to use a strong sampling approach and world-renowned diagnostic methods. This was one of the first population-based, randomised, cross-sectional surveys done in a rural area of a Sub-Saharan country focusing on the prevalence and burden of COPD (90,97). The study identified COPD in younger age groups where the prevalence was highest in people aged 30–39 years (17 [38%] of 45 men, 20 [40%] of 50 women). The overall COPD prevalence in the study was 16.2% (15.4% in men and 16.8% in women). As in many other studies, key risk factors were biomass smoke for both sexes (93% were exposed to biomass smoke), and tobacco smoke for men (97). In addition, COPD was correlated with being a former smoker and having a wheeze (97).

In Rwanda, another study aimed to estimate the prevalence of Atopy, asthma and COPD (101), using a study group aged 15-80 in Kigali town or Huye District. The study estimated prevalence of airflow obstruction was 14%. The overall prevalence of COPD was 4.5% while asthma prevalence was 8.9%. COPD prevalence was found to be associated with smoking, being male and aging. In older participants (45 and older), COPD prevalence was 9.6%. This was fairly consistent with findings of studies from Europe, Asia and America. In current and ex-smokers prevalence rates were 11.2% and 8.6% respectively and this was also consistent with previous findings (101). Asthma prevalence was higher in urban than rural areas, while no differences were found between rural and urban areas regarding COPD. As reported in the same study, having two thirds of the participants aged below 45 resulted in a lower prevalence of COPD when compared with data in the few existing studies where prevalence ranges from 5.3% to 47.4% (101).

2.14 Risk factors for COPD in SSA and MENA

There are several common environmental risk factors for CRD including tobacco smoking, household and outdoor air pollution and exposure to dust, gases or fumes in occupational settings (36). Genetic factors are also implicated, though this is beyond the scope of this review. It has, however, been recently acknowledged that for both the asthma and COPD burden in LMICs, other causes are also contributing, particularly tuberculosis (TB), HIV and rapid urbanisation.

2.14.1 Tobacco

Tobacco smoking, alongside population aging, are causes widely regarded as the most important risk factors for COPD globally (66,69,94). The WHO reports that smoking alone causes about 42% of CRD (120). Maternal smoking during pregnancy is a risk factor for asthma in paediatric patients (121,122). The sharp increase in smoking rates in LMICs reflecting the 'success' of intensive efforts by the Tobacco Industry to expand into African markets will see the global prevalence of COPD increase over coming decades (69,89,101,123).

The burden of tobacco use in African countries is estimated to be between 8% and 43% for men and between 5% and 30% for women (101). COPD prevalence in

current smokers in men ranges from 9.4% to 56.9%, with comparable broad ranges seen for other risk factors such as history of tuberculosis, exposure to biomass fuels smoke or occupational fumes (91,92). Smoking is also increasing in the MENA region. An epidemiological study in Turkey reported that COPD prevalence in current male smokers older than 40 was 18.1%, and was 4.5% amongst younger smokers. Furthermore, 25.5% of the women and 57.2% of the men were current smokers. The rate of smoking varies greatly within the region, from 20% of men in Iran to 63% in Turkey (93). The Burden of Obstructive Lung Disease (BOLD) study analysed COPD prevalence and mortality in association with smoking and poverty, and reports that tobacco and exposure to environmental tobacco smoke remain the greatest risk factors for airflow obstruction (36). However, many areas with high COPD mortality rates have a low consumption of tobacco (36,75). Tobacco alone, therefore, does not fully explain the varying prevalence globally, and other factors need to be investigated in LMICs (36,69,91,97,117).

2.14.2 Household air pollution

Exposure to household air pollution from biomass fuels smoke is a recognised risk factor for CRD, particularly for COPD, and mostly among women (88,124). Biomass fuels contain material from plants or animals burnt by humans such as wood, animal dung, crop residue and grass (38). It is estimated that over 80% of homes in SSA and 90% of rural houses use biomass fuels (38,117). A Malawian study found that women and people of lower socioeconomic status in SSA are particularly affected by biomass fuels smoke exposure (125). In MENA countries, household air pollution from biomass fuels smoke is also considered a risk factor for CRD, but to a lesser extent (47,96). The link between asthma and biomass fuels exposure is less clear (126,127), though a recent systematic review reported a relationship between these fuels and asthma symptoms (128). In MENA, 25% to 45% of patients with COPD were known to have been exposed to biomass fuels smoke and were reported non-smokers (93). Ben Abdallah *et al* estimates that 54.5% of the Turkish, rural, female participants with COPD that were studied were exposed to biomass fuels smoke. However, the same study reports that the relative risk from smoking was 3.4 times greater than biomass fuels exposure and 3.3 times greater than occupational exposure (83,93).

2.14.3 Outdoor air pollution

Outdoor air pollution is variable, differing greatly between urban and rural environments and with the degree and nature of local industry. Outdoor air pollution tends to be a combination of wood smoke and vehicle exhaust (129), with higher levels of nitrogen dioxide, ozone, particulate matter and sulphur dioxide in urban areas (130). There has been a rise in the prevalence of asthma that corresponds with increasing urbanisation over the last three decades (131) although, in some high income countries there has been a decline in asthma prevalence, hospitalisation and death from asthma(52). There is evidence that high levels of vehicle emissions and living in an urban environment are correlated with the rising trend in allergic respiratory diseases (130). Air pollution has a quantifiable impact on COPD mortality and morbidity and is also recognised to have a negative influence on lung development in children (80,132). Research on outdoor air pollution and CRD in SSA and MENA is limited, and the majority of the data in these regions is extrapolated from studies observing other risk factors.

The global population living in urban areas is predicted to increase from 45% to 59% by 2025. Africa's urban population in particular is growing rapidly and predicted to increase from 40% to 56% by 2050. The impact of air pollution on CRD can therefore also be expected to increase (133). Studies looking at wheezing, asthma and COPD in Africa illustrate rural-urban gradients, with generally low levels in the villages and increasing prevalence with urbanization (38,134).

2.14.4 Occupational exposures

There is little evidence regarding the burden of asthma due to occupational exposure in LMICS, particularly African countries outside South Africa (135). Hoy *et al* estimates 15% to 20% of population burden of asthma are attributable to occupational exposure. However, this is only valid in developed countries which have strong occupational health data (135). Similarly, the American Thoracic Society (ATS) reported occupational exposure as the main cause of 15% prevalence of COPD and asthma and was associated with an increased mortality rate in the COPD population (136). GINA also reported that occupational exposure can trigger asthma in 5% to 20% of adults (71). These findings have been replicated by a study on a 'never-smoked population' in two industrialised areas of Sweden, where 24% of the

study population was found to have occupational exposure (35). A Nigerian study reported a high prevalence of occupational asthma (6.5%) and rhinitis (78%) in woodworkers, which increased with duration of employment (137). As reported by Finney et al, COPD was prevalent in 13.4% of South African gold miners and 33.1% of Nigerian shoe factory workers (92).

In MENA, there are variable reports regarding occupational exposure. A study from Sudan reported that 26% of miners had symptoms of chronic bronchitis where mine dust was the leading cause (27,138). The non-smoker BOLD study in Tunisia reported 92% of those exposed to occupational pollutants from dust, gas and fumes suffered from chronic bronchitis and a significant association (OR 1.87, 95% CI 1.14 - 12.86) was found between occupational exposure and COPD as well as having more respiratory symptoms (103). This is further evidenced by a recent study in Dubai which showed a significant association between occupational exposure to dust and airflow limitation (OR 2.07, 95% CI 1.20 - 3.59) (139).

2.14.5 Pulmonary tuberculosis (TB)

According to the WHO stop TB partnership, there are more than 2.4 billion people infected with TB globally and 9.6 million new cases are diagnosed every year, with the majority occurring in LMICs. TB patients often have airflow obstruction; studies have found prevalence varies from 28% to 68% (140,141). A large study based in South Africa in 2004 reported that the strongest predictor of COPD was history of TB (OR 4.9, 95% CI 2.6 - 9.2 in men) and (OR 6.6, 95% CI 3.7 - 11.9 in women), an association stronger than both smoking and biomass fuels exposure (142). A recent study in previously-treated TB patients in Sudan concluded that clinical features of CRDs are strongly associated with a history of Previously Treated TB (PTB) (143). Additionally, previous studies have found that TB was strongly associated with CRDs in areas highly endemic of TB (144). The recent BOLD multicentre study stated that self-reported TB was associated with airflow obstruction (Adjusted odds ratio 2.51, 95% CI 1.83–3.42) (43).

The ISAAC study found an inverse relationship between asthma symptom prevalence and estimated TB incidence (145). It has been hypothesised that exposure to *mycobacterium tuberculosis* may reduce the risk of developing asthma through the

induction of a Th1-like immune response (99). However, further studies are required as research is lacking.

2.14.6 HIV

The link between HIV and chronic respiratory disease is unclear, however in both children and adults, HIV patients are reported to have a higher risk of respiratory disease (146,147). Countries with a high reported prevalence of HIV also have high reported prevalence of asthma (38) and children with HIV on anti-retroviral therapy have higher rates of recurrent wheeze (146). Similarly, a study in Cameroon reported a positive association between COPD and HIV infection (OR 2.85, CI 1.20-6.74, p=0.017). This study found a COPD prevalence of 2.2% in HIV positive patients compared to 0.7% in HIV negative participants. It did, however, note the main determinants of COPD to be TB, weight and chronic respiratory symptoms (119). Similar studies in South Africa and Nigeria have also found an association between HIV and airflow obstruction (146). The pathophysiology of the link between obstructive lung disease and HIV is not understood but thought to involve the development of lung inflammation and a low lung diffusing capacity (147). A rapid decline in lung function, obliterative bronchiolitis and severe airflow limitation in children with HIV has also been reported (146).

2.14.7 Socioeconomic status

Low socioeconomic status is an independent risk factor for COPD and there is a significant correlation with lung function, even after adjustment for smoking, occupational exposure and ethnicity (90,148). The interplay of several risk factors is complex but is thought to include low birth weight, recurrent respiratory infections, poor nutrition, poor housing conditions and air pollution (149). A similar pattern of exposure to risk factors that impact health care access may also influence the development of asthma. Pallasaho et al interviewed 44,483 participants in Finland, Sweden and Estonia and reported a significant link between low socioeconomic status and asthma-like symptoms (150). In addition, a recent BOLD study from 12 sites found that airflow obstruction is always associated with poverty and low socioeconomic status at both individual and community level (151). These issues need to be further explored in SSA and MENA.

2.14.8 Chronic Asthma

Chronic airway inflammation and obstruction from uncontrolled asthma has been hypothesised as a cause of lung remodelling, leading to fibrosis and the irreversible airflow obstruction of COPD (53). Globally the increasing prevalence and ongoing lack of access to effective treatment (such as inhaled corticosteroids) will likely be contributing to the development of COPD in asthma patients. In addition asthma can co-exist with COPD and be a risk factor for COPD development (79).

2.14.9 Other risk factors that have been implicated globally for asthma

A recent study in Aberdeen, Scotland targeting school children aged 8–13 reported that the associations between asthma and known risk factors had changed over a 50 year period (152). However, the risk factors known and implicated globally for asthma are the following**:**

2.14.9.1 Atopic sensitisation

Indoor allergens such as house dust, cockroaches and furry pets can sensitize asthmatic patients and are considered important risk factors in the emergence of the disease in SSA (138,153). The risk of developing asthma is higher in children than in adults (153). In polluted urban areas, the prevalence of allergic respiratory diseases can be increased by exposure to inhaled allergens, which foster airway sensitization and result in a more severe immunoglobulin arbitrated reaction to further aeroallergens and airway inflammation (132). A rapid asthmatic reaction can be triggered by allergen inhalation. These create immunoglobulin mediated mast cell degranulation, downstream inflammation and a late asthmatic reaction, including activation of T-helper 2 lymphocytes (154). In many African countries, asthma and allergic sensitization are becoming more widespread, a trend supported by studies in Ghana, Kenya, Ethiopia and Rwanda. This rising tendency is mostly associated with sensitisation to house dust mites, tobacco smoking and living in urbanised areas (155). Other specific allergic sensitizers in Africa are span trees, grasses and weeds as well as airborne mould spores. In MENA countries, increased asthma prevalence has been shown to be associated with increased rates of sandstorms (155).

Cow milk, eggs, nuts, fish and shellfish are the most allergenic foods, causing an IgE-mediated reaction (153,154). About 40% of allergic children have asthma and 30% will have allergic rhinitis (153). Food induced asthma appears to be less frequent

in SSA than in the developed world, though data are limited (154). In a Zimbabwean study, tropical dietary lifestyles were considered a probable cause of allergen sensitization in Africa as these diets include grains, plants, fruits and even insects (155).

2.14.9.2 Infections

In SSA, the incidence of acute respiratory infections is one of the highest in the world. Household air pollution is considered to be a risk factor for acute respiratory tract infections in children, which in turn may increase the risk of asthma (47). Several viral infections can result in asthma in children by causing wheezy bronchitis (154). Children who experience severe respiratory infections in early childhood have up to a 50% risk of developing asthma in subsequent years of childhood and COPD in later life (153,156).

Other important factors implicated in asthma are drugs, exercise, obesity and diet. The intake of fruit and vegetables, vitamins A, D and E, zinc and selenium have been reported to have a negative association with risk of asthma whilst junk food, salt and trans fatty acid intake reported to have a positive association with the risk of asthma(157). Obesity is also known to be risk factor for asthma(158).

2.15 Comorbidities

Patients with COPD often suffer different comorbidities, including cardio-vascular disease, osteoporosis, anxiety and depression, malnutrition, metabolic syndrome, diabetes, skeletal muscle dysfunction, cachexia, gastrointestinal diseases, lung cancer and other respiratory conditions (159–161). Comorbidities can include a wide range of diseases that coincide with COPD (162). These diseases can contribute to COPD burden, survival, quality of life, degree of severity and are associated with poor clinical outcomes (160). Asthma can exist with COPD in clinical settings and is a risk factor in the development of COPD as stated above (159).

2.16 Conclusions

NCLD is a present and growing problem across SSA and MENA. There is, however, limited epidemiological evidence resulting in gaps in the evidence base and a need

for further research. Across both regions, asthma and COPD are likely to be under-estimated, under-diagnosed, under-treated as well as inadequately prevented (38,98,107). Although there have been many global strategies put forward for management and control, the implementation of these guidelines inconsistent and logistically challenging, especially in LMICs. In these areas, which are facing threats from the tobacco epidemic, household and outdoor air pollution and urbanisation, there is often limited adoption of international guidelines within resource-limited health systems. There are important challenges regarding the lack of diagnostic equipment, treatment and trained and experienced health care professionals which need to be addressed through strengthening of health systems (138,163).

Chapter 3 Prevalence and determinants of chronic obstructive pulmonary disease in Khartoum, Sudan

3.1 Introduction

The previous chapter summarised the existing literature on CRD globally and identified that there is a lack of information about the burden of disease in SSA and MENA. This chapter outlines a study which documents the burden of COPD in Khartoum State.

The global burden of CRDs and COPD has been discussed in the previous chapter. There has been little research on COPD in Africa outside of South Africa. The prevalence estimates for COPD in SSA (90,91,164) are based on limited epidemiological data which lack a standardized definition of COPD. A systematic review by Finney et al. (2013) reported only 9 cross-sectional studies from SSA (two from South Africa, two from Nigeria, one from Malawi and one from Cape Verde). These studies used various diagnostic methods and found a prevalence of COPD ranging from 4.1% to 24.8% (92).

The Burden of Obstructive Lung Disease (BOLD) Initiative was established to develop standardized methods in order to estimate the prevalence of COPD and associated risk factors in populations aged 40 and older (66,68). It also aims to measure the influence of COPD on quality of life, ability to perform activities of daily living, respiratory symptoms and use of health care services(68,70). BOLD study methods have been used in a PLATINO study to assess COPD prevalence in five Latin American countries. This was followed by piloting the BOLD study in Turkey and China and lessons learned from both PLATINO and the pilot study formed the current BOLD study methodology which was developed by the BOLD Executive Committee (68). BOLD study objectives and rationale has been discussed in section 2.4.2.1 of Chapter 2.

So far, results have been published in local African BOLD studies from Fez in Morocco (165), Sousse in Tunisia (104), Blantyre in Malawi (166) and Ile-Ife in Nigeria (167).

To date, there are no published data on the prevalence and determinants of COPD in Sudan. To help fill this knowledge gap, a population-based, cross-sectional BOLD study of the prevalence of COPD in urban Khartoum and the impact of risk factors on disease prevalence was conducted. The study discussed in this chapter aimed to measure the prevalence and investigate the main risk factors of AFO in Khartoum State as well as identify risk factors associated with airflow obstruction in Khartoum state.

3.2 Methodology

3.2.1 Study settings, location, and participants

Khartoum state is divided into 7 localities, across which there is a mix of urban, semi-urban, rural, and internally displaced populations. The total population of Khartoum state is 5,274,321 (Figure 3.1). Three of the 7 localities, with a total population of 661,617, were randomly selected for sampling in this study. Clusters were formed within each locality, comprising 19 in Jabel Awlya, 17 in Sharg Alneel and 11 in Omdurman. Each cluster was comprised of 15 households. A total of 280, 258 and 158 households were then randomly selected from Jabel Awlya, Sharg Alneel and Omdurman respectively.

The study aimed to collect spirometry and questionnaire data from 600 participants. The sample size was selected to provide an acceptable level of precision for estimating prevalence in accordance with BOLD protocol(67) See Appendix (4) for sampling plan.

The target population was defined by meaningful administrative borders for which other types of routinely collected information are available. In order to avoid sampling populations that may have only limited generalizability, the area should have a total population, including all ages, of at least 150,000 people (67).

Pre-selection and randomization of clusters and households were carried out before the field visits. The selected houses in each cluster were consecutively numbered and all eligible adults aged 40 or older in these households were interviewed. Field workers returned up to three times to locate absent households at interview time. Each participant package had a unique 6-digit identifier that contained both the

country and city code.
Ethical approval was obtained from the Imperial College London and the Ministry of Health in Khartoum state ethics committee prior to the start of the study. All participants gave written informed consent prior to any data being collected (Appendix (2)).

The study participants were aged 40 or older and were selected using a 3-stage stratified cluster sampling plan. The exclusion criteria were; aged younger than 40, being institutionalized (e.g., living in a community-based care centre or in prison) or being medically unfit to perform spirometry (e.g., pregnant women in their third trimester and individuals with a history of myocardial infarction or major surgery in the previous 3 months).

Where participants were not willing to participate in the study in its entirety, a minimal dataset - also used as a refusal questionnaire - was obtained. All study participants completed a structured interview administered by a trained interviewer. Anthropometric measurements along with pre-bronchodilator and post-bronchodilator spirometry data were then collected in accordance with the American Thoracic Society guidelines using an Easy One System (ndd Medizintechnik, Zurich, Switzerland) by three trained and certified technicians in accordance with BOLD protocol (68). The questionnaire was administered in an approved translated local language (Arabic) and included questions about respiratory symptoms, medical history, medications, smoking history, use of biomass fuel, and occupational exposure. The clinical data obtained included height, weight, resting heart rate and waist and hip circumference (Appendix (3)).

Quality control was carried out at the central BOLD centre at Imperial college London. Local training on study standardised methodology was carried out covering both questionnaire administration and spirometry test. Piloting of study and assessment of data quality was done prior to the start of the main study with technical assistance from the BOLD centre.

All study data were pseudo-anonymised and entered in the BOLD online platform of Imperial College, London.

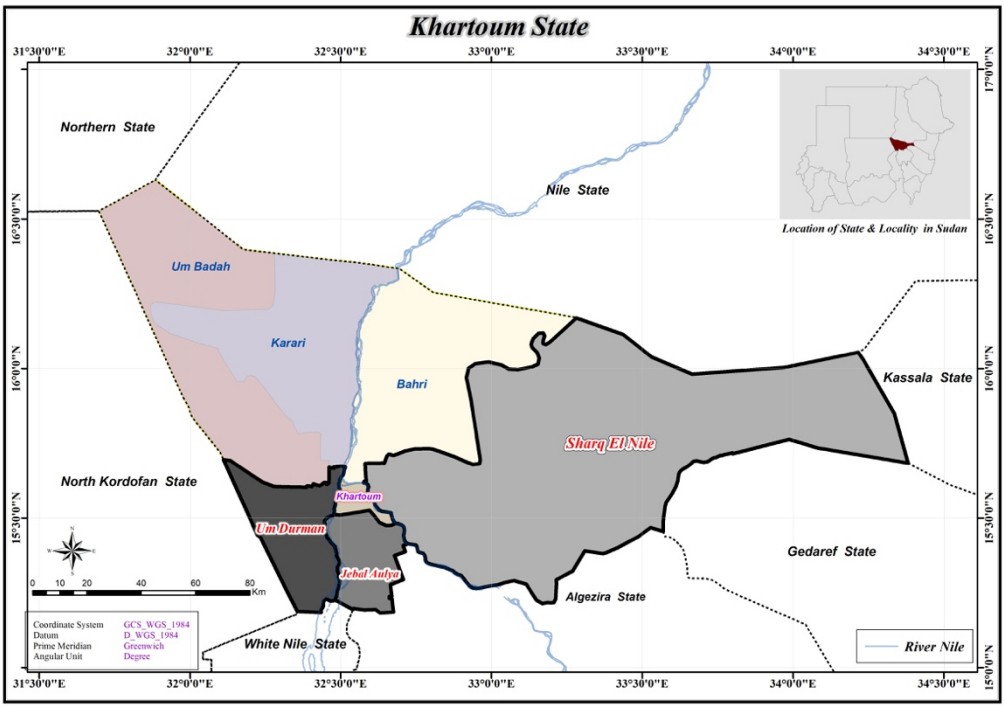


Figure 3.1 Khartoum state locality division. Study areas in grey and black (Sharg Elnile, Jabel-Awlya and Omdurman)

3.2.2 Definitions

Spirometric definitions are illustrated in Table 3.1. Both GOLD definitions and Lower Limit of Normal (LLN) as recommended by the ATS/ERS are used to report disease prevalence and associated risk factors in this study. Predicted values based on standardized values for age, sex and height were calculated based on the third National Health and Nutrition Examination Survey (NHANES) (1988–1994) (168). This reference range has been used as standard reference that provides ethnically appropriate equations for Caucasian Americans, African Americans, and Mexican Americans. The use of NHANES enabled comparability with other published BOLD studies. The local values were derived from the spirometry results of healthy Sudanese adults who had never smoked; did not report any respiratory symptoms, did not report current asthma or chronic bronchitis; did not report emphysema or COPD and did not report tuberculosis that participated in this survey.

Table 3.1 Spirometric definitions (161,168,169)

Findings	Spirometric definition
Post-bronchodilator obstruction (GOLD stage 1 or higher COPD)[1]	FEV_1/FVC ratio <0.7
Post-bronchodilator moderate-severe obstruction (GOLD stage 2 or higher COPD)[1]	FEV_1/FVC ratio <0.7 and FEV_1 <80% predicted*
Modified stage 1 or higher COPD (LLN)[2]	Post-BD FEV1/FVC < LLN
Modified stage 2 or higher COPD (LLN)[2]	Post-BD FEV1/FVC < LLN and post-BD FEV1 < 80% predicted
Low FVC	FEV_1/FVC ratio >0.7 and FVC<80% predicted*
Airway reversibility	FEV_1 increase >200ml and >12% following bronchodilator
predicted values based on ages-sex and height standardized taken from NHANES III or local values derived from the spirometry of non-smoking and healthy Sudanese adults, 1, definitions based on GOLD global burden of lung disease initiative, 2, a definition based on below lower limit of normal (LLN).	

3.2.3 Statistical analysis

Subjects who completed full data and minimal questionnaires with acceptable or unacceptable spirometry readings were compared using the chi-square test. Prevalence estimates of spirometric abnormalities stratified by subject age and sex were reported using the NHANES III reference range (68). In addition, prevalence estimates were also reported using locally derived spirometry ranges for non-smoking Sudanese adults with no history of respiratory disease or symptoms.

Univariate and logistic regression analyses were used to test the associations between spirometry abnormalities and several exposure variables including age, sex, educational level, self-reported history of tuberculosis (TB), hypertension, diabetes and/or heart disease, body mass index, smoking status, smoking pack years, exposure to indoor biomass fuel and occupational exposure.

Asset-based measures have been commonly used in LMIC as they offer an easily collected variable that is constant over short term economic instabilities(170). A Mokken scale analysis, which is based on a count of assets owned by the study subjects and ranked for their ability to differentiate between different levels of wealth; has been used in this study as a proxy of socioeconomic status(170). The analysis included 14 asset related questions included in the BOLD core questionnaire. The questions recorded the assets in current time and in the time when the participant was 5 years old with a binary (yes/no) responses. Study participants were questioned whether their household has any of the following: electricity, flush toilet, fixed phone, cell phone, television, radio, refrigerator, car, moped/scooter/motorcycle, washing machine, owns their own home, indoor bath or shower, indoor tap, or an outdoor tap of their own. A score of 1 to 10 was created and used to test the association between socioeconomic status and spirometric abnormality. Only results related to the current owned assets were reported in this study.

In addition, occupations reported by participants were grouped into three categories: a) Organic, such as working in flour milling cotton jute and farming; b) Inorganic, such as working in hard rock, coal mining sand blasting, asbestos, steel milling and construction; c) Fumes such as chemical plastics manufacturing, welding firefighting and cleaning. Associations between occupation groups and spirometric abnormality were tested. In addition, the association with those who had >5 years of occupational exposure has been reported.

Multivariable logistic regression models that included sex, age, and all variables from the univariate analysis with a *p*-value <0.2 were developed. The prevalence of respiratory symptoms was reported and associations with the study variables were tested using regression analysis. A description of the associations between abnormal spirometry and respiratory symptoms was reported. The data were analysed using Stata IC 14 (StataCorp, College Station, TX). Prevalence estimates and regression models were developed using survey weighting with the Svy package in Stata (14). Both univariate and multivariate analysis were reported for the prevalence estimates using below Lower Limit of Normal (LLN) and GOLD standards.

The response rate was calculated based on total recruited subjects as enumerator while having the denominator limited to responders and non-responders.

3.3 Results

The flow of subjects through the study is shown in Figure 3.2 and Table 3.2. Of the 998 participants approached, 300 were not traceable, 698 were interviewed and 516 provided full questionnaire data and had BOLD centre-approved spirometry results. Eleven of the 698 consented subjects declined to participate fully in the study but completed the minimal data questionnaire, while 2 were ineligible. Of the eligible subjects, 54 (7.74%) provided only spirometry readings. The final response rate was 85.5% (n=696).

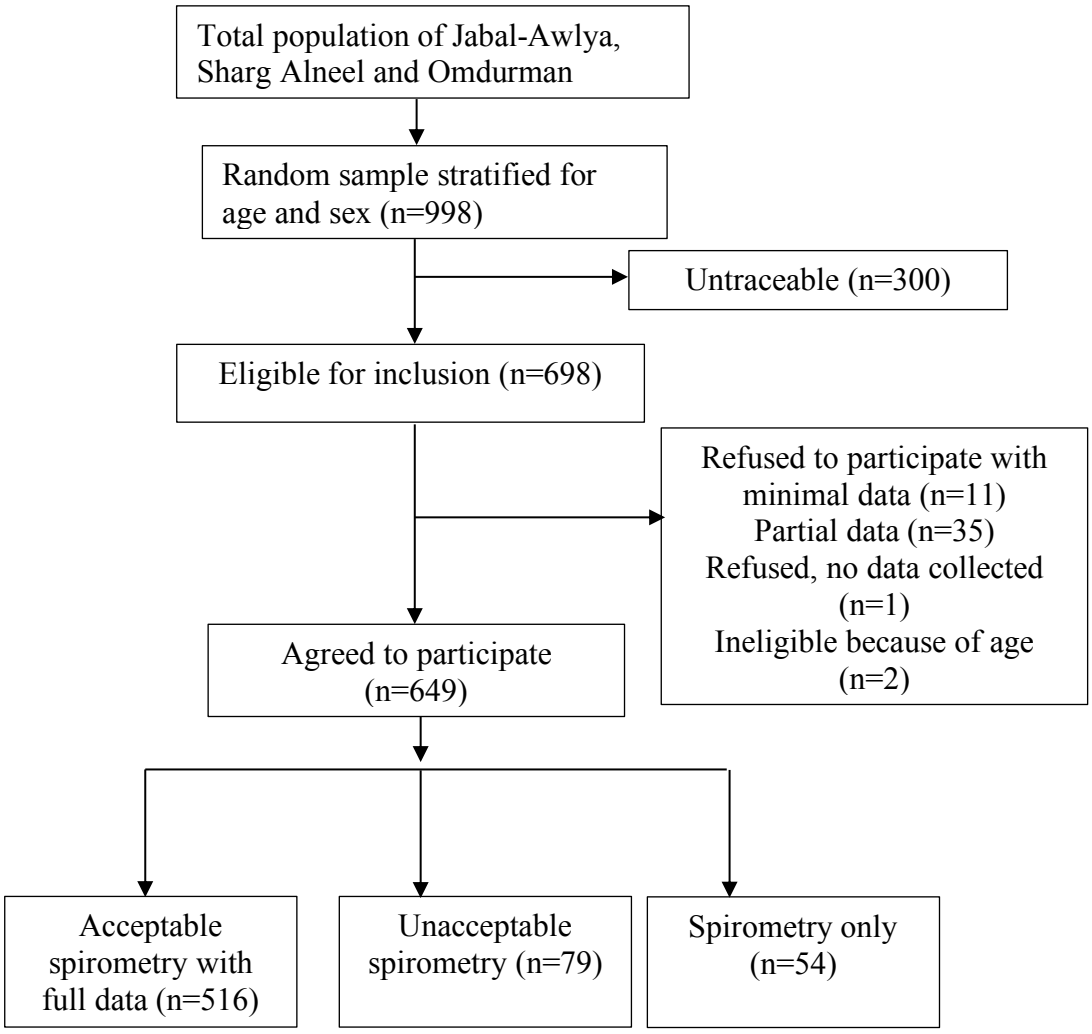


Figure 3.2: Participant flow diagram

3.3.1 Subject characteristics

The characteristics of the subjects are presented in Tables 3.3 and 3.4. Their mean age was 53.8 ± 10.4 (SD) years and 59.3% were men. Out of the total approached subjects, 72% conducted a spirometry test, 15% either refused or provided partial spirometry data and 13% provided no data. People who refused to participate tended to be older (p=0.003, Pearson's χ^2=14.0048). Overall, 35% completed primary school education. Men tended to have a higher level of education compared to women, as did the group aged 40–49 when compared to other age groups. In total, 70.9% of participants owned their own home and 66.2% had their own water source. Only 20.8% had access to a flush toilet. The mean number of household members was 7.8 ± 3.56. No statistically significant difference were seen between those with or without usable spirometry results (Table 3.3).

3.3.2 Environmental Exposures

Among the respondents, 24% had smoked cigarettes. Of current smokers, 15% were men and 0.8% were women. About 24% of smokers had more than 20 pack-years of exposure. The age group of 60-69 had the highest smoking exposure compared to other groups and 24.6% of them had smoking history. Exposure to indoor biomass fuel for more than 6 months was reported by 82% of subjects. In total, 78% reported having used an open, indoor fire fuelled by coal or charcoal for cooking for ≥6 months, while 35% used firewood and 21% used kerosene. Overall, women tended to have a higher mean number of hours of exposure to indoor biomass fuel per year than men (70% vs. 54%). Twenty five percent of the responders were working in agriculture, textile or food industry and farming was the most commonly reported occupation (24%) while 15% of them had more than 5 years of exposure. 50% of participants work in mining and construction industry had >5 years of exposure. (See Table 3.4).

3.3.3 Other diseases

In total, 23% of subjects were obese and 7% were underweight. Hypertension was self-reported by 20% of all subjects, of whom 55% were women. Diabetes was reported by 9% (9.5% of women and 8.8% of men), heart disease by 2% (2.3% of women and 1.7% of men), lung cancer by 0.5%, stroke by 0.5% and TB by 0.8%

(1.2% of women and 0.6% of men). None of these diseases were associated with any type of obstruction or low FVC using either local or NHANES reference ranges, except tuberculosis associated with stage 1 COPD or higher using the NHANES reference range (OR 0.08, 95% CI 0.01- 0.59).

Table 3.2 Comparison of responders[1] and non-responders[2] for Khartoum, Sudan

		Responders	**Non-responders**	**P-value[3]**
		N=917	N=52	
Age	40-49	226 (38%)	7 (22%)	0.015
	50-59	200 (34%)	8 (25%)	
	60-69	108 (19%)	9 (28%)	
	70+	61 (10%)	8(25%)	
Gender	Male	353 (59%)	18 (55%)	0.587
	Female	242 (41%)	15 (46%)	
Smoking status	Current	55 (9%)	0 (0%)	0.362
	Ex	86 (14%)	1 (8%)	
	Never	454 (76%)	12 (92%)	
Doctor diagnosed asthma, emphysema, CB or COPD	Yes	44 (7%)	0 (0%)	0.309
	No	551 (93%)	13 (100%)	
Other disease	Yes	152 (26%)	1 (8%)	0.265
	No	443 (74%)	12 (92%)	

1. Responders are those who completed post-BD spirometry (regardless of QC scores) and the core questionnaire.
2. Non-responders are eligible individuals who are missing the core questionnaire and/or post-BD spirometry, but for whom the tabulated variable is known.
3. Two-sided p-value based on Pearson chi-square test.

Table 3.3 Comparison of responders[1] with and without usable spirometry for Khartoum, Sudan

		With useable spirometry	Without useable spirometry	P-value
Age	40-49	192(37%)	34(43%)	0.783
	50-59	176(34%)	24(30%)	
	60-69	94(18%)	14(18%)	
	70+	54(10%)	7(9%)	
Gender	Male	306(59%)	47(59%)	0.974
	Female	210(41%)	32(41%)	
Smoking status	Current	50(10%)	5(6%)	0.217
	Ex-smoker	70(14%)	16(20%)	
	Never	396(77%)	58(73%)	
Doctor diagnosed asthma	Yes	34(7%)	5(6%)	0.931
	No	482(93%)	74(94%)	
Doctor diagnosed COPD	Yes	2(0%)	0(0%)	0.579
	No	514(100%)	79(100%)	
Cough	Yes	58(11.2%)	8(10.1%)	0.769
	No	458(88.8%)	71(89.9%)	
Phlegm	Yes	59(11.4%)	8(10.1%)	0.732
	No	457(88.6%)	71(89.9%)	
Wheeze	Yes	17(3.3%)	1(1.3%)	0.327
	No	499(96.7%)	78(98.7%)	
Shortness of breathe	Yes	53(11.1%)	9(12%)	0.816
	No	425(89%)	66(88%)	
Any Symptoms	Yes	122(24.7%)	17(22.4%)	0.667
	No	373(75.4%)	59(77.6%)	

1. Responders are those who completed post-BD spirometry (regardless of QC scores) and the core questionnaire.

2. Usable spirometry defined as post-BD quality scores>1 for each of FEV1 and FVC

3. Two-sided p-value based on Pearson chi-square test. NOTE: In some cases numbers are too small for meaningful statistical analysis.

Table 3.4 Characteristics of all subjects who completed a full BOLD core questionnaire, including those with and without spirometry results.

Variable (n)	N(%)
Age group, years (n=595)	
40–49	226 (38.0)
50–59	200 (33.6)
60–69	108 (18.2)
70+	61 (10.3)
Sex (n=595)	
Male	353 (59.3)
Female	242 (40.7)
Level of education (n=593)	
None	125 (21.1)
Primary school	207 (34.9)
Middle school	69 (11.6)
High school or above	192 (32.4)
Mean years of education (n=595)	6.49 (5.5)
Home ownership (n=595)	
Yes	422 (70.9)
No	168 (28.2)
Access to private indoor or outdoor water supply (n=595)	
Yes	394 (66.2)
No	199 (33.5)
Access to flush toilet in home (n=595)	
Yes	124 (20.8)
No	466 (78.3)
Smoking status (n=595)	
Current smoker	55 (9.2)
Ex smoker	86 (14.5)
Never smoked	454 (76.3)
Pack-years of smoking (n=595)	
Never smoked	454 (76.3)
>0 and <10	71 (11.9)
≥10	70 (11.8)
Biomass exposure (n=532)	

Yes	422 (82.4)
No	90 (17.6)
Farm work for ≥3 months (n=527)	
Yes	126 (23.9)
No	401 (76.1)
Body mass index (n=588)	
Underweight (<18.5)	39 (6.6)
Normal (18.5–24.9)	226 (38.4)
Overweight (25.0–29.9)	189 (32.1)
Obese (≥30)	134 (22.8)
Reported history of tuberculosis (n=595)	
Yes	5 (0.8)
No	590 (99.2)
Reported history of hypertension (n=595)	
Yes	118 (19.8)
No	477 (80.2)
Reported history of diabetes (n=595)	
Yes	54 (9.1)
No	541 (90.9)
Reported history of heart disease (n=595)	
Yes	12 (2.0)
No	583 (98.0)
Current Mokken scale (Mean ± SD)	5.18 ±2.67
0	50 (8.6)
1	30 (5.1)
2	27 (4.6)
3	42 (7.2)
4	53 (9.1)
5	88 (15.0)
6	90 (15.4)
7	91 (15.6)
8	64 (10.9)
9	32 (5.5)
10	18 (3.1)
Occupation group 1	137(25.8)

>5 years of exposure in group 1	104 (14.9)
Occupation group 2	61(11.5)
>5 years of exposure in group 2	40(50.7)
Occupation group 3	25(5.7)
>5 years of exposure in group 3	19(2.7)
Occupation group 1: Working in agriculture, textile or food industry **Occupation group 2: Working in Mining and construction industry)** **Occupation group 3: Welders, firefighters, cleaners or exposed to chemicals and fumes during work**	

3.3.4 Respiratory symptoms

At least one respiratory symptom was reported by 23% (SE 1.9) of subjects and respiratory symptoms that interfered with daily activities was reported by 1.9% (SE 0.5). A cough was reported by 10.4% (SE 1.3), with the highest prevalence recorded in subjects aged 70+ years (11.9% [SE 4.9]). The prevalence of cough was higher in men than in women (10.6% [SE 1.6] vs. 10.1% [SE 2.0]. Chronic cough (lasting for more than 3 months per year) was reported by 4.0% (SE 0.8) of the study population. Production of sputum was reported by 11% (SE 1.3) and chronic production of sputum (for more than 3 months per year) was reported by 5% (SE 0.9). Shortness of breath was reported by 11% (SE 1.3), and 41% (SE 6.5) of this group stopped walking after 100 yards because of breathing problems. A wheeze in the past 12 months in the absence of a cold was the least commonly reported symptom (3.0% [SE 0.7], Table 3.5, Figure 3.3). A small positive correlation was found between all respiratory symptoms ($p<0.05$, Pearson's r correlation <0.4) except a medium positive correlation between sputum production and cough ($p<0.001$, Pearson's r correlation = 0.43).

Medically diagnosed respiratory disease was reported by 7.4% of the participants that contributed full data sets. Medically diagnosed asthma and COPD was reported by 6.6% and 2.1% of subjects respectively. Medically diagnosed COPD, chronic bronchitis or emphysema was reported by 2.0%.

Table 3.5: Age and gender stratified prevalence of respiratory symptoms among participants with complete core questionnaires

Definition of symptom*	Age group	Male (n=353) prevalence (SE)	Female (n=242) prevalence(SE)	Total (n=595) prevalence (SE)
Cough (do you usually cough when you don't have a cold?)	40-49	9% (2.7)	9.1% (2.6)	9.4% (1.9)
	50-59	10% (2.7)	10.6% (3.4)	10.7% (1.9)
	60-69	12% (3.8)	9.9% (5.4)	11.6% (3.2)
	70+	11% (4.7)	13.1% (8.8)	11.9% (4.9)
	Total	10.6% (1.6)	10.1% (2.0)	10.4% (1.3)
Sputum (do you usually bring up phlegm from your chest?)	40-49	16% (3.4)	10.8% (2.8)	13.6% (2.3)
	50-59	10.9% (2.7)	5.8% (2.5)	8.6% (1.9)
	60-69	10.2% (3.2)	13% (6.1)	11.4% (3.2)
	70+	11.9% (5.1)	0	6.4% (2.9)
	Total	13.2% (1.9)	8.5% (1.7)	11.1% (1.3)
Wheeze (have you had wheezing / whistling in your chest at any point in past 12m, in the absence of a cold)	40-49	4.5% (2.0)	3.3% (1.6)	4% (1.3)
	50-59	1.7% (1.1)	1.1%(1.1)	1.4 (0.8)
	60-69	7.6% (3.0)	0	4.3% (1.7)
	70+	0	0	0
	Total	3.7% (1.1)	1.8%(0.91)	2.9% (0.7)
Shortness of breath (Currently do you have shortness of breath when hurrying on the level or walking up a slight hill?)	40-49	10.5% (3.0)	17.8%(3.6)	13.8% (2.3)
	50-59	6.1% (2.2)	12.3%(3.7)	9.04% (2.1)
	60-69	7.5% (3.2)	6.7%(4.6)	7.2% (2.7)
	70+	10.7% (4.6)	5.5%(5.4)	8.3% (3.5)
	Total	8.9% (1.7)	13.2%(2.2)	10.9% (1.3)
Any respiratory symptom (any of cough, sputum, wheeze without cold, exertional	40-49	25.8% (4.2)	25.3%(4.1)	25.6% (2.9)
	50-59	21.1% (3.7)	19.2%(4.4)	20.2% (2.8)
	60-69	26.5% (5.2)	22.7%(7.5)	24.8% (4.4)
	70+	23.7% (6.7)	18.4%(9.8)	21.8% (5.8)
	Total	24.5% (2.4)	22.4%(2.7)	23.5%(1.9)

breathlessness as above?)				
Functional limitation (have breathing problems interfered with your usual daily activities?)	40-49	0.9% (0.9)	5%(2.0)	2.8% (1.1)
	50-59	0	3.7% (2.1)	1.6% (0.9)
	60-69	1.3% (1.3)	0	0.7% (0.7)
	70+	1.8% (1.7)	0	0.9% (0.9)
	Total	0.8% (0.5)	3.4%(1.1)	1.9%(0.5)

** Presence of respiratory symptoms were determined using 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 usually 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 12 months? In the last 12 months have you had this wheeze or whistling only when you have had a cold? Functional limitation: did you have an attack of breath shortness that kept you from going out, or putting on your clothes?*

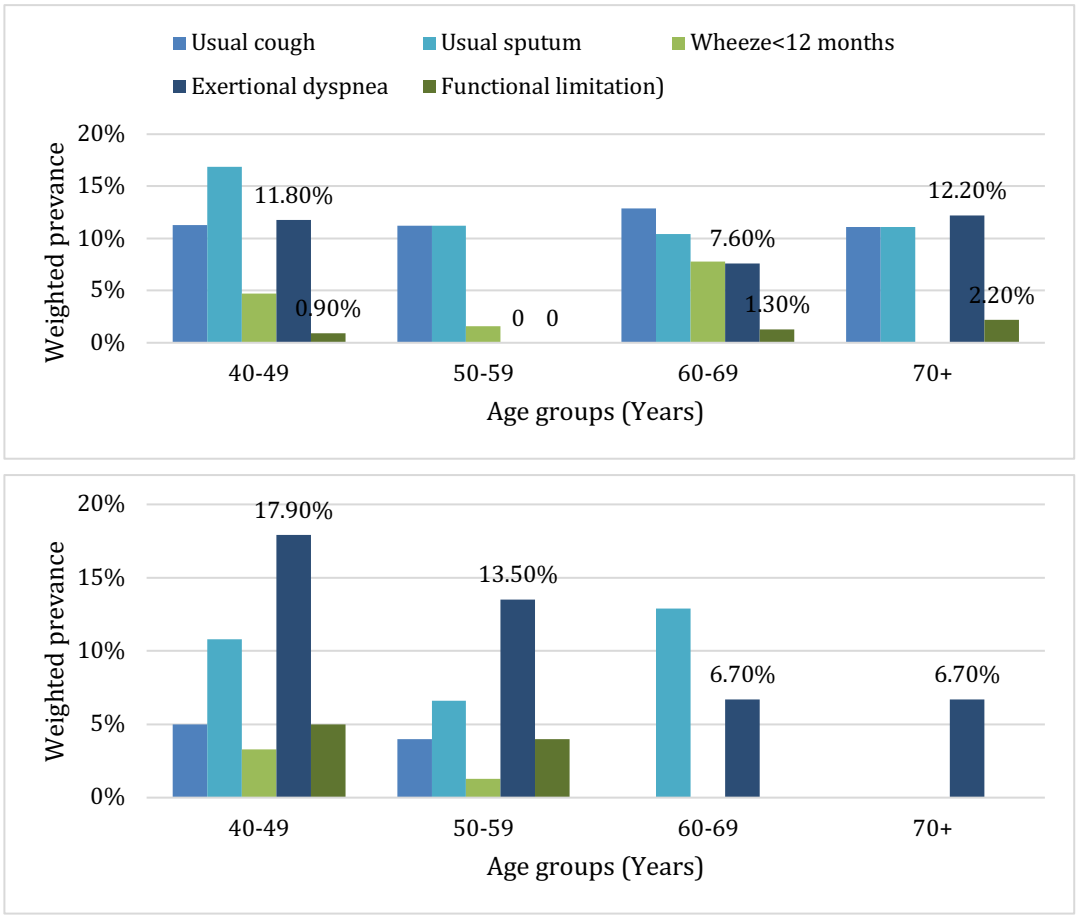


Figure 3.3: Prevalence of respiratory symptoms among the study participants. The upper bar represents symptom prevalence in women (n=242) and the lower bar represents symptom prevalence in men (n=353).

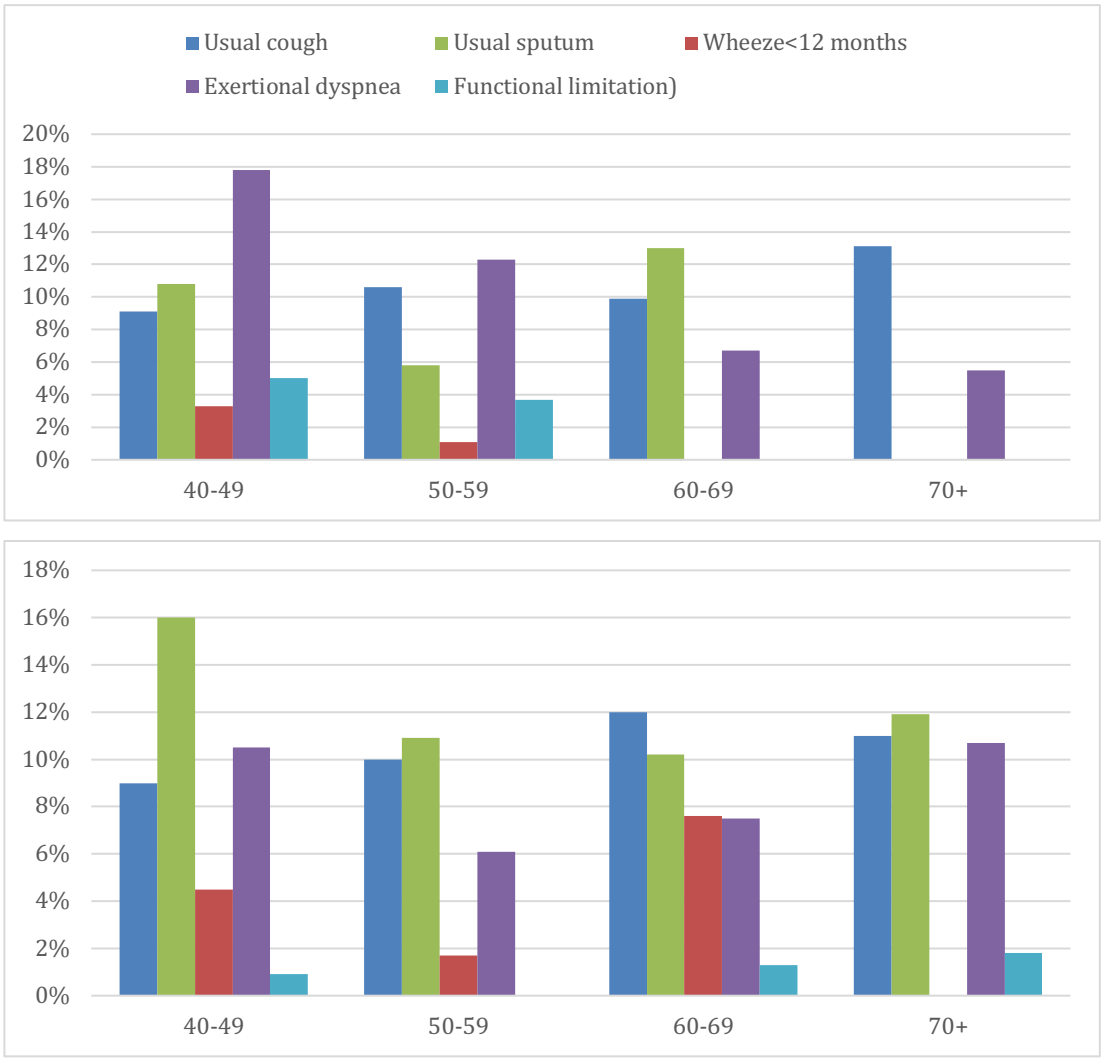


Figure 3.4: Prevalence of respiratory symptoms among the study participants. The upper bar represents symptom prevalence in women (n=242) and the lower bar represents symptom prevalence in men (n=353).

3.3.5 Spirometry

No statistically significant differences were found between age and gender groups who did and did not complete the spirometry test, (p=0.783, Pearson's χ^2=1.0774) and (p=0.974, Pearson's χ^2=0.001) respectively.

3.3.5.1 Spirometry results based on GOLD definitions

Post-bronchodilator obstruction (GOLD stage 1) was seen in 14.8% (SE 1.6) of the total study population (16.6% [SE 2.1] of men and 12.5% [SE 2.5] of women). Subjects aged 60–69 had the highest prevalence of GOLD stage 1 or higher COPD (31.6% [SE 4.9]). According to the NHANES III reference range, 12.6% (SE 1.5) of

the overall population had GOLD stage 2 or higher (13.9% [SE 1.9] of men and 10.9% [SE 2.3] of women). Male smokers with more than 20 packs per years had the highest prevalence of GOLD stage 1 and stage 2 COPD (19.8% [SE 6.6] and 17.3 [SE 6.2]) compared to other smoking groups. Using the locally derived reference range, 5.2% (SE 0.9) of the total study population had GOLD stage 2 COPD (6.1% [SE 1.3] of men and 4% [SE 1.4] of women). Similarly, subjects aged 60–69 had the highest prevalence of GOLD stage 2 using both the local and NHANES reference ranges (27.6% [SE 4.8] vs.12.6% [SE 3.5], Table 3.6 and 3.7, Figure 3.4 and 3.6).

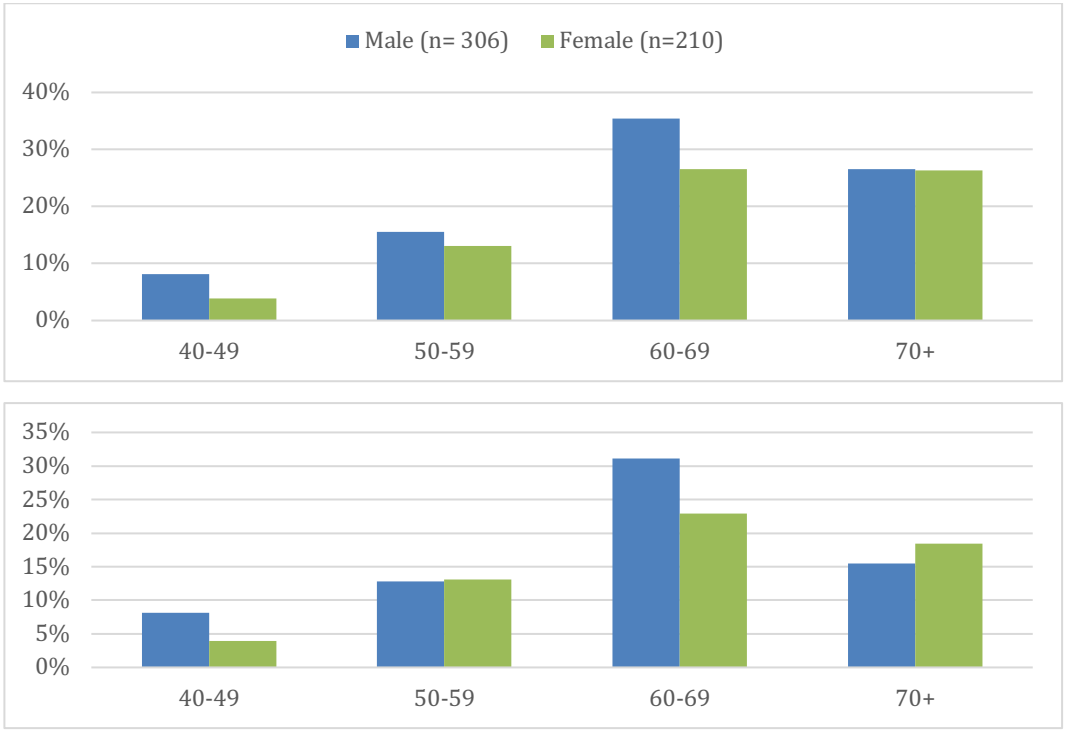


Figure 3.5 Estimated Population Prevalence of airway obstruction by age and sex using (NHANES) reference range for the Sudanese population in subjects completing standard ATS spirometry (n=516). The upper graph represents the prevalence of GOLD Stage 1 or higher COPD (Post-BD FEV1/FVC <0.7) and the lower graph represents the prevalence of GOLD Stage 2 or higher COPD ((Post-BD FEV1/FVC < 0.7 and post-BD FEV1 < 80% predicted).

3.3.5.2 Spirometry results based on LLN definition

Using below LLN of the NHANES reference range for white Americans, modified stage 1 or higher COPD prevalence was 10.3% [SE 1.4] (9.2 [SE 1.7] of men and

11.2 [SE 2.4] of women). On other hand using the locally derived reference range the prevalence was 5.7% [SE 1.1] (5.2% [SE 1.3] of men and 6.3 [SE 1.9] of women). Subjects aged 60–69 had the highest prevalence of modified stage 1 or higher COPD using below LLN (13.4% [SE 3.8]). According to the NHANES III reference range, prevalence of modified stage 2 or higher COPD using below LLN was 9.4% [SE 1.4) (8.8% [SE 1.7] of men and (10.1% [SE 2.2] of women). Males with 0-10 pack years of smoking exposure had the highest prevalence of modified stage 1 and 2 COPD using below LLN compared to other smoking groups (15.3% [SE 5.2] and 14% [SE 5.1]). Using the locally derived reference range, 3.0% [SE 0.8] of the study population had modified stage 2 or higher COPD (2.9% [SE 0.9] of men and 3.1% [SE 1.3] of women). Similarly, subjects aged 60–69 had the highest prevalence of stage 2 or higher COPD using both the local and NHANES reference ranges (17.6% [SE 4.2] vs. 6.7% [SE 2.6]), Table 3.7 and 3.8, Fig 3.5 and 3.6).

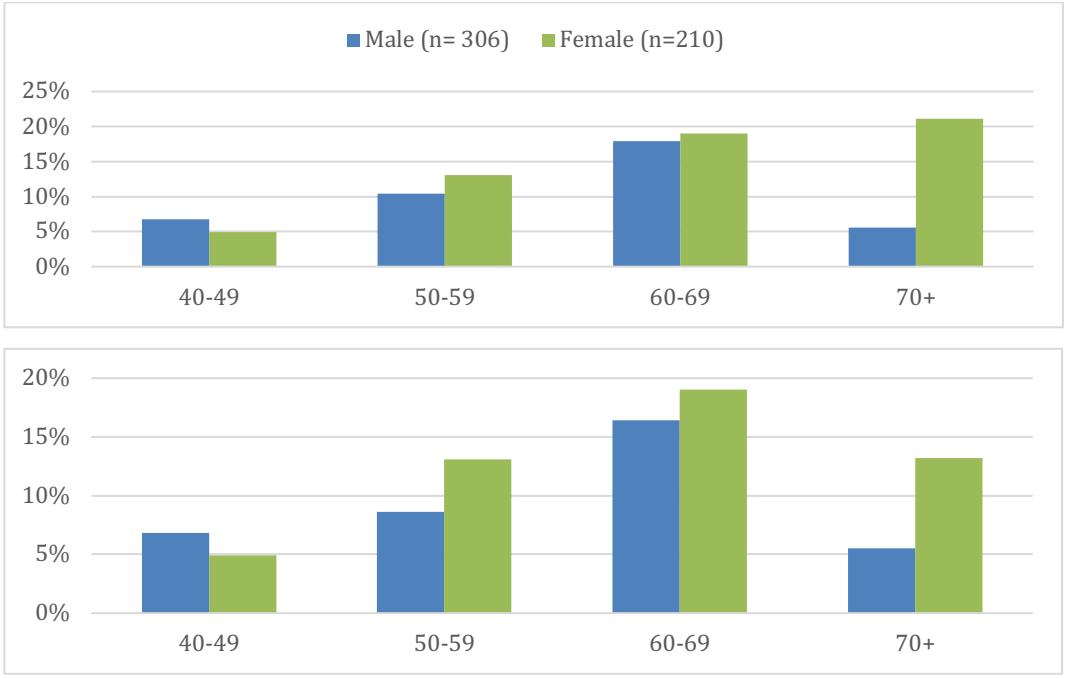


Figure 3.6*:* Estimated Population Prevalence of airway obstruction by age and sex using (NHANES) reference range for the Sudanese population in subjects completing standard ATS spirometry (n=516). The upper graph represents the prevalence of LLN Modified Stage 1 or higher COPD (Post-BD FEV1/FVC < LLN) and the lower graph represents the prevalence of LLN Modified Stage 2 or higher COPD ((Post-BD FEV1/FVC < LLN and post-BD FEV1 < 80% predicted).

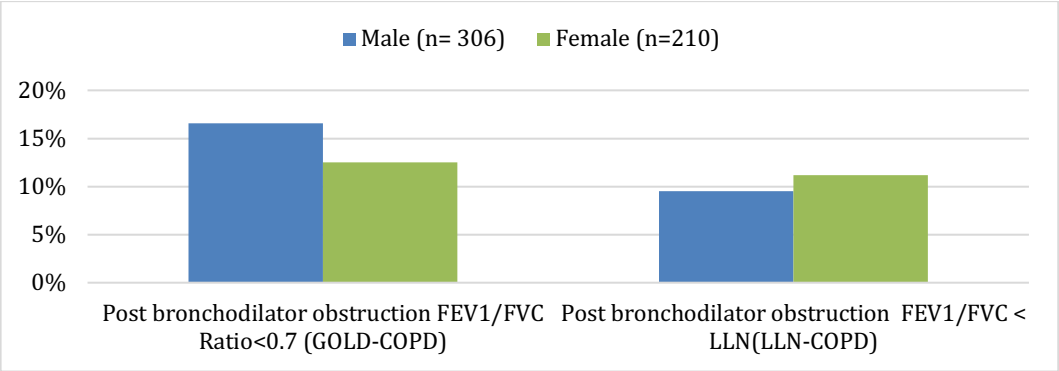


Figure 3.7 Estimated Prevalence of airway obstruction by sex using National Health and Nutrition Examination Survey reference ranges (NHANES) for the Sudanese population in subjects completing standard ATS spirometry (n=516). The graph represents the prevalence of GOLD Stage 1 or higher COPD (Post-BD FEV1/FVC <0.7) and the prevalence of LLN Modified Stage 1 or higher COPD (Post-BD FEV1/FVC < LLN).

3.3.5.3 Airway reversibility

Airway reversibility was found in 6.1% [SE 1.1] of the total study population and was more prevalent in women than in men (8% [SE 1.9] vs. 4.4% [SE 1.1]). Airway obstruction persisted after use of a bronchodilator in 10.5% (SE 5.1) of subjects with reversibility. Prevalence was higher using LLN (18.5% [SE 4.0]) – see Table 3.9.

3.3.5.4 Low FVC

Low FVC was more prevalent than obstruction in both sexes and in all age groups. Using the NHANES III reference range, the overall estimated prevalence was 58.8% (SE 2.2). Low FVC was more slightly common in men than in women (59.5% [SE 2.9] vs. 58.1% [SE 3.6]). Respiratory symptoms were more present in those with low FVC as 53.3% of those with respiratory symptoms had low FVC (52.5% phlegm and 56.6% shortness of breath). However, having cough was significantly higher in those without spirometric restriction (Table 3.10). However, using the local reference range, a far lower prevalence estimate of low FVC (11.3% [SE 1.4]) was found (12.1% [SE 1.9]) in men and 10.3% [SE 2.1] in women; Table 3.11, Figure 3.5).

Table 3.6 Age and gender stratified prevalence estimates for abnormal spirometry among participants with full spirometry data using GOLD definition

Spirometric definition (reference range)	Age group (n=328)	Male (n= 306) Prevalence (SE)	Female (n=210) Prevalence (SE)	Total (n= 516) Prevalence (SE)
Post bronchodilator obstruction FEV1/FVC ratio<70% (GOLD Stage1)	40-49	8.1% (2.9)	3.9% (1.9)	6.1% (1.8)
	50-59	15.5% (3.4)	13.1% (4.3)	14.4% (2.7)
	60-69	35.4 (5.8)	26.5% (8.5)	31.6% (4.9)
	70+	26.6 (7.3)	26.3% (11.4)	26.5% (6.9)
	Total	16.6% (2.1)	12.5% (2.5)	14.8% (1.6)
Post bronchodilator moderate to severe obstruction FEV1/FVC ratio<70% and FEV1 <80% predicted (NHANES ref range) (GOLD stage 2)	40-49	8.1% (2.9)	3.9% (1.9)	6.2% (1.8)
	50-59	12.8% (3.1)	13.1% (4.3)	12.9% (2.6)
	60-69	31.1% (5.7)	22.9% (8.2)	27.6% (4.8)
	70+	15.5% (5.9)	18.4%(9.8)	17.0% (5.8)
	Total	13.9% (1.9)	10.9% (2.3)	12.6% (1.5)
Post bronchodilator moderate to severe obstruction FEV1/FVC ratio<70% and FEV1 <80% PREDICTED (locally derived ref range) (GOLD stage 2)	40-49	3.4% (1.9)	3.0% (1.6)	3.1% (1.3)
	50-59	6.2% (2.3)	3.1% (2.2)	4.9% (1.6)
	60-69	16.2% (4.5)	7.8% (5.3)	12.6% (3.5)
	70+	2.2% (2.2)	5.3% (5.2)	3.8% (2.8)
	Total	6.1% (1.3)	4.0% (1.4)	5.2% (0.9)

Table 3.7 Age and gender stratified prevalence estimates for abnormal spirometry among participants with full spirometry data using below limit of normal (LLN) definition

Spirometric definition (reference range)	Age group (n=516)	Male (n= 306) Prevalence (SE)	Female (n=210) Prevalence (SE)	Total (n=516) Prevalence (SE)
Post bronchodilator obstruction (FEV1/FVC < LLN) (NHANES ref range)	40-49	6.8 (2.7)	4.9 (2.1)	5.9 (1.7)
	50-59	10.4 (2.9)	13.1 (4.4)	11.5 (2.5)
	60-69	17.9 (4.7)	19.0 (7.6)	18.4 (4.2)
	70+	5.6 (3.9)	21.1 (10.8)	13.4 (6.0)
	Total	9.5 (1.7)	11.2 (2.4)	10.3 (1.4)
Post bronchodilator obstruction (FEV1/FVC < LLN) (locally derived ref range)	40-49	4.7 (2.3)	3.0 (1.7)	3.9 (1.5)
	50-59	4.3 (1.9)	3.1 (2.2)	3.8 (1.4)
	60-69	11.9 (3.9)	15.4 (7.1)	13.4 (3.8)
	70+	-	13.2 (8.8)	6.7 (4.6)
	Total	5.2 (1.3)	6.2 (1.9)	5.7 (1.1)
Post bronchodilator moderate to severe obstruction (FEV1/FVC < LLN and **POST-BD FEV1 < 80% predicted) (NHANES ref range)**	40-49	6.8 (2.6)	4.9 (2.1)	5.9 (1.7)
	50-59	8.6 (2.6)	13.1 (4.3)	10.5 (2.4)
	60-69	16.4 (4.5)	18.9 (7.6)	17.6 (4.2)
	70+	5.6 (3.9)	13.2 (8.8)	9.4 (4.9)
	Total	8.8 (1.7)	10.1 (2.2)	9.4 (1.4)
Post bronchodilator moderate to severe obstruction FEV1/FVC < LLN and post-BD FEV1 < 80% predicted (locally derived ref range)	40-49	1.1 (1.1)	3.0 (1.7)	2.0 (1.0)
	50-59	3.5 (1.7)	1.8 (1.8)	2.8 (1.3)
	60-69	8.8 (3.4)	3.9 (3.9)	6.7 (2.6)
	70+	-	5.3 (5.2)	2.7 (2.6)
	Total	2.9 (0.9)	3.1 (1.3)	3.0 (0.8)

Table 3.8 Estimated Population Prevalence (SE) of abnormal spirometry by pack years and sex

		Pack-years				
	Sex	**Never smokers**	**0-10**	**10-20**	**20+**	**Total**
Estimated Population Prevalence (SE) of GOLD Stage 1 or higher COPD	Male	15.4 (2.6)	19.3 (5.7)	16.9 (7.0)	19.8 (6.6)	16.7 (2.1)
	Female	12.9 (2.6)	*	*	*	12.5 (2.6)
	Total	14.0 (1.9)	17.3 (5.2)	16.5 (6.8)	19.8 (6.6)	14.8 (1.6)
Estimated Population Prevalence (SE) of GOLD Stage 2 or higher COPD	Male	13.0 (2.4)	14.0 (5.1)	16.9 (7.0)	17.3 (6.2)	14.0 (2.0)
	Female	11.3 (2.4)	*	*	*	11.0 (2.3)
	Total	12.0 (1.7)	12.6 (4.6)	16.5 (6.8)	17.3 (6.2)	12.6 (1.5)
Estimated Population Prevalence (SE) of LLN Modified Stage 1 or higher COPD	Male	8.9 (2.1)	15.3 (5.2)	4.5 (3.2)	7.4 (4.2)	9.5 (1.7)
	Female	11.5 (2.5)	*	*	*	11.2 (2.4)
	Total	10.4 (1.7)	13.7 (4.7)	4.4 (3.1)	7.4 (4.2)	10.3 (1.4)
Prevalence (SE) of LLN Modified Stage 2 or higher COPD	Male	8.1 (2.1)	14 (5.1)	4.5 (3.2)	7.4 (4.2)	8.8 (1.7)
	Female	10.4 (2.3)	*	*	*	10.1 (2.2)
	Total	9.4 (1.6)	12.6 (4.6)	4.4 (3.1)	7.4 (4.2)	9.4 (1.4)
*** No observation in this group**						

Table 3.9 Age and gender stratified prevalence estimates for airway reversibility based on ATS/ERS definition (n=33/516)

Spirometric definition (reference range)	**Age group (n=516)**	**Male (n= 305) Prevalence (SE)**	**Female (n=211) Prevalence (SE)**	**Total (n= 516) Prevalence (SE)**
Airway reversibility fev1 increase ≥200ml and ≥12% following bronchodilator	40-49	1.3% (1.3)	4.9% (2.2)	3% (1.2)
	50-59	7.2% (2.5)	9.1% (3.6)	8.1% (2.1)
	60-69	5.9% (2.9)	18.3% (7.4)	11.2% (3.6)
	70+	7.5% (4.3)	5.3% (5.2)	6.4% (3.4)
	Total	4.4% (1.1)	8% (1.9)	6.1% (1.1)

Table 3.10 Presence of respiratory symptoms in those with/without low FVC

Spirometric restriction	Abnormal FVC N(%)	Normal FVC N(%)	P-value
Cough	25(43.1)	33(56.9)	0.025
Phlegm	31(52.5)	28(47.5)	0.476
Wheeze	8(47.1)	9(52.9)	0.406
Shortness of breathe	30(56.6)	23(43.4)	0.874
Functional limitation	6(60)	4(40)	0.84
Any respiratory symptoms	65(53.3)	57(46.7)	0.332

Table 3.11 Age and gender stratified prevalence estimates for low FVC using both NHANES and local reference ranges (n=293/516)

Spirometric definition (reference range)	Age group (n=516)	Male (n= 306) Prevalence (SE)	Female (n=210) Prevalence (SE)	Total (n=516) Prevalence (SE)
Low FVC (FEV1/FVC ratio>0.7, and FVC<80% predicted) (NHANES ref range)	40-49	75.7% (4.6)	65% (4.7)	70.6% (3.3)
	50-59	56% (4.7)	60.6% (6.2)	57.9% (3.7)
	60-69	37.5% (5.9)	44% (9.6)	40.3% (5.3)
	70+	35.4% (7.8)	44.7% (12.7)	40.1% (7.5)
	Total	59.5% (2.9)	58.1% (3.6)	58.8% (2.2)
Low FVC (FEV1/FVC ratio>0.7, and FVC<80% predicted) (locally derived ref range)	40-49	11.1% (3.3)	11.5% (3.1)	11.3% (2.3)
	50-59	16.5% (3.4)	12.5% (4.2)	14.7% (2.7)
	60-69	5.9% (2.8)	7.2% (4.9)	6.4% (2.7)
	70+	14.3% (5.6)	5.3% (5.2)	7.7% (3.9)
	Total	12.1% (1.9)	10.3% (2.1)	11.3% (1.4)

3.3.5.5 Factors associated with respiratory symptoms

There was no significant association between a cough and any of the risk factors investigated in either bivariate or multivariate analysis.

In both multivariate and bivariate analyses, regular production of sputum was negatively associated with age (Table 3.12). Subjects aged 60–69 were less likely to report regular sputum production (OR 0.39, 95% CI 0.16–0.93) than those aged 40–49. There was a significantly increased likelihood of regular sputum production if the patient was an ex-smoker (OR 2.66, 95% CI 1.09–6.50) and had diabetes (OR 4.04, 95% CI 1.82–8.96). There was no observed trend in Mokken scale points and all respiratory symptoms. Participants with lower socioeconomic status; who scored 2 in Mokken scale tend to have higher odds of sputum production in both bivariate and multivariate analysis (OR 7.18, 95% CI 1.16-44.53).

In multivariate analysis, the likelihood of having shortness of breath was significantly greater in subjects exposed to indoor biomass fuel (OR 4.56, 95% CI 1.44–14.43). The presence of wheeze was only associated with currently being a smoker (OR 3.49, 95% CI 1.02–11.96).

Cough was less commonly reported in those with low FVC using LLN (odds ratio [OR] 0.48, 95% confidence interval [CI 0.27-0.87]) and NHANES (odds ratio [OR] 0.55, 95% confidence interval [CI 0.30–0.99]). There were no other significant associations between spirometric abnormality and respiratory symptoms.

Table 3.12 Multivariate associations between respiratory symptoms and risk factors (all variables significant at level <0.2 in bivariate analysis are included)

Variable	Usual cough (n=66/ 596)		Usual sputum (n=67/ 596)		Exertional dyspnoea (n=62/545)		Wheeze without cold (n= 18/596)	
	Odds ratio	95% CI	Odds ratio	95% CI	Odds ratio	95% CI	Odds ratio	95% CI
Age group								
40-49	1.0	-	1.0	-	1.0	-	1.0	-
50-59	1.05	0.54-2.03	0.36*	0.17-0.75	0.49	0.22-1.09	0.34	0.09- 1.33
60-69	0.99	0.43- 2.29	0.39*	0.16-0.94	0.81	0.31-2.14	1.28	0.45- 3.70
70+	0.97	0.36-2.66	0.41	0.15-1.11	0.29	0.05-1.72	-	-
Gender								
Male	1.0	-	1.0	-	1.0	-	1.0	-
Female	0.79	0.43-1.45	0.93	0.44-1.96	1.37	0.63-2.99	0.61	0.19-1.98
Year of education	0.96	0.91-1.02			1.03	0.97- 1.09		
Smoking status								
Never			1.0	-	1.0	-	1.0	-
Current			2.25	0.77- 6.55			3.49*	1.02-11.96
Ex-smoker			2.67*	1.09-6.50			0.26	0.03-2.07
BMI (kg/m^2)								

Underweight (BMI<18.5)			0.19	0.03-1.43	0.53	0.10-2.74	-	-
Normal (BMI 18-25)			1.0	-	1.0	-		
Overweight (BMI 25-30)			0.64	0.30-1.35	2.09	0.91-4.76		
Obese (BMI>30)			0.75	0.34-1.68	2.31	0.94- 5.66		
Reported diabetes								
No			1.0	-	1.0	-		
Yes			4.04*	1.82-8.96	0.26	0.03-1.94		
Have a flush toilet								
No			1.0	-	1.0	-	1.0	-
Yes			1.24	0.53- 2.87	0.62	0.29-1.33	5.61	0.71-44.36
Number of people living in house	1.05	0.99-1.12						
Any biomass exposure								
No	1.0	-	1.0	-	1.0	-	-	-
Yes	1.69	0.70-4.09	1.93	0.71- 5.23	4.56 *	1.44 -14.43		
Current Mokken scale	**OR**	**P-value**	**OR**	**P-value**	**OR**	**P-value**	**OR**	**P-value**
	-	-	-	-	1.03	0.686	0.06	0.681
***indicates p<0.05**								

3.3.5.6 Factors associated with post-bronchodilator airway obstruction defined by LLN

Using LLN, subjects aged 60–69 had the highest risk of COPD modified stage 1 or higher (OR 3.16, 95% CI 1.20-8.31) and modified stage 2 or higher (OR 3.39, 95% CI 1.04- 6.93) compared to those aged 40–49. In contrast, having a higher educational level was protective against LLN modified stage 1 or higher COPD in bivariate analysis (OR 0.31, 95% CI 0.13–0.76), though no association was identified after adjustment. Those who were overweight or obese were less likely to have LLN modified stage 1 or higher COPD (OR 0.38, 95% CI 0.17–0.82 and OR 0.34, 95% CI 0.13–0.99, respectively). Those with a history of TB were less likely to have LLN modified stage 1 or higher COPD (OR 0.08, 95% CI 0.01- 0.59). No other factor was significantly associated with airway obstruction (Tables 3.13 and 3.14).

Using the local reference range, subjects aged 60–69 were more likely to have COPD stage 1 or higher than their younger counterparts (OR 3.10, 95% CI 1.01-9.57), and being obese was negatively associated with obstruction (OR 0.29, 95% CI 0.09- 0.97) in multivariable analysis. Having a higher educational level was protective against COPD in the bivariate analysis (OR 0.23, 95% CI 0.063 - 0.83), though no association was identified after adjustment. Using firewood for cooking for more than 6 months was protective against COPD modified stage 2 or higher (OR 0.11, 95% CI 0.03 - 0.44) in bivariate analysis though no association was identified after adjustment. No other association was identified between possible risk factors and abnormal spirometry.

3.3.5.7 Factors associated with post-bronchodilator airway obstruction defined by GOLD

Older age was significantly associated with airway obstruction. The 70+ age group had increased odds of 3.94 (95% CI 1.62-9.56) compared to the younger group (40-49), though the (60-69) age group had the highest odds of 6.25 (95% CI 2.85-13.72) of airway obstruction and 5.21 (95% CI: 2.35-11.55) of moderate-severe obstruction compared to those in the 40-49 group. Being a current smoker had an increased chance of 2.56 (95% CI 1.06-6.18) of having a GOLD stage 2 or higher COPD. Being obese and having TB were protective against GOLD stage 2 or higher COPD and the odds were (OR: 0.48; 95% CI: 0.23-1.00) and (OR 0.18; 95% CI: 0.04-0.91)

respectively. Years of Education was significantly associated with obstruction in the bivariate analysis (OR: 0.92; 95% CI: 0.87-0.97) but once the adjustment was made no association was identified (Table 3.15 and 3.16). Using the Mokken scale, no association observed between socio economic status and both gold stage 1 and stage 2 COPD.

Using the local reference range in GOLD stage 2 or higher COPD, the age group 60-69 had increased odds of 3.79 compared to the younger group (95% CI: 1.33-10.81), while self-reported TB and being obese were negatively associated with obstruction (OR 0.07; 95% CI: 0.01-0.43) and (OR 0.17; 95% CI: 0.03-0.90) in the multivariable analysis. No other associations were seen between possible risk factors and abnormal spirometry.

Table 3.13 Bivariate and multivariable associations of risk factors with Modified Stage 1 or higher COPD defined using NHANES reference range (Post-BD FEV1/FVC < LLN; n=64/590)

Variable	Bivariate association		Multivariable association	
	Odds ratio	**95% CI**	**Odds ratio**	**95% CI**
Age group				
40-49	1.0	-	1.0	-
50-59	2.08 ±	0.95-4.53	2.13	0.84-5.41
60-69	3.58 *	1.56-8.22	3.16 *	1.20-8.32
70+	2.47	0.76-9.10	1.91	0.60-6.10
Gender				
Male	1.0	-	1.0	-
Female	1.20	0.65-2.23	1.31	0.61-2.84
Level of education				
None			1.0	-
Primary school	0.46±	0.21-1.02	0.610	0.27-1.34
Middle school	0.72	0.27-1.91	1.23	0.40-3.81
High school or above	0.32*	0.134-0.76	0.71	0.28-1.78
Self-reported TB				
No			1.0	-
Yes	4.53±	0.72-28.68	0.08	0.01-0.59

Body Mass Index (kg/m2)				
Underweight (BMI<18.5)	2.04±	0.72-5.77	1.87	0.66-5.30
Normal (BMI 18-25)	1.0	-	1.0	-
Overweight (BMI 25-30)	0.38*	0.18-0.82	0.43	0.18-1.01
Obese (BMI>30)	0.34*	0.13-0.89	0.35*	0.11-1.17
Smoking status				
Never	1.0	-	1.0	-
Current	1.21	0.48-3.05	1.95	0.83-4.59
Ex smoker	0.76	0.29-1.97	0.72	0.32-1.60
Smoking pack years				
<10 years	1.0	-	-	-
<= 10 years	0.51±	0.19-1.36	-	-
Home ownership				
No	1.0	-	-	-
Yes	1.11	0.55-2.23	-	-
Access to private water supply (indoors or outdoors)				
No	1.0	-	-	-
Yes	1.60 ±	0.41-1.82	-	-

Household has flush toilet				
No	1.0	-	-	-
Yes	0.86	0.41-1.82	-	-
Number of people living in house	1.051	0.97-1.14	-	-
Any biomass exposure				
No	1.0	-	-	-
Yes	1.80	0.65-4.97	-	-
Use of firewood in cooking >6 month				
No	1.0	-	-	-
Yes	0.60±	0.30-0.17	-	-
Occupation group 1	0.87	0.42-1.83	-	-
>5 years of exposure in group1	0.9	0.40-2.05	-	-
Occupation group 2	0.84	0.30-2.41	-	-
>5 years of exposure in group2	0.16±	0.02-1.24	-	-
Occupation group 3	1.63	0.44-6.09	-	-
>5 years of exposure in group3	1.33	0.27-6.66	-	-
Working in farming				
No	1.0	-	-	-
Yes	0.95	0.45-1.98	-	-
Current Mokken scale	**OR**	**P-value**	**OR**	**P-value**
	0.96	0.478	-	-

[±] indicates p<0.2; *p<0.05. CI, confidence interval; OR, odds ratio; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity ratio; LLN, lower limit of normal; TB, tuberculosis

Occupation group 1: Working in agriculture, textile or food industry

Occupation group 2: Working in Mining and construction industry

Occupation group 3: Welders, firefighters, cleaners or exposed to chemicals during work

Table 3.14 Bivariate and multivariable associations of risk factors with Modified Stage 2 or higher COPD defined using NHANES reference range (Post-BD FEV1/FVC < LLN and post-BD FEV1 < 80% predicted; n=58/590)

Variable	Bivariate association		Multivariable association	
	Odds ratio	95% CI	Odds ratio	95% CI
Age group				
40-49	1.0	-	1.0	-
50-59	1.88±	0.85-4.15	1.85	0.72-4.71
60-69	3.39*	1.46 -7.84	2.61*	1.01 - 6.77
70+	1.65	0.46-6.01	1.08	0.29- 4.00
Gender				
Male	1.0	-	1.0	-
Female	1.17	0.62-2.20	1.55	0.71-3.39
Years of education	0.91*	0.85-0.97	0.95	0.88-1.04
Self-reported TB				
No	1.0	-	1.0	-
Yes	5.02±	0.79-31.80	0.05*	0.01-0.34
Body Mass Index (kg/m2)				
Underweight (BMI<18.5)	1.42	0.46 - 4.31	1.19	0.34-4.16
Normal (BMI 18-25)	1.0	-	1.0	-
Overweight (BMI 25-30)	0.36*	0.16-0.81	0.73 *	0.15-0.93
Obese (BMI>30)	0.31*	0.11- 0.85	0.29	0.08-1.05
Smoking status				
Never	1.0	-	1.0	-
Current	1.35	0.53-3.41	2.28	0.96-5.41
Ex smoker	0.74	0.26-2.05	0.59	0.23-1.49
Home ownership				
No	1.0	-		
Yes	0.90	0.44-1.86		

Access to private water supply (indoors or outdoors)				
No	1.0	-		
Yes	1.42	0.74 - 2.74		
Household has flush toilet				
No	1.0	-	-	-
Yes	0.88	0.41-1.89	-	-
Number of people living in house	1.06 ±	0.98-1.15	1.04	0.96-1.14
Any biomass exposure				
No	1.0	-		
Yes	1.92	0.63-5.82		
Occupation group 1	1.01	0.48- 2.12	-	-
>5 years of exposure in group1	1.02	0.45-2.32	-	-
Occupation group 2	0.96	0.33-2.73	-	-
>5 years of exposure in group2	0.18±	0.02-1.37	-	-
Occupation group 3	1.83	0.49-6.86	-	-
>5 years of exposure in group3	1.47	0.29-7.403	-	-
Working in farming				
No	1.0	-		
Yes	0.91±	0.44-1.92	0.61	0.32-1.16
Current Mokken scale	**OR**	**P-value**	**OR**	**P-Value**
	0.94	0.360	-	-

± indicates p<0.2; *p<0.05. CI, confidence interval; or, odds ratio; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity ratio; LLN, lower limit of normal; TB, tuberculosis

Table 3.15 Bivariate and multivariable associations of risk factors with post bronchodilator airway obstruction defined using GOLD and NHANESIII reference range (FEV1/FVC ratio <0.7), n= 96 /590)

Variable	Bivariate association		Multivariable association	
	Odds ratio	95% CI	Odds ratio	95% CI
Age group				
40-49	1.0	-		
50-59	2.58*	1.22- 5.47	2.58*	1.18- 5.63
60-69	7.07*	3.29- 15.21	6.25*	2.85- 13.72
70+	5.51*	2.18 -13.92	3.94*	1.62- 9.57
Gender				
Male	1.0	-		
Female	0.72	0.41- 1.24	0.77	0.40- 1.49
Years of education	0.92*	0.87- 0.97	0.96	0.91- 1.01
Self-reported TB				
No	1.0	-		
Yes	2.96	0.47- 18.58		
Body Mass Index (kg/m2)				
Underweight (BMI<18.5)	1.75	0.69- 4.43	2.04	0.77- 5.38
Normal (BMI 18-25)	1.0	-		
Overweight (BMI 25-30)	0.42 *	0.23 - 0.78	0.51	0.26 - 1.02
Obese (BMI>30)	0.27*	0.12 - 0.62	0.43	0.16 - 1.11
Smoking status				
Never	1.0	-		
Current	1.79±	0.85 -3.76	1.95	0.83 - 4.59
Ex smoker	1.01	0.48 - 2.14	0.72	0.32 -1.60
Home ownership				
No	1.0	-		
Yes	0.85	0.46 - 1.56		
Access to private water supply				
No	1.0	-		
Yes	1.30	0.76 - 2.24		

Household has flush toilet				
No	1.0	-		
Yes	0.88	0.47 - 1.63		
Number of people living in house	1.05±	0.98 -1.12	1.04	0.96 -1.12
Any biomass exposure				
No	1.0	-	-	-
Yes	1.62	0.70 - 3.74	-	-
Occupation group 1	1.09	0.60-1.97	-	-
>5 years of exposure in group1	0.79	0.50-1.87	-	-
Occupation group 2	0.92	0.41-2.09	-	-
>5 years of exposure in group2	0.35±	0.10-1.19	-	-
Occupation group 3	1.73	0.58-5.14	-	-
>5 years of exposure in group3	1.37	0.36-5.23	-	-
Working in farming				
No	1.0	-	-	-
Yes	1.19	0.65 - 2.15	-	-
Current Mokken scale	**OR**	**P-value**	**OR**	**P-value**
	0.99	0.784	-	-

±indicates p<0.2; *p<0.05. CI, confidence interval; or, odds ratio; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity ratio; LLN, lower limit of normal; TB, tuberculosis

Occupation group 1: Working in agriculture, textile or food industry

Occupation group 2: Working in Mining and construction industry

Occupation group 3: Welders, firefighters, cleaners or exposed to chemicals during work

Table 3.16 Bivariate and multivariable associations of risk factors with moderate-severe post bronchodilator airway obstruction, defined using GOLD and NHANES III reference range (FEV1/FVC ratio <0.7 and FEV1 <80% predicted) n=81/590

Variable	Bivariate association		Multivariable association	
	Odds ratio	95% CI	Odds ratio	95% CI
Age group				
40-49	1.0	-	1.0	-
50-59	2.27*	1.06- 4.87	2.18	0.98-4.82
60-69	5.82*	2.68-12.67	5.21*	2.40-11.55
70+	3.13*	1.13- 8.65	1.57	0.53-4.63
Gender				
Male	1.0	-	1.0	-
Female	0.76	0.43-1.34	1.18	0.58-2.38
Years of education	0.92*	0.88- 0.98	0.96	0.90-1.01
Self-reported TB				
No	1.0	-	1.0	-
Yes	3.58±	0.57-22.51	0.16*	0.03-0.90
Body Mass Index (kg/m2)				
Underweight (BMI<18.5)	1.52	0.57-4.03	1.47	0.47-4.58
Normal (BMI 18-25)	1.0	-	1.0	-
Overweight (BMI 25-30)	0.43*	0.22-0.83	0.48 *	0.23-0.10
Obese (BMI>30)	0.29*	0.12-0.71	0.38	0.12-1.17
Smoking status				
Never	1.0	-	1.0	-
Current	1.96±	0.91-4.22	2.56*	1.06 - 6.18
Ex	0.82	0.35-1.90	0.70	0.28 -1.81
Home ownership				
No	1.0	-		
Yes	0.83	0.43-1.63		

Access to private water supply (indoors or outdoors)				
Yes	1.09	0.61-1.96		
No	1.0	-		
Household has flush toilet				
No	1.0	-		
Yes	0.99	0.52-1.87		
Number of people living in house	1.06 ±	0.98-1.13	1.05	0.97-1.14
Any biomass exposure				
No	1.0	-		
Yes	1.69	0.66-4.31		
Occupation group 1	1.4	0.78-2.57	-	-
>5 years of exposure in group1	1.21	0.62-2.36	-	-
Occupation group 2	1	0.42-2.36		
>5 years of exposure in group2	0.43±	0.12-1.44	-	-
Occupation group 3	2.11±	0.71-6.29	-	-
>5 years of exposure in group3	1.66	0.44-6.37	-	-
Working in farming				
No	1.0	-		
Yes	1.53±	0.83-2.80	1.62	0.81- 3.21
Current Mokken scale	**OR**	**P-value**	**OR**	**P-Value**
	0.99	0.850	-	-

± indicates p<0.2; *p<0.05. CI, confidence interval; or, odds ratio; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity ratio; LLN, lower limit of normal; TB, tuberculosis

Occupation group 1: Working in agriculture, textile or food industry

Occupation group 2: Working in Mining and construction industry

Occupation group 3: Welders, firefighters, cleaners or exposed to chemicals during work

3.3.5.8 Factors associated with low FVC

Using the NHANES III reference range, low FVC was associated with a 10-20 pack year smoking history, having a primary or higher level of education, having more people in-house and being obese (OR 2.79; 95% CI: 1.11- 7.00; OR 2.42; 95% CI: 1.43- 4.09; OR 0.94; 95% CI: 0.89 - 0.99 and OR 1.73; 95% CI: 1.04 - 2.86 respectively) in bivariate analysis. After adjustments, the younger age group were less likely to have low FVC. No other factors were associated with low FVC in multivariate analysis (Table 3.17).

Table 3.17 Multivariate associations of risk factors with low FVC, defined using NHANES III reference range (FEV1/FVC ratio >0.70 and FVC <80% predicted), n= 328/590

Variable	**Multivariable association**	
	Odds ratio	**95% CI**
Age group		
40-49	1	-
50-59	0.75*	0.50-1.13
60-69	0.35*	0.21-0.57
70+	0.36*	0.19-0.66
Gender		
Male	1	-
Female	1.14	0.78-1.65
Body Mass Index (kg/m2)		
Underweight (BMI<18.5)	1.1	0.54-2.25
Normal (BMI 18-25)	1	-
Overweight (BMI 25-30)	1.32	0.88-2.00
Obese (BMI >30)	1.38	0.85-2.23
Home ownership		
Yes	1.15	0.79-1.69
No	1	-
Number of people living in house	0.95*	0.90-0.99
***indicates p<0.05**		

3.4 Discussion

In this population-based cross-sectional study, we aimed to investigate the prevalence and determinants of COPD in adults in urban Sudan. Our main finding was that 14.8% of people in this age group had spirometric findings consistent with COPD using GOLD criteria while prevalence was lower using the below LLN definition (10%). A high prevalence of low FVC (58.8%) was identified using the NHANES III reference range for Caucasian Americans. GOLD stage 2 or higher COPD was detected in 12.6% vs 9.4% of the overall population using the same reference range, though this decreased to 5.2% vs 3.0% when the local reference range was used according to GOLD versus below LLN definitions respectively. These findings might be compatible with the ATS/ERS recommendations to use the LLN for FEV1/FVC to avoid over-diagnosis of COPD in elderly populations (171). However, other studies argued that using LLN might underdiagnose COPD in elderly population compared to an expert diagnosis (172).

Using the NHANES III reference range, older age protected against low FVC. However, using the local reference range, no association was found between spirometric restriction and any of the risk factors.

Our finding of a higher prevalence of obstruction when using the NHANES III reference range compared to the local reference range has been reported previously (166). The NHANES III reference range is a standardized, validated set of spirometric measurements for asymptomatic, Caucasian, non-smoking Americans and adjusted for age, sex, and height. However the use of other reference ranges such as Global Lung Function Initiative 2012 (GLI 12) might be more suitable in this study, NHANES allowed comparability with other published BOLD studies. In the present study, the local ranges reported are based on healthy non-smoking Sudanese adults participated in this study. In spite of it being the only available data, values of the local methodology might be ethnically more suitable compared to NHANES, however, different exposures in this settings may constrain it (166).

There is a lack of evidence to explain the finding of low FVC in this population. However, low FVC has been reported in other BOLD research in SSA (166,173).

Our findings are consistent with other studies in resource-poor settings, but the literature in this area is still limited and there is still no valid explanation (36). Literature suggested that unidentified environmental factors, low birth weight, early exposure to biomass fuel, air pollution and poor diet are common factors associated with lung restriction in developing countries (36). In addition, the findings of having higher prevalence of respiratory symptoms in those with lung restriction may suggest that reduced FVC is associated with burden of lung disease in urban Sudan.

The prevalence of spirometric obstruction in our study is consistent with that in similar studies from SSA, where the prevalence of smoking is high (92,94). Previous BOLD studies found a prevalence of COPD of 23% in men and 16.9% in women in South Africa (36) and an overall prevalence of 7.7% in Nigeria (69,92,167). Additionally, the median reported prevalence in Africa in a recent systematic analysis of spirometric-based studies was 13.4%, which is in line with our results (94). When compared with studies from MENA, our findings for the prevalence of COPD in Sudan using both LLN and GOLD definitions are higher than those in Saudi Arabia (174), Abu Dhabi (106), Tunisia (103,104), Morocco (165), Algeria (175) and Lebanon (93).

Older age was the main risk factor for airflow obstruction in our study, which is consistent with both regional and global findings (69,92,94,97,138,166,176). The highest prevalence estimates of spirometric obstruction using both LLN and GOLD definitions was among 60-69 year olds. This age group also reported a higher prevalence of both chronic cough and chronic phlegm and this might be because of a higher smoking prevalence when compared to other age groups. In contrast, being 70+ appeared to be protective against low FVC when compared to the 40–49 age group, which contrasts GOLD definitions (161).

A higher educational level was protective against COPD which is consistent with other studies, suggesting that airway obstruction is associated with having a lower level of education (66,69,79). The significant association between smoking and moderate to severe obstruction using the GOLD definition, in the absence of an association with spirometric obstruction using LLN, might not be the result of heavy smoking given that 50% of the smokers in our study reported a smoking history of

less than 10 pack years. Countries with lower smoking rates, such as Malawi and Rwanda, have a lower reported prevalence of COPD (138,166).

In our study, participants with high body mass index were less likely to have airflow obstruction and low FVC. This contrasts with other studies that have suggested an association between high BMI and reduced airflow obstruction(177,178). Moreover, the negative association with low FVC is in contrast with previous studies reported that obesity is a cause of low FVC as a result of restriction coming from the accretion of body fat (173).

Conversely, no significant association between the socioeconomic status, identified by using the Mokken scale, and developing post bronchodilator airway obstruction using both LLN and GOLD. This is contrasting with other studies suggesting that low socioeconomic status may be associated with a progression of airflow limitation (94,179).

The lack of a significant association between greater numbers of people per household and either obstruction or low FVC is in contrast with other studies suggesting that crowded housing and low socioeconomic status may be associated with progression of airflow limitation (94,179).

However, participants with low socioeconomic standing and with a greater number of people in household were less likely to have low FVC. This contrasts with studies that suggest that poverty, low socioeconomic status and crowded housing may be associated with a progression of airflow limitation and low FVC in individuals in in LMIC (36,94,179). A possible reason for this difference may be due to the low intensity of environmental exposure in this setting. However, using the wealth score have been widely used for assessing the socioeconomic status, the Mokken scale has been proven to be a valuable tool that provide an indication of individuals' wealth in BOLD studies (170).

We did not observe any association between occupational exposure, whether categorised into organic, inorganic or fumes, and developing airway obstruction. Twenty-three percent of the subjects in this study were farmers and no association

with lung disease was observed. Furthermore, no association between exposure to biomass fuel and obstruction was identified except when using firewood for more than six months in cooking, which was inversely associated with modified stage 2 COPD or higher using the local reference range. This is in contrast with published reports which assert that exposure to biomass fuel is the biggest risk factor for lung disease in Africa (90–92,94). However, a recent study that included 25 BOLD sites stated that airflow obstruction measured by post-bronchodilator spirometry was not associated with the use of solid fuels for cooking or heating (180). Although causality cannot be assumed from this cross-sectional study, it seems reasonable that a positive association would be found in this high-use population. It is also plausible that people using biomass fuel would experience more symptoms (181), such as shortness of breath, which is considered as one of the most common symptoms of COPD. It is possible that this group of patients would suffer from chronic bronchitis or non-obstructive lung diseases. Moreover, the findings of airway reversibility in the whole population was 6%. While in participants with post bronchodilator obstruction, airway reversibility was 10% and 18% using LLN and GOLD respectively. These percentages of airway reversibility (10-18%) might be compatible with asthma diagnosis, which is consistent with the prevalence of asthma in Sudanese adults from previous studies(182).

Additionally, we found that only 0.2% of reported TB might account for the significant negative association between TB and obstruction, which again conflicts with the published literature (43,143). Identification of TB was based on self-reporting, and many factors might affect the validity of the answers provided, given that TB is a highly stigmatized clinical condition the proportion reported here may be an underestimate (183).

This study is the first, to our knowledge, to provide prevalence estimates of COPD in Sudanese adults using internationally accepted methods and procedures as well as an appropriate sampling technique. Following the BOLD project protocol will also allow for future comparisons with other COPD studies.

One limitation of our study is that we did not reach the target sample size of 600 adults above 40 years. This was because 79 participants (12%) had unacceptable

spirometry data while 54 participants (8%) had spirometry data only with no linked questionnaire data. In addition, missing information for a proportion of the study participants limited the cluster-weighted analysis as estimating prevalence based on localities and areas was not possible. Furthermore, information on reasons for exclusion were not recorded, meaning those who were excluded for medical reasons were not separated from those who were excluded for other reasons.

3.5 Conclusions

In conclusion, the findings of this study suggest that CRD is an important public health problem in Sudan and needs to be considered in future public health policies. The overall prevalence of COPD in urban Sudan is similar to that found by other BOLD centres in countries with similar smoking rates, such as South Africa. However, the prevalence of COPD in urban Sudan was relatively high when compared with other countries in SSA and MENA. A high prevalence of low FVC was also identified, the aetiology and pathophysiology of which is unknown and requires further investigation.

Chapter 4 The burden of non-communicable lung diseases in adults, rural Sudan: A population-based cross-sectional study

4.1 Introduction

The previous chapter summarised the prevalence and main determinant of COPD in urban Sudan while reported a high prevalence of the disease in Khartoum State . This chapter outlines a study which documents the burden of chronic non-communicable lung diseases in Gezira State.

Global and regional prevalence estimates of the burden of COPD have been discussed in previous chapters and estimates of the burden of asthma have been addressed in chapter 2 (section 2.5).

In Sudan, asthma is the third most frequent cause of hospitalisation after pneumonia and malaria, and there has been a striking increase in the number of asthma-related emergency admissions (26). While COPD has a prevalence rate of 14% and 10% using GOLD and LLN definitions as found in previous study of urban Sudan (see section 3.3.5, chapter 3), published data on the burden, prevalence, and determinants of COPD and asthma in Sudan are scarce (164).

Following the BOLD study conducted in urban Sudan (see chapter 3), this study conducted another population-based cross-sectional BOLD study in Gezira state, Sudan to provide data regarding the prevalence and determinants of chronic lung diseases such as COPD, asthma and other chronic respiratory diseases. The findings of the previous BOLD study suggested a high prevalence of lung obstruction and an even higher prevalence of low FVC in urban Sudan. Consequently, this study aimed to investigate the burden of chronic lung diseases in different settings in Sudan by selecting Gezira state - a more rural area. The study expanded the scope of the previous work and included a younger population of ≥18 years to explore the prevalence of COPD and other chronic lung diseases such as asthma, as well as related factors that might contribute to the burden of chronic lung disease in Sudan.

4.2 Methodology

4.2.1 Study settings, location and participants

Gezira State is one of the 18 states in Sudan. The state is in the eastern central region of country and has an area of 27,549 km² and an estimated population of approximately 3,780,915. Almost 80.4% live in rural areas, with 19.1% living in urban areas according to the 2008 national census of Sudan (20). The Blue Nile River dissects the state and Wad Medani is its capital. The state is bordered by Khartoum State to the north, Sinnar State to the south, Gadarif State to the east and White Nile State to the west. The population of Gezira is distributed across 7 localities, 40 administrative units and approximately 689 villages, all of which vary in size and population. It split by the Blue Nile with further divisions into administrative units, capital cities, secondary villages and villages (Figure 4.1).

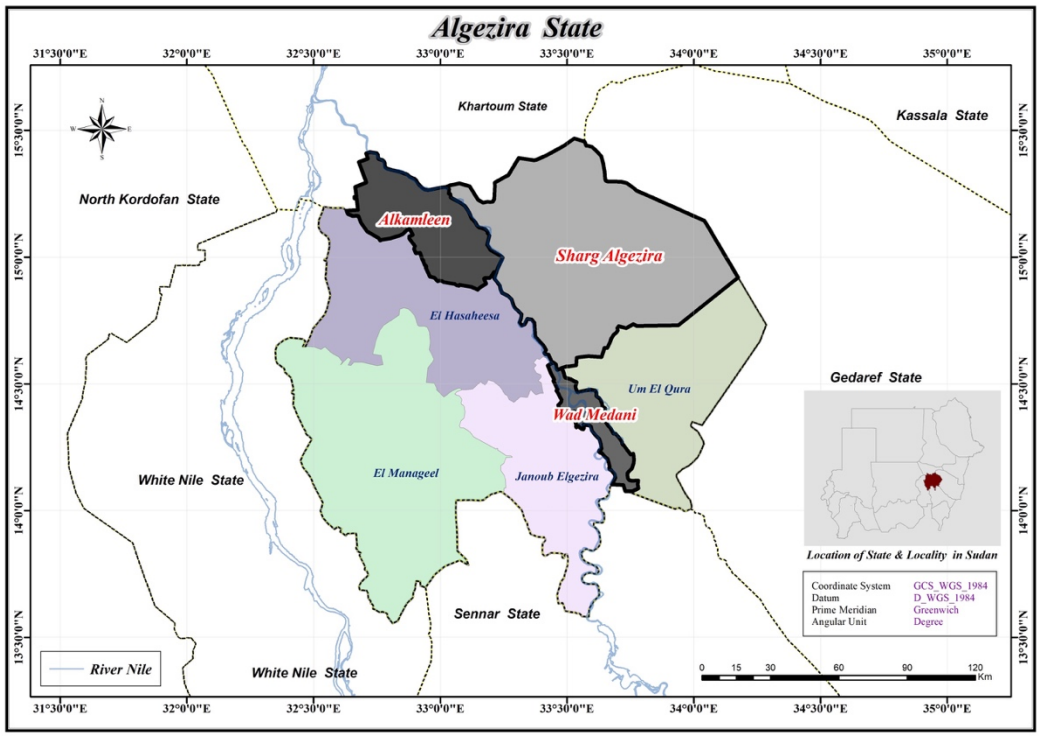


Figure 4.1 Gezira State, Sudan. Locality divisions with study areas in grey and black (Alkamleen, Sharg algezira, Wad Medani)

Ethical approval was obtained prior to the start of the study from Imperial College London, the ethics committee at the ministry of health in Gezira State and the Liverpool School of Tropical Medicine (11.03RS). All participants were given

written informed consent prior to data collection (See Appendix (2 and 5)).

This study followed a multistage sampling design. Three localities (Sharg Algezira, Alkamleen and Wad Medani) were randomly selected from seven localities using a simple random sampling approach. The total population of the three selected localities is 1,288,947.

Each of the three localities is divided into several administrative units, each of which is sub-divided into villages/areas. A simple random sample of 5% of the villages (n=35) was selected.

By including 1000 households, we anticipated being able to sample 2000-3000 adults. All eligible individuals in these households were included. Thirty households per village were then sampled. This was followed by a mapping exercise to count and locate all households, including nomadic households present at the time of the mapping and campo (migrants from other states) residents. In each area/village, households were numbered serially and each locality and village was ascribed unique numbers. As there were no available data for the number of households at the village level, study researchers used simple random sampling to obtain households after mapping (Appendix (4) sampling plan). A strategic data management plan was developed prior to the start of the data collection which covered all standard operating procedures (see Appendix (6)). Pre-selection of areas was carried out prior to field visits. Each participant had a unique identification number composed of 9 digits.

This study included participants aged ≥18 years, living in rural Gezira state. All institutionalised people, the medically unfit and pregnant women in their last trimester were excluded.

The data were collected through standardised, pre-tested BOLD project questionnaires between 25th Aug 2015 and 30th Dec 2016. All consenting participants completed structured questionnaires and underwent pre- and post-bronchodilator spirometry testing. Data were collected by seven trained data collectors and spirometry testing was carried out by a team of five certified technicians.

Anthropometric and pre- and post-bronchodilator spirometry testing was performed in accordance with the BOLD protocol and the American Thoracic Society (ATS) guidelines using the Easy OneTM (NDD Medizintechnic, Zurich, Switzerland) spirometer (68).

This study used the same standardised BOLD questionnaires and data collection methodology described in the previous study (see section 3.2.1, chapter 3).
Local training for the data collection team was conducted prior to the start of the household survey. Training on performing spirometry testing and associated measurements was delivered to the technicians locally by Imperial College London.
To avoid data loss and the complex data management faced in the previous urban study, comprehensive data verification for the whole data set and documentation of field challenges was carried out both in the field and before data entry process. Cross-checking of data was carried out through a field data registry, as well as entry and follow-up sheets.
Data were anonymised and entered into the BOLD international platform at Imperial College London.

4.2.2 Definitions

COPD disease definitions have been discussed in section 3.2.2, chapter 3

4.2.3 Statistical analysis

Statistical analyses were done as discussed in section 3.2.3, chapter 3.

4.3 Results

3281 participants were approached from 35 villages in rural Gezira, of which 9 were Cambo (a rural, mixed-composition, displaced community) (184), 25 were regular villages and 1 was Nomadic. There were 2030 subjects with either partial or complete pre/post spirometry test data and 1308 subjects with full spirometry test and questionnaire data. On the other hand, 542 subjects were having unacceptable spirometry results. The participant recruitment diagram is shown below (Figure 4.2). The total response rate was 59.1%.

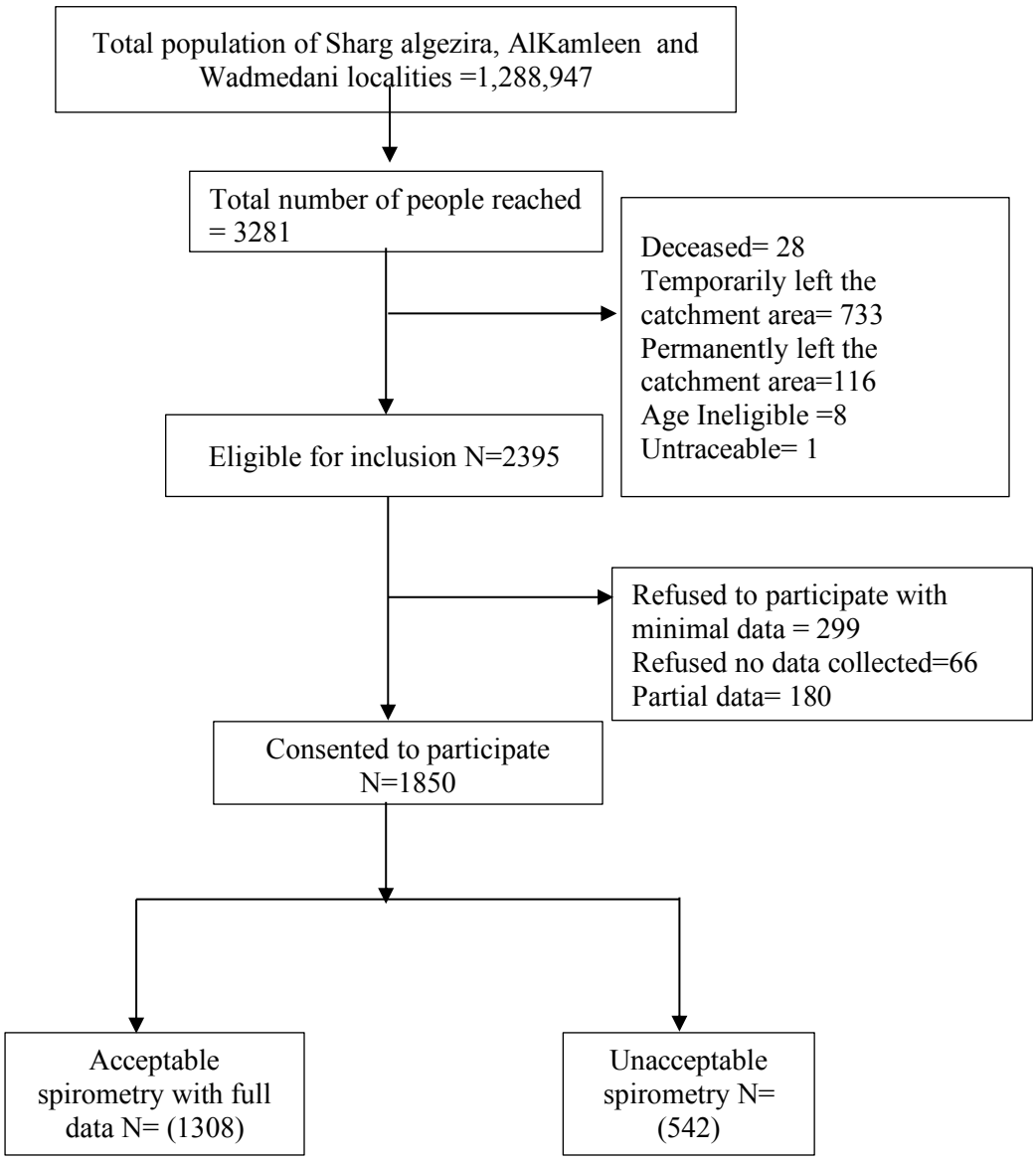


Figure 4.2 Participant recruitment diagram

4.3.1 Participant characteristics

The mean age (SD) was 39.3 (17) years and 55% were <40 years. Women and men were equally distributed (50%). Participants with higher education represented 44.3%. There was no significant difference between men and women with respect to education while the age groups <40 tended to be more educated when compared to older groups (66% vs 36% higher education attainment respectively). There were no significant differences between sexes, age groups and educational level groups for those who did and did not complete spirometry testing.

Responders tended to be <40 years old (P<0.001, Pearson's $\chi 2$= 29.5) when compared to non-responders. Women tended to refuse participation more than men (p<0.001, Pearson's $\chi 2$= 82.4). Those who had never smoked were more likely to fully participate in the study (p<0.001, Pearson's $\chi 2$= 40.1) compared to other smoking groups (Table 4.1). There were no significant differences between those who did and did not complete spirometry test (Table 4.2). Disposition of study participant is shown in Table 4.3.

In total, 17.3% owned more than 6 assets using the Mokken scale, and 92% of participants owned their own home and 85% had their own water source. Only 15% had access to a flush toilet. The mean number of household members was 7.4 ± 3.3. Forty percent of the responders were working in agriculture, textile or food industry and farming was the most commonly reported occupation (39%),15% of which had more than 5 years of exposure (Table 4.4).

4.3.2 Environmental Exposures

Current smokers represented 10.6% of participants. While 9.9% [SE, 2.9] had ever smoked in their life. Among total participants, 13.3% [SE 2.2] had a 10 pack-year smoking history or more while 1.9% [SE, 0.2] had a ≥20 pack-year smoking history (Table 4.4).

Forty-eight percent of participants had exposure to biomass fuels for more than 6 months in their life (36.8% fire coal and 30.5% firewood). On average, those who were exposed to biomass fuels had 1.49 ± 1.4 hours of fire coal and 1.13 ± 1.4 hours of firewood per day (Table 4.4).

4.3.3 Other diseases

In total, 47% of subjects had a normal Body Mass Index (BMI). Hypertension was self-reported by 6.4% of all subjects, of whom 70% were women. Diabetes was reported by 3.3% (57% were women) and both heart disease and TB were reported by 0.3%. None of these diseases were associated with any type of obstruction or low FVC using either local or NHANES reference ranges.

Table 4.1 Comparison of responders[1] and non-responders[2] for Gezira, Sudan

		Responders	**Non-responders**	**P-value[3]**
		N=1,843	N= 1,278	<0.001
	18-29	626(34%)	565(43.5%)	
	30-39	386(20.9%)	270(21.1)	
Age	40-49	328(17.8%)	172(13.5%)	
	50-59	240(13%)	134(10.5)	
	60-69	173(9.5%)	80(6.3%)	
	70+	90(4.9%)	66(5.2%)	
Gender	Male	932(49.9%)	551(43.1%)	<0.001
	Female	926(50.1%)	728(56.9%)	
Smoking status	Current	196(10.7%)	18(5.2%)	<0.001
	Ex	191(10.4%)	7(2%)	
	Never	1445(78.9%)	323(92.8)	
Doctor diagnosed asthma, emphysema, CB or COPD	Yes	134(7.4%)	12(3.5%)	0.008
	No	1689(92.6%)	336(96.6%)	
Other disease	Yes	165(9.1%)	28(8.1%)	0.533
	No	1651(90.9%)	320(92%)	

1. Responders are those who completed post-BD spirometry (regardless of QC scores) and the core questionnaire.
2. Non-responders are eligible individuals who are missing the core questionnaire and/or post-BD spirometry, but for whom the tabulated variable is known.
3. Two-sided p-value based on Pearson chi-square test.

Table 4.2 Comparison of responders[1] with and without usable spirometry for Gezira, Sudan

		With useable spirometry	Without useable spirometry	P-value
Age	18-29	438(33.5%)	188(35.1%)	0.949
	30-39	281(21.5%)	105(19.1%)	
	40-49	234(17.9%)	94(17.5%)	
	50-59	170(13%)	70(13.1%)	
	60-69	122 (9.3%)	51(9.5%)	
	70+	62(4.7%)	28(5.2%)	
Gender	Male	651(49.8%)	272(50.3%)	0.843
	Female	657(50.2%)	269(49.7%)	
Smoking status	Current	133(10.2%)	63(11.7%)	0.638
	Ex-smoker	137(10.6%)	54(10.1%)	
	Never	1,025(79.2%)	420 (78.2%)	
Doctor diagnosed asthma	Yes	80(6.2%)	37(6.9%)	0.561
	No	1211(93.8%)	497(93.1%)	
Doctor diagnosed COPD	Yes	2(0.2%)	0	0.362
	No	1,292 (99.9%)	55(100%)	
Cough	Yes	241(18.7%)	100(18.8%)	0.94
	No	1,049 (81.3%)	431 (81.2%)	
Phlegm	Yes	181(14%)	80(15%)	0.591
	No	1,113(86%)	455 (85.1%)	
Wheeze	Yes	60(4.6%)	33(6.2%)	0.177
	No	1,235(95.4%)	503(93.8%)	
Shortness of breathe	Yes	191(18.4%)	82(18.9%)	0.797
	No	849(81.6%)	351 (81.1%)	
Any Symptoms	Yes	460(40.6%)	189 (40.8%)	0.946
	No	672(59.4%)	274(59.2%)	

1. Responders are those who completed post-BD spirometry (regardless of QC scores) and the core questionnaire.

2. Usable spirometry defined as post-BD quality scores>1 for each of FEV1 and FVC

3. Two-sided p-value based on Pearson chi-square test. NOTE: In some cases numbers are too small for meaningful statistical analysis.

Table 4.3 Disposition of Study Participants

Outcome	Men	Women	Total
Responders:			
Full data collected (Core Ques plus acceptable post BD spirometry)	651	657	1,308
Full data collected (Core Ques plus unacceptable post BD spirometry)	273	269	542
Total responders	924	926	1850
Non-responders:			
Partial data collected	46	134	180
Refused (minimal data collected)	65	234	299
Refused (no minimal data collected)	31	35	66
Only Spirometry data collected	0	0	0
Unreachable	0	0	0
Total non-responders	142	403	545
Ineligible:			
Deceased*	17	11	28
Temporarily left catchment area	408	325	733
Permanently left catchment area	72	44	116
Age ineligible	4	4	8
Institutionalised	0	0	0
Untraceable (inaccurate address and phone)	0	1	1
Total ineligible	501	385	886
Total selected for recruitment[1]	1567	1714	3281

1. Number of responders + non-responders + ineligibles

* Deceased after the start of survey time

Table 4.4 Characteristics of all participants who completed a full BOLD core questionnaire, including those with and without spirometry results

Variable (n)	N (%)
Age group, years (n= 1,844)	
18-29	626 (34)
30-39	387 (21)
40–49	328 (17.8)
50–59	240 (13.0)
60–69	173 (9.4)
70+	90 (4.9)
Sex (n=1,850)	
Male	924 (50)
Female	926 (50)
Level of education (n=1,804)	
None	398 (22.1)
Primary school	483 (26.8)
Middle school	124 (6.9)
High school or above	799 (44.3)
Home ownership (n=1,831)	
Yes	1,679 (91.7)
No	151 (8.3)
Access to private indoor or outdoor water supply (n=1,831)	
Yes	1,551 (84.7)
No	280 (15.3)
Access to flush toilet in home (n=1,831)	
Yes	269 (14.7)
No	1,562 (85.3)
Number of people in households (1,832)	
<5 people	290 (15.9)
5-9 people	1,163 (63.5)
>=10 people	379 (20.7)
Smoking status (n=1,833)	
Current smoker	197 (10.8)
Ex-smoker	191 (10.4)
Never smoked	1,445 (78.8)

Pack-years of smoking (n=1809)	
Never smoked	1,445 (79.9)
>0 and <10	252 (13.9)
≥10	112 (6.2)
20 pack-years of smoking (n=1809)	
<20 years	1,764 (97.5)
>=20 years	45 (2.5)
Biomass fuel exposure (n= 1,814)	
Yes	876 (48.3)
No	938 (51.7)
Farm work for ≥3 months (n= 1,774)	
Yes	697 (39.3)
No	1,077 (60.7)
Construction work for ≥3 months (n=1,774)	
Yes	342 (19.2)
No	1,434 (80.8)
Body Mass Index (n=1700)	
Underweight (BMI<18.5)	173 (10.2)
Normal (BMI 18.5–24.9)	800 (47.1)
Overweight (BMI 25.0–29.9)	415 (24.4)
Obese (BMI ≥30)	312 (18.4)
Reported history of tuberculosis (n=1825)	
Yes	6 (0.3)
No	1,819 (99.7)
Reported history of hypertension (n=1829)	
Yes	117 (6.4)
No	1,712 (93.6)
Reported history of diabetes (n=1828)	
Yes	60 (3.3)
No	1,768 (96.7)
Reported history of heart disease (n=595)	
Yes	6 (0.3)
No	1,821 (99.7)
Current Mokken scale (Mean ± SD)	5.21±2.36
0	43 (2.4)

1	121 (6.6)
2	148 (8.1)
3	150 (8.2)
4	165 (9.0)
5	262 (14.3)
6	318 (17.4)
7	311 (17)
8	213 (11.6)
9	88 (4.8)
10	11 (0.6)
Occupation group 1	712(40)
>5 years of exposure in group 1	506(15)
Occupation group 2	403(22)
>5 years of exposure in group 2	145(4.4)
Occupation group 3	95(5.3)
>5 years of exposure in group 3	27(0.8)
Occupation group 1: Working in agriculture, textile or food industry **Occupation group 2: Working in Mining and construction industry)** **Occupation group 3: Welders, firefighters, cleaners or exposed to chemicals and fumes during work**	

4.3.4 Respiratory symptoms

At least one respiratory symptom, usually present without having a cold, was reported by 40.7% [SE 3.1] of subjects, and the 70+ age group had the highest prevalence (60.6% [SE 4.3]). Respiratory symptoms that interfered with daily activities was reported by 8.4% [SE 1.6] of subjects. Usual cough was the most frequently reported symptom (19.5% [SE 1.7]), with the highest prevalence recorded in subjects aged 18-29 years (22.5% [SE2.7]. A chronic cough (lasting for more than 3 months per year) was reported by 2.4% [SE 0.02]. Production of usual sputum was reported by 14% [SE 1.9] and chronic production of sputum (for more than 3 months per year) was reported by 2.7% [SE 0.001]. Shortness of breath was reported by 18.7% [SE 0.9], and 38.7% [SE 3.5] of these subjects were unable to walk further than 100 yards because of breathing problems. A wheeze in the past 12 months in the absence of a cold was the least commonly reported symptom (4.9% [SE 1.2],

Table 4.5, Figure 4.3). Overall, females and participants aged 70+ tended to be more symptomatic when compared to other groups. However, those aged 60-69 had the highest prevalence of sputum production, wheeze and functional limitation due to breathing problems.

Participants aged ≥40 years tended to have a higher prevalence of any respiratory symptoms 42.2% [SE 2.1], wheeze and sputum production. However, the younger group, aged 18-39, had a higher prevalence of a cough, shortness of breath and functional limitation due to breathing problems (Table 4.6 and Figure 4.4). A small positive correlation was found between all respiratory symptoms ($p<0.05$, Pearson's r correlation <0.3).

Medically diagnosed respiratory disease was reported by 7.4% of the participants that contributed full data sets. Medically diagnosed asthma and COPD was reported by 6.4% and 7.4% of subjects respectively. Medically diagnosed COPD, chronic bronchitis or emphysema was reported by 1.7%.

Table 4.5 Age and gender stratified prevalence of respiratory symptoms among participants with complete core questionnaire

Definition of symptom	**Age group**	**Male (n=924) prevalence (SE)**	**Female (n=926) prevalence (SE)**	**Total (n=1850) prevalence (SE)**
Cough (do you usually cough when you don't have a cold?)	18-29	20.3 (2.3)	24.3 (3.2)	22.5 (2.7)
	30-39	18.9 (0.6)	18.3 (2.6)	18.5 (1.7)
	40-49	14 (2.7)	17.1 (3.1)	15.7 (1.1)
	50-59	18.6 (2.4)	16.5 (4.7)	17.7 (0.8)
	60-69	9.1 (1.3)	22.8 (0.5)	15.9 (0.6)
	70+	17 (5.2)	15.2 (3.4)	16.2 (2.6)
	Total	17.9 (0.8)	20.9 (2.6)	19.5 (1.7)
Sputum (do you usually bring up	18-29	14.2 (2.8)	12.7 (2.4)	13.4 (2.3)
	30-39	18.7 (3)	12.2 (5.3)	14.9 (4.4)
	40-49	9.7 (1.5)	13.8 (1.1)	11.9 (0.3)

phlegm from your chest?)	50-59	15.1 (3.3)	9.8 (4.7)	12.8 (0.7)
	60-69	13.3 (5.3)	20.7 (4.8)	16.9 (4.8)
	70+	22.4 (8.3)	25.2 (0.1)	23.7 (2.7)
	Total	14.7 (2.1)	13.4 (2.1)	14 (1.9)
Wheeze (have you had wheezing / whistling in your chest at any point in past 12 months, in the absence of a cold)	18-29	5.1 (2.2)	3.8 (1.1)	4.4 (1.1)
	30-39	6.5 (0.4)	3.9 (2.3)	5 (1.4)
	40-49	2.2 (2.6)	5.6 (1.5)	4 (2)
	50-59	4.6 (0.1)	7.8 (2.7)	6 (1.2)
	60-69	6.1 (1.4)	10.3 (4.6)	8.1 (2.9)
	70+	7.4 (4.1)	2.6 (1.7)	5.3 (2.7)
	Total	5 (1.2)	4.7 (1.4)	4.9 (1.2)
Currently, do you have shortness of breath when hurrying on the level or walking up a slight hill?)	18-29	15.2 (1.4)	23.3 (0.7)	19.5 (0.5)
	30-39	18.3 (2.2)	17.7 (6.6)	17.9 (3.7)
	40-49	12.3 (1.2)	22.8 (2.9)	17.1 (1.9)
	50-59	15.5 (1.6)	18.9 (2.5)	16.9 (2)
	60-69	16.6 (1.7)	27 (9.1)	20.8 (3.8)
	70+	10.2 (4.2)	42.8 (16.5)	22.7 (7.2)
	Total	15.2 (0.9)	22 (2.1)	18.7 (0.9)
Any respiratory symptom (any of usual cough, usual sputum, wheeze without cold in the last 12 months, exertional breathlessness as above)	18-29	38.4 (4.5)	44.5 (1.8)	41.7 (2.8)
	30-39	40.3 (2.6)	35.1 (7.3)	37.2 (5.5)
	40-49	27.8 (2.8)	45.2 (5.5)	36.2 (3.8)
	50-59	37.6 (1.4)	41.8 (6.4)	39.4 (2.3)
	60-69	34.4 (2.9)	65.1 (2.9)	49 (0.9)
	70+	52.1 (3.7)	72.4 (16)	60.6 (4.3)
	Total	37.3 (2.8)	43.9 (3.6)	40.7 (3.1)
Functional limitation (have breathing problems interfered with your usual daily activities)	18-29	5.8 (0.1)	11.9 (3.4)	9.1 (2)
	30-39	8.1 (0.9)	8.8 (3.2)	8.5 (1.9)
	40-49	4.9 (1.6)	8 (3.2)	6.6 (2.6)
	50-59	8.1 (1.9)	6.4 (4.9)	7.4 (3.0)
	60-69	10.5 (1.3)	10.4 (3.6)	10.4 (2.4)
	70+	7.2 (1.8)	2.6 (1.7)	5.2 (1.5)
	Total	6.9 (0.7)	9.8 (2.6)	8.4 (1.6)

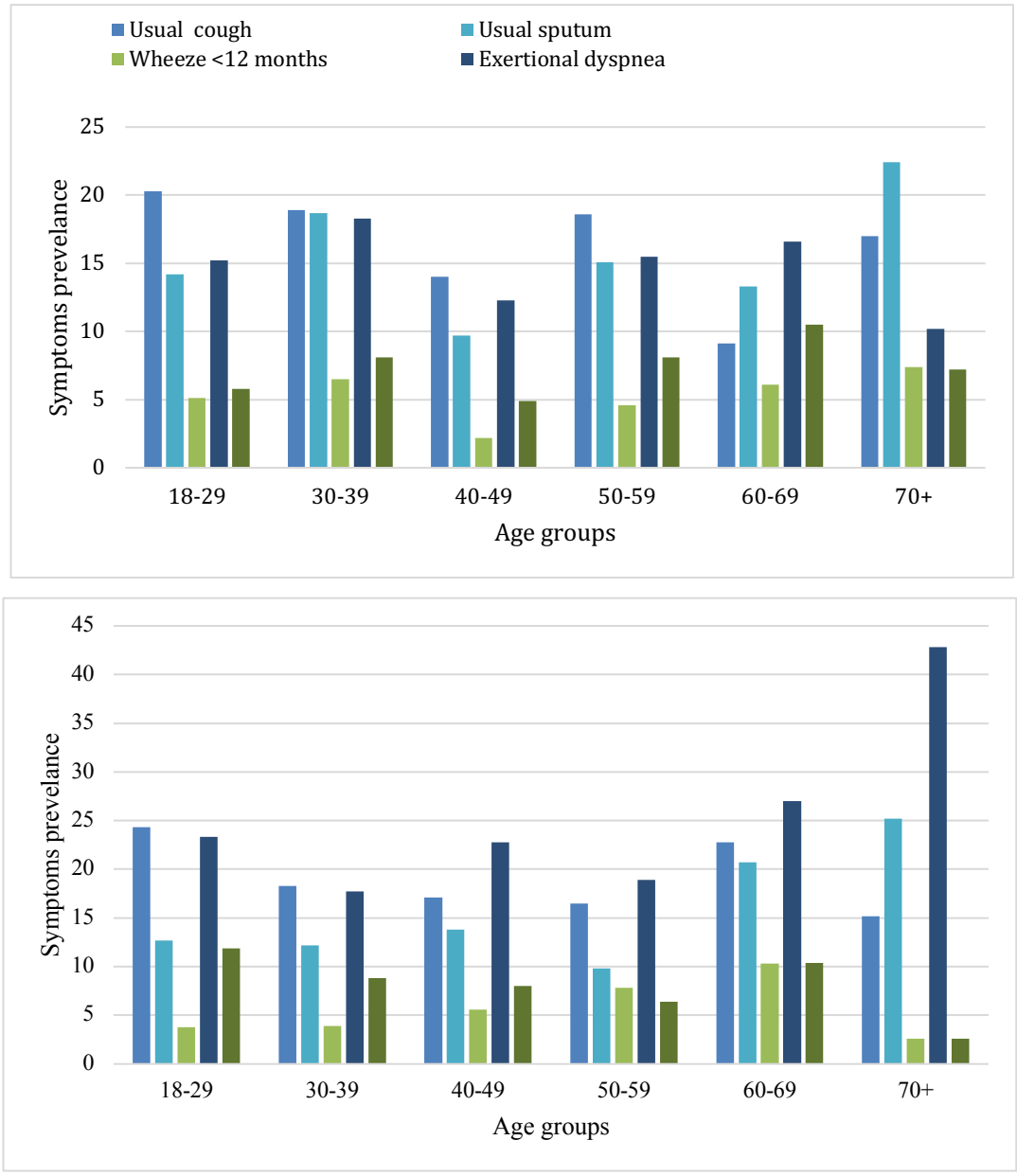


Figure 4.3 Prevalence of respiratory symptoms among the study participants. The upper bar represents symptom prevalence in men (n=924) and the lower bar represents symptom prevalence in women (n=922).

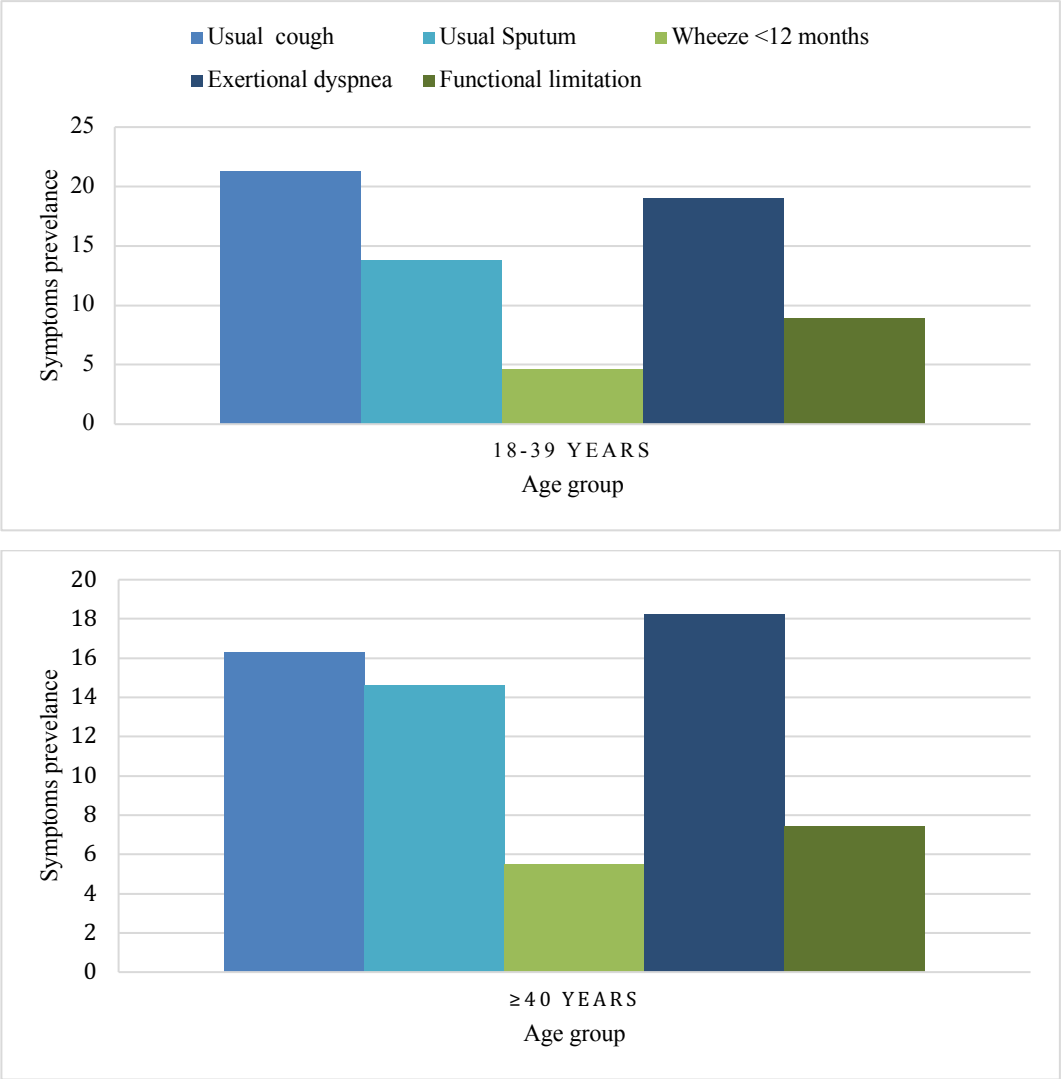


Figure 4.4 Prevalence of respiratory symptoms among the study participants. The upper bar represents symptom prevalence in younger groups (18-39) years (n= 1,917) and the lower bar represents older groups ≥40 years (n= 1,362).

Table 4.6 Age and gender stratified prevalence of respiratory symptoms among participants with complete core questionnaire (<40 years and ≥40 years old)

Definition of restriction	Age group	Male (n=924) prevalence (SE)	Female (n=922) prevalence (SE)	Total (n=1838) prevalence (SE)
Cough (do you usually cough when you don't have a cold?)	18-39	19.9 (1.8)	22.4 (2.9)	21.3 (2.4)
	≥40	14.8 (1.5)	17.8 (2)	16.3 (0.2)
	Total	17.9 (0.8)	20.9 (2.6)	19.5 (1.7)
Sputum (do you usually bring up phlegm from your chest?)	18-39	15.4 (2.8)	12.6 (3.3)	13.8 (3)
	≥40	13.7 (1.1)	15.5 (1.1)	14.6 (0.8)
	Total	14.7 (2.1)	13.4 (2.1)	14 (1.9)
Wheeze (have you had wheezing / whistling in your chest at any point in past 12m, in the absence of a cold?)	18-39	5.5 (1.6)	3.9 (1.2)	4.6 (1.2)
	≥40	4.4 (1.7)	6.7 (2.3)	5.5 (1.9)
	Total	5 (1.2)	4.7 (1.4)	4.9(1.2)
Do you have shortness of breath when hurrying on the level or walking up a slight hill?)	18-39	16 (1.6)	21.6 (2)	19 (0.8)
	≥40	13.8 (0.5)	24.1 (2.1)	18.2 (1.3)
	Total	15.2 (0.9)	22 (2.1)	18.7 (0.9)
Any respiratory symptom (any of cough, sputum, wheeze without cold, exertional breathlessness)	18-39	38.9 (3.9)	41.6 (3.5)	40.4 (3.6)
	≥40	34.8 (1.3)	50.9 (3.1)	42.2 (2.1)
	Total	37.3 (2.8)	43.9 (3.6)	40.7 (3.1)
Functional limitation (have breathing problems interfered with your usual daily activities?)	18-39	6.4 (0.9)	11 (3.1)	8.9 (1.9)
	≥40	7.2 (1.1)	7.5 (2.4)	7.4 (1.7)
	Total	6.9 (0.7)	9.8 (2.6)	8.4 (1.6)

4.3.5 Spirometry

4.3.5.1 Spirometry results based on GOLD definitions

GOLD stage 1 or higher COPD was seen in 3.4% (SE 0.7) of the total study population (3.9% [SE 0.4) of men and 3.1% [SE 1.5] of women). Subjects aged 70+ years and smokers of 20+ packs per year had the highest prevalence of GOLD stage 1 COPD (14.1% [SE 5.0] vs. 15% [SE 5.1] respectively) and the highest prevalence

of GOLD stage 2 or higher using the locally derived range (7.5% [SE 2] vs. 8% [SE 3.7] respectively). According to the NHANES reference range, 3% (SE 0.6) of the overall population had GOLD stage 2 or higher COPD (3.2% [SE 0.2] of men and 2.8% [SE 1.4] of women). Using the locally derived reference range, 2% (SE 0.6) of the total study population had GOLD stage 2 or higher COPD (1.7% [SE 0.07] of men and 2.3% [SE 1.1] of women). Similarly, participants with a smoking history of 20+ packs per year had the highest prevalence of GOLD stage 2 or higher using NHANES (12% [4.1]). However, subjects aged 60–69 years had the highest prevalence of GOLD stage 2 or higher COPD using NHANES (11.9% [SE 5.2]) (Table 4.7 and Figure 4.5).

Table 4.7 Age and gender stratified prevalence estimates for abnormal spirometry, among participant with full spirometry data using GOLD definition

Spirometric definition (Reference range)	**Age group (n=1,307)**	**Male (n= 651) Prevalence (SE)**	**Female (n=657) Prevalence (SE)**	**Total (n= 1308) Prevalence (SE)**
Post bronchodilator obstruction FEV1/FVC Ratio<70% (GOLD stage 1 or higher)	18-29	0.5 (0.4)	0.6 (0.7)	0.55 (0.34)
	30-39	1.1 (0.9)	3.5 (2.4)	2.5 (1.0)
	40-49	4.3 (1.7)	4.8 (2.1)	4.6 (0.32)
	50-59	6.5 (2.5)	5.8 (1.4)	6.2 (1.4)
	60-69	14.6 (2.4)	10.6 (7.1)	12.6 (4.7)
	70+	23.8 (7.8)	3.5 (1.9)	14.1 (5.0)
	Total	3.9 (0.3)	3.1 (1.5)	3.4 (0.8)
Post bronchodilator moderate to severe obstruction FEV1/FVC ratio<70% and FEV1 <80% predicted (NHANES) GOLD stage 2 or higher	18-29	0.5 (0.5)	0.5 (0.6)	0.6 (0.2)
	30-39	1.1 (0.9)	3.5 (2.4)	2.5 (1.0)
	40-49	3.6 (1.1)	4 (1.6)	3.8 (7.6)
	50-59	6.5 (2.5)	5.8 (1.4)	6.2 (1.4)
	60-69	13.2 (3.4)	10.6 (7.1)	11.9 (5.2)
	70+	14.0 (5.1)	3.5 (1.9)	9.1 (3.8)
	Total	3.2 (0.2)	2.8 (1.4)	3.0 (0.6)

Post bronchodilator moderate to severe obstruction FEV1/FVC ratio<70% and FEV1 <80% predicted (Locally derived ref range)	18-29	0.5 (0.5)	0.6 (0.7)	0.5 (0.2)
	30-39	-	2.5 (1.8)	1.5(1)
	40-49	3.6 (1.1)	3.1 (1.1)	3.3 (0.4)
	50-59	1.2 (1.4)	4.5 (1.4)	2.6 (1.4)
	60-69	4.6 (1)	8.1 (5.8)	6.4 (3.2)
	70+	11.1 (2.3)	3.5 (1.9)	7.5 (2)
	Total	1.7 (0.1)	2.3 (1.1)	2 (0.6)

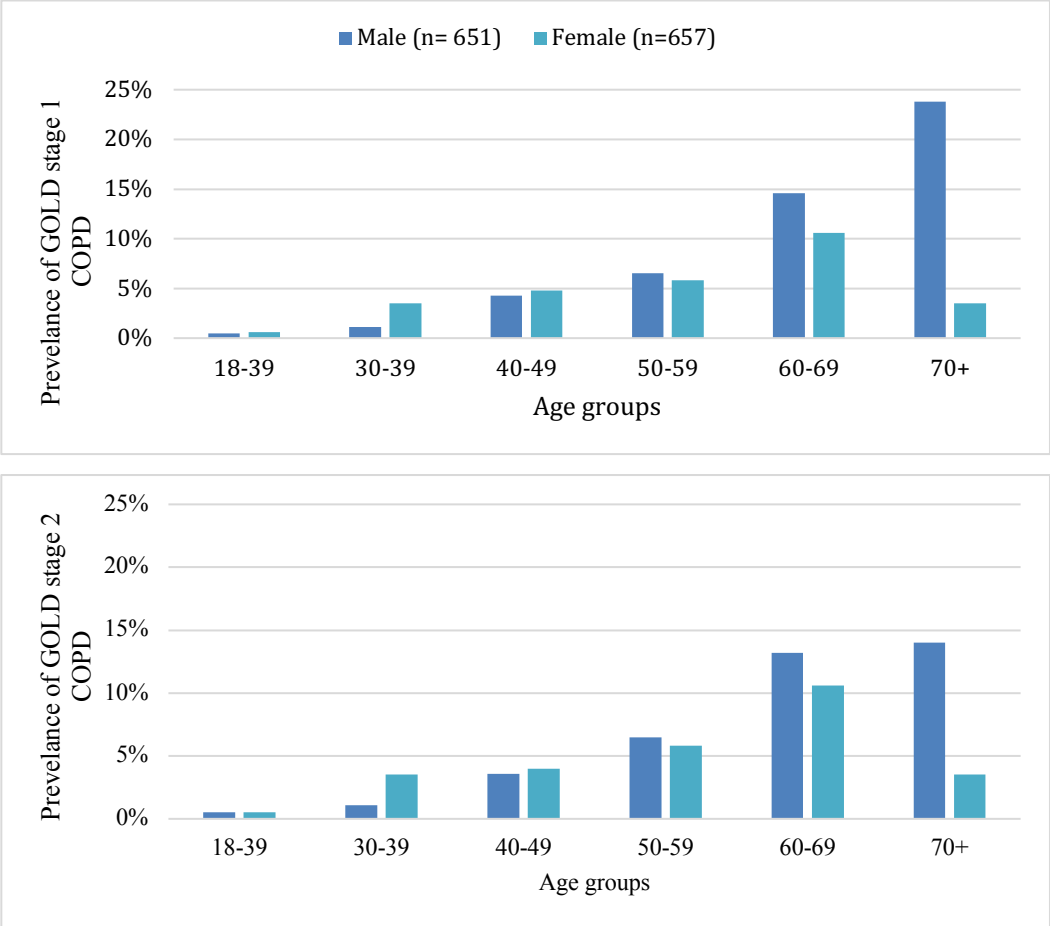


Figure 4.5 Estimated Population Prevalence of airway obstruction by age and sex using NHANES for the Sudanese population in subjects completing standard ATS spirometry (n=1308). The upper graph represents the prevalence of GOLD Stage 1 or higher COPD (Post-BD FEV1/FVC <0.7) and the lower graph represents the prevalence of GOLD Stage 2 or higher COPD (Post-BD FEV1/FVC < 0.7 and post-BD FEV1 < 80% predicted).

4.3.5.2 Spirometry results based on LLN definitions

Using LLN, COPD prevalence was 4.1% [SE 0.5] in the total population (3.1% [SE 0.5] in men and 4.8% [SE1.4] in women) using NHANES and was slightly lower using the locally derived range at 3.2% [SE 0.4] in total population (3.4 [SE0.6] in men and 3.1% [SE1.3] in women). The prevalence of modified stage 2 COPD or higher was 3.6% [SE 0.4] (2.75 [SE0.7] in men and 4.4% [SE 1.3] in women). Using the locally derived ranges, modified stage 2 COPD or higher was prevalent in 2.1% [SE 0.4] of the total population (2% [SE 0.5] in men and 1.9% [SE 1.1] in women). Subjects aged 60–69 years and subjects who smoked ≥20 years had the highest prevalence of modified stage 1 or higher and modified stage 2 or higher LLN-COPD (8.2% [SE2.3] vs. 7.1% [SE4.2]) and (7.6% [SE 2.7] vs. 4.1% [SE 2.5] respectively). Males with >20 packs of smoking exposure had the highest prevalence of modified stage 1 and 2 COPD using below LLN compared to other smoking groups (7% [SE 4.2] and 4.2% [SE 2.5]) - Tables 4.8, 4.9 and Figure 4.6).

Table 4.8 Age and gender stratified prevalence estimates for abnormal spirometry, among participants with full spirometry data using below LLN

Spirometric definition (reference range)	**Age group (n= 1,307)**	**Male (n= 651) Prevalence (SE)**	**Female (n=657) Prevalence (SE)**	**Total (n= 1308) Prevalence (SE)**
Prevalence of LLN Modified Stage 1 or higher COPD (Post-BD FEV1/FVC < LLN) by age and sex (NHANES Equations)	18-29	1.9 (0.4)	2.3 (1.3)	2.1 (0.6)
	30-39	2.1 (1.8)	8 (3.1)	5.7 (1)
	40-49	4.3 (1.7)	6.6 (3.2)	5.5 (1.1)
	50-59	2.1 (1.1)	5.8 (1.4)	3.6 (1.2)
	60-69	10.5 (4)	6 (4)	8.2 (2.3)
	70+	6.1 (2.6)	3.5 (1.9)	4.8 (0.9)
	Total	3.1 (0.5)	4.8 (1.4)	4.1 (0.5)

Estimated Population Prevalence of LLN Modified Stage 1 or higher COPD (Post-BD FEV1/FVC < LLN) by age and sex (locally derived ref range)	18-29	2.6 (0.8)	1.9 (1.6)	2.3 (0.8)
	30-39	2.1 (1.8	5.3 (1.5)	4 (0.1)
	40-49	4.3 (1.7)	4 (1.8)	4.2 (0.3)
	50-59	2.1 (1.2)	2.9 (2.1)	2.4(1.4)
	60-69	9.5 (4.7)	2.1 (2.1)	5.8 (1.1)
	70+	6.1 (2.6)	3.5 (1.9)	4.8 (0.9)
	Total	3.4 (0.6)	3.1 (1.3)	3.2 (0.4)
Prevalence of LLN Modified Stage 2 or higher COPD (Post-BD FEV1/FVC < LLN and post-BD FEV1 < 80% predicted) by age and sex (NHANES ref range)	18-29	1.4 (0.8)	1.6 (1.3)	1.5 (0.6)
	30-39	2.1 (1.8)	8 (3.1)	5.7 (1.1)
	40-49	3.6 (1.1)	5.7 (3.1)	4.7 (1.5)
	50-59	2.1 (1.1)	5.8 (1.4)	3.6 (1.2)
	60-69	9.1 (3.7)	6 (4)	7.6 (2.7)
	70+	6.1 (2.6)	3.4 (1.9)	4.8 (0.9)
	Total	2.7 (0.7)	4.4 (1.3)	3.6 (0.4)
Prevalence of LLN Modified Stage 2 or higher COPD (Post-BD FEV1/FVC < LLN and post-BD FEV1 < 80% predicted) by age and sex (locally derived ref range)	18-29	1.4 (0.8)	1.4 (1)	1.4 (0.4)
	30-39	1.1 (0.9)	2.5 (1.8)	1.9 (0.7)
	40-49	3.6 (1.1)	2.4 (0.8)	2.9 (0.1)
	50-59	1.2 (1.4)	1.6 (2)	1.6 (1.7)
	60-69	3.6 (1.1)	2.1 (2.2)	2.8 (0.9)
	70+	6.1 (2.6)	3.5 (1.9)	4.8 (0.9)
	Total	2 (0.5)	1.9 (1.1)	2.1 (0.4)

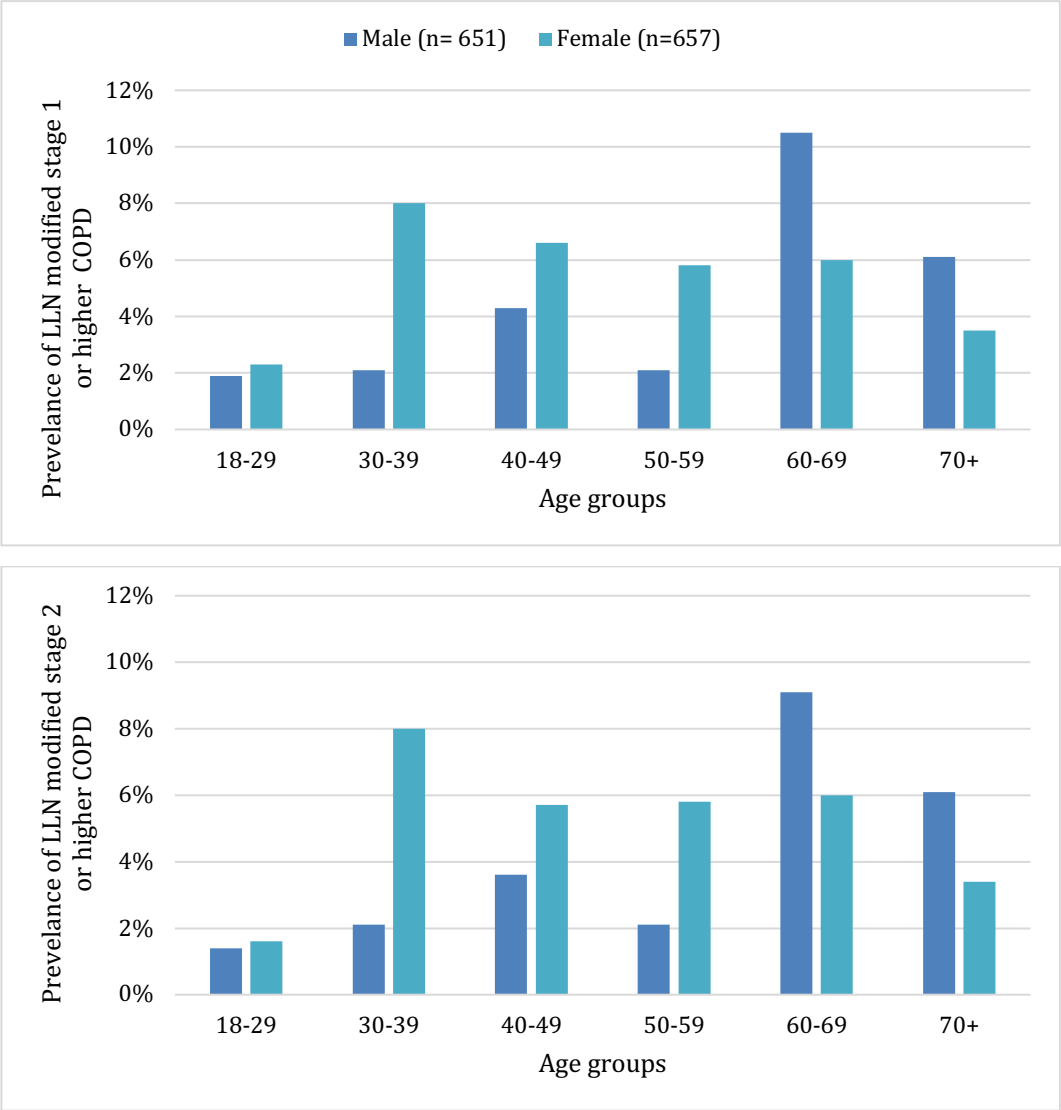


Figure 4.6 Estimated Population Prevalence of airway obstruction by age and sex using National Health and Nutrition Examination Survey reference ranges (NHANES) for the Sudanese population in subjects completing standard American Thoracic Society spirometry (n=1308). The upper graph represents the prevalence of LLN Modified Stage 1 or higher COPD (Post-BD FEV1/FVC < LLN) and the lower graph represents the prevalence of LLN Modified Stage 2 or higher COPD (Post-BD FEV1/FVC < LLN and post-BD FEV1 < 80% predicted).

Table 4.9 Estimated Population Prevalence (SE) of abnormal spirometry by pack years and sex

		Pack-years				
	Sex	**Never smokers**	**0-10**	**10-20**	**20+**	**Total**
Estimated Population Prevalence (SE) of GOLD Stage 1 or higher COPD	Male	3.5 (1.5)	2.4 (0.5)	8.1 (4)	15(5.1)	3.9 (0.4)
	Female	2.9 (1.4)	*	*	*	3 (1.5)
	Total	3.1 (1)	2.4 (0.5)	8.1 (4)	15(5.1)	3.4 (0.8)
Estimated Population Prevalence (SE) of GOLD Stage 2 or higher COPD	Male	2.8 (0.9)	2 (0.3)	8.1 (4)	12.2(4.1)	3.2 (0.2)
	Female	2.7 (1.2)	*	*	*	2.8 (1.4)
	Total	2.7 (0.6)	1.9 (0.3)	8.1 (4)	12.2(4.1)	3 (0.6)
Estimated Population Prevalence (SE) of LLN Modified Stage 1 or higher COPD	Male	3.1 (0.8)	2.3 (0.6)	3.5(3.4)	7(4.2)	3.1 (0.5)
	Female	4.7 (1.3)	*	*	*	4.8 (1.4)
	Total	4.2 (0.6)	2.2 (0.6)	3.5(3.4)	7(4.2)	4 (0.5)
Prevalence (SE) of LLN Modified Stage 2 or higher COPD	Male	2.6 (1.2)	2.3 (0.6)	3.5(3.4)	4.2(2.5)	2.7 (0.7)
	Female	4.3 (1.2)	*	*	*	4.4 (1.3)
	Total	3.7 (0.5)	2.2 (0.6)	3.5(3.4)	4.2(2.5)	3.6 (0.4)
*** No observation in this group**						

4.3.5.3 Airway reversibility

Airway reversibility was reported by 6.4% [SE 0.3] of the total population. Men tended to have more airway reversibility when compared with women (7.2% [SE 0.2] vs. 5.7% [0.5]). Airway obstruction defined using LLN persisted after use of a bronchodilator in 18.5% [SE 2.6] of subjects with reversibility. Prevalence was lower using GOLD definitions (15.1% [SE 2.4]) (Table 4.10).

Table 4.10 Age and gender stratified prevalence estimates for airway reversibility

Spirometric definition (Reference range)	**Age group (n= 1,307)**	**Male (n= 651) Prevalence (SE)**	**Female (n=657) Prevalence (SE)**	**Prevalence (SE) Total (n= 1308)**
Airway reversibility FEV1 increase ≥200ml and ≥12% following bronchodilator	18-29	3.3 (2)	3 (1.8)	3.1 (0.3)
	30-39	9.7 (5.7)	4.6 (2.1)	6.7 (2.1)
	40-49	7.5 (0.6)	7.3 (3.3)	7.3 (1.6)
	50-59	9.9 (4.8)	11.8 (3.3)	10.6 (3.8)
	60-69	12.6 (3.8)	11.2 (3.9)	11.9 (1.0)
	70+	12.9 (5)	15 (8.9)	13.9 (6.9)
	Total	7.2 (0.2)	5.7 (0.5)	6.4 (0.3)

4.3.5.4 Low FVC

A low FVC was more prevalent than obstruction in both sexes and in all age groups. Using the NHANES III, overall estimated prevalence was 53.8% [SE 2.7]. Low FVC was more common in women when compared with men (56.3% [SE4.3] vs. 50.9% [SE1.5]). Similar to the urban findings; respiratory symptoms were more common in those with reduced FVC; 53% (Phlegm 53% and shortness of breath 56%) however, no significance differences were observed (Table 4.11). Using the local reference range, a far lower prevalence estimate of 7.3% [SE1.3] was found (5.3% [SE 0.2] in men and 9.1% [SE 2.4] in women) (Table 4.12).

Table 4.11 Presence of respiratory symptoms in those with/without low FVC

Spirometric restriction	Abnormal FVC N(%)	Normal FVC N(%)	P-value
Cough	119(49.17)	123(50.83)	0.794
Phlegm	96(53.04)	85(46.96)	0.527
Wheeze	30(50.00)	30(50.00)	0.707
Shortness of breathe	107(56.02)	84(43.98)	0.127
Functional limitation	51(47.22)	57(52.78)	0.629
Any respiratory symptoms	244(52.93)	217(47.07)	0.794

Table 4.12 Age and gender stratified prevalence estimates for low FVC

Spirometric definition (Reference range)	Age group (n=1,307)	Male (n= 651) Prevalence (SE)	Female (n=657) Prevalence (SE)	Prevalence (SE) Total (n= 1308)
Restriction FEV1/FVC Ratio>0.7 AND FVC<80% predicted (NHANES ref range)	18-29	57.2 (1.3)	51.6 (5.3)	54.2 (3.6)
	30-39	49.5 (5.8)	57.7 (6.6)	54.4 (5.7)
	40-49	51.4 (3.8)	66.2 (1.6)	59.3 (3.1)
	50-59	47 (2.8)	62.6 (3.4)	53.6 (0.9)
	60-69	38 (3.4)	59.2 (2.8)	48.7 (3.3)
	70+	20.5 (5.2)	51.0 (6.9)	35.1 (5.2)
	Total	50.9 (1.5)	56.3 (4.3)	53.8 (2.7)
Restriction FEV1/FVC Ratio>0.7, AND FVC<80% predicted (Locally derived ref range)	18-29	5.3 (1.3)	8.9 (3.5)	7.3 (1.4)
	30-39	5.4 (0.4)	6.5 (2.1)	6.1 (1.3)
	40-49	2.5 (2.9)	9.5 (2.2)	6.2 (0.5)
	50-59	9.5 (0.5)	14.7 (6.9)	11.6 (3)
	60-69	1.5 (1.4)	13.4 (5.4)	7.6 (2.9)
	70+	8.9 (4.2)	7 (3.8)	8 (1.9)
	Total	5.3 (0.2)	9.1 (2.4)	7.3 (1.3)

4.3.5.5 Factors associated with respiratory symptoms

The 60-69 age group were less likely to have a cough (OR 0.53; 95% CI: 0.31-0.92) while years of education was significantly associated with having a cough (OR 1.02; 95% CI: 1.00-1.04). In bivariate analysis, sputum production was associated with having hypertension (OR 1.89; 95% CI: 1.34-2.68) though no association was identified after adjustment. Having more than 10 people in the household was protective against sputum production (OR 0.73; 95% CI: 0.58-0.92) in bivariate analysis, but no association was identified after adjustment. Being female resulted in the highest odds of having shortness of breath (OR 2.4; 95% CI: 1.6-3.2) in multivariate analysis. No association was identified with wheeze or any of the risk factors in both bivariate and multivariate analysis (Tables 4.13 and 4.14).

Having a wheeze was associated with COPD stage 1 and 2 using the GOLD definition (OR 3.7; 95% CI: 2.1-6.5 vs. OR 4.3; 95% CI: 1.9-9.5) while sputum production was significantly associated with modified stage 1 COPD using the local range and LLN definition (OR 1.1; 95% CI: 1.0-1.2).

Table 4.13 Bivariate associations between respiratory symptoms and risk factors

Variable	Usual Cough (n= 343/1,829)		Usual Sputum (n= 262/1837)		Exertional dyspnoea (n= 276/1,481)	
	Odds Ratio	**95% CI**	**Odds Ratio**	**95% CI**	**Odds Ratio**	**95% CI**
Age Group						
18-29	1	-	1	-	1	-
30-39	0.78*	0.61-1.0	1.13	0.60-2.11	0.9	0.27-3.06
40-49	0.64±	0.33-1.23	0.87	0.41-1.87	0.85	0.41-1.74
50-59	0.74±	0.47-1.17	0.95	0.42-2.12	0.84	0.41-1.74
60-69	0.65±	0.39-1.07	1.32	0.13-12.97	1.08	0.35-3.33
70+	0.67	0.18-2.46	2	0.80-5.01	1.21	0.24-6.16
Gender						
Male	1	-	1	-	1	-
Female	1.21±	0.78-1.88	0.9	0.46-1.77	1.57	0.83-2.98
Year of education	1.02±	0.98-1.05	1.01	0.96-1.06	1.01	0.96-1.06
Smoking						
Never	1	-	1	-	1	-
Ever smoked	1.29	0.38-4.37			1.28	0.49-3.33
Smoking Status						
Current smoker	1.38	0.37-5.18	1.73±	0.53- 5.62	1.4	0.37-5.30
Ex-smoker	1.18	0.39-3.63	1.29	0.30-5.55	1.13	0.75-1.71

Packs per year						
Never	1	-	1	-	1	-
0-10 packs year	1.15	0.26-5.09	1.08	0.46-2.56	1.11	0.36-3.46
≥10 packs years	1.66[±]	0.58-4.73	2.82	0.63-12.65	1.55[±]	3.07
BMI (kg/m^2)						
Underweight (BMI <18.5)	1.02	0.29-3.56	1.12	0.33-3.74		
Normal (18.5-25)	1	-	1	-	1	-
Overweight (25-30)	0.92[±]	0.80-1.06	1.14	0.52-2.49		
Obese (BMI>30)	0.95	0.38-2.35	1	0.34-2.89		
Self-reported TB						
No	1	-	1	-	1	-
Yes	0.79	0 - 406.68	4.48[±]	0.28-71.57	-	-
Reported Hypertension						
No	1	-	1	-	1	-
Yes	1.39	0.49- 3.92	1.89*	1.34-2.68		
Number of people living in house	0.96[±]	0.92-1.02	-	-	-	-
Any biomass fuel exposure						

No	1	-	1	-	1	-
Yes	1.38[±]	0.85-2.25	1.56[±]	0.93-2.62		
Working in a Farm						
No	1	-	1	-	1	-
Yes	-	-	1.11	0.47-2.59	0.79[±]	0.48-1.30
Working as welder						
No	1	-	1	-	1	-
Yes	1.16[±]	0.92-1.45	1.22[±]	0.94-1.59	1.11	0.38 -3.27
Current Mokken scale	**OR**	**P-value**	**OR**	**P-value**	**OR**	**P-value**
	1.02	0.564	1.02	0.701	1.06[±]	0.149
*** Indicates p<0.05; [±] indicates p<0.2**						

Table 4.14 Multivariate associations between respiratory symptoms and risk factors, all variables significant at level <0.2 are included

Variable	Usual Cough (n= 343/1,829)		Usual Sputum (n= 262 /1837)		Exertional dyspnoea (n= 276/1,481)	
	Odds Ratio	95% CI	Odds Ratio	95% CI	Odds Ratio	95% CI
Age Group						
18-29	1	-	1	-	1	-
30-39	0.67	0.39-1.14	0.9	0.39-2.04	0.77	0.24-2.42
40-49	0.52	0.24-1.14	0.65	0.25-1.64	0.76	0.40-1.45
50-59	0.67	0.43-1.06	0.75	0 .41-1.35	0.76	0.29-2.00
60-69	0.53*	0.31-0.92	0.91	0.16-5.11		
70+	0.66	0.22-2.03	1.38	0.58-3.34	1.04	0.27-4.04
Gender						
Male	1	-	1	-	1	-
Female	1.72	0.84-3.52			2.36*	1.67-3.33
Years of education	1.02*	1.00-1.04	-	-	-	-
Packs per year						
Never	1	-	1	-	1	-
0-10 packs year	1.4	0.17-11.88			1.95	0.74-5.16
≥10 packs years	2.99	0.88-10.12			2.28	0.64-8.12
BMI (kg/m^2)						

Underweight (BMI <18.5)	0.98	0.32-3.034			3.93	0 .12-129.57
Normal (18.5-25)			1	-	1	-
Overweight (25-30)	0.93	0.80-1.09				
Obese (BMI>30)	0.98	0.50-1.92				
Number of people living in house	0.97	0.88-1.06	-	-	-	-
Any biomass fuel exposure						
No	1	-	1	-	1	-
Yes	1.53	0.92-2.53	-	-	1.67	0.80-3.51
Work as welder						
No	1	-	1	-		
Yes	1.33	0.31-5.68	0.92	0.27-3.14		
Work in a Farm						
No	-	-	-	-	1	-
Yes	-	-	-	-	0.94	0.82-1.07
Current Mokken scale	**OR**	**P-value**	**OR**	**P-value**	**OR**	**P-value**
	-	-	-	-	1.06	0.231
***Indicates a P<0.05**						

4.3.5.6 Factors associated with post-bronchodilator airway obstruction defined by GOLD

The 70+ age group had the highest odds of having GOLD stage 1 or higher COPD using the NHANES range and GOLD stage 2 or higher COPD using the local reference range, as well as GOLD stage 2 or higher COPD ((OR 34.97; 95% CI: 4.70-257.48), (OR 13.07; 95% CI: 2.38-71.71), (OR 16.61; 95% CI: 3.48-79.28)) when compared to the 18-29 age group respectively. Years of education was also associated with GOLD stage 1 COPD and GOLD stage 2 or higher in bivariate analysis, while no association was identified after adjustment (Table 4.15 and 4.16). Participants who reported exposure to biomass fuels were less likely to have GOLD stage 2 or higher COPD using the local reference range (OR 0.7; 95% CI: 0.56-0.88). Those who had >5 years of occupational exposure working in agriculture, textile or food industry had higher odds of developing GOLD stage 1 or higher COPD (OR 2.08; 95% CI: 1.19-3.65) in bivariate analysis, while no association identified in multivariate analysis. No other association was identified between obstruction and any of the risk factors.

Table 4.15 Bivariate and multivariable associations of risk factors with Stage 1 or higher COPD defined using GOLD definitions and NHANESIII reference range (Post-BD FEV1/FVC < 0.7; n=95/1320)

Variable	Bivariate association		Multivariable association	
	Odds Ratio	95% CI	Odds Ratio	95% CI
Age Group				
18-29	1	-	1	-
30-39	4.61±	0 .56-38.27	4.07	0.29-58.02
40-49	8.61*	1.67-44.79	9.41*	2.28-38.87
50-59	11.82*	4.57-30.54	11.68*	5.88-23.20
60-69	25.86*	2.62-254.94	30.07*	2.16-417.89
70+	29.45*	5.69-152.33	34.97*	4.70-257.48
Gender				
Male	1	-	1	-
Female	0.76	0.07-7.72	0.83	0.03-20.24
Smoking				
Never	1	-	-	-
Ever smoked	1.53	0.15-15.17	-	-
Smoking Status				
Never	1	-	-	-
Current	0.9	0.04-22.97	-	-
Ex-smoker	2.23	0.17-28.87	-	-
Packs per year				
Never	1	-	1	-
0-10 packs year	0.77	0.12-4.93	0.83	0.09-7.43
≥10 packs years	3.76±	0.37-37.63	1.52	0.06-41.14
Years of education	1*	0 .87-0.98	1.03	0.95-1.10
Reported Hypertension				
No	1	-	1	-
Yes	2.18±	0.86-5.54	1.37	0.17-10.73
Reported Diabetes				
No	1	-	1	-
Yes	1.35	0.04-44.88		
BMI (kg/m2)				

Underweight (BMI<18.5)	0.9	0.25-3.27	-	-
Normal (BMI 18-25)	1	-	1	-
Overweight (BMI 25-30)	0.86	0.19-3.99	-	-
Obese (BMI >30)	1.2	0.10-14.22	-	-
Number of people living in house	1.02	0.84-1.25	-	-
Any biomass fuel exposure				
No	1	-	1	-
Yes	1.33	0.68-2.61	-	-
Use of firewood in cooking >6 months				
No			1	-
Yes	0.76	0.15-3.80		
Occupation group 1	1.62	0.19-13.22	-	-
>5 years of exposure in group1	2.08*	1.19-3.65	0.75	0.34-1.65
Occupation group 2	0.68	0 .14-3.39	-	-
>5 years of exposure in group1	1.42	0.61-3.31	-	-
Occupation group 3	0.55	0.12-2.47	-	-
>5 years of exposure in group1	2.03	0.46-9.05	-	-
Working in Farming				
No	1	-	1	-
Yes	1.57	0.19-12.73	-	-
Current Mokken scale	**OR**	**P-value**	**OR**	**P-value**
	0.94	0.514	-	-

***indicates p<0.05; ± indicates p<0.2**

Occupation group 1: Working in agriculture, textile or food industry

Occupation group 2: Working in Mining and construction industry)

Occupation group 3: Welders, firefighters, cleaners or exposed to chemicals during work

Table 4.16 Bivariate and multivariable associations of risk factors with moderate-severe post bronchodilator airway obstruction, defined using GOLD and NHANES III reference range (FEV1/FVC ratio <0.7 and FEV1 <80% predicted) n=52/1320

Variable	Bivariate association		Multivariable association	
	Odds Ratio	95% CI	Odds Ratio	95% CI
Age Group				
18-29	1	-	1	-
30-39	4.62	0.56-38.27	3.13	0.08-126.3
40-49	7.04±	0.85-58.44	7.39*	1.20-45.40
50-59	11.82*	4.57-30.54	10.94*	3.69-32.40
60-69	24.26*	1.91-308.76	26.25	0.90-766.6
70+	17.75*	8.24-38.24	16.61*	3.48-79.28
Gender				
Male	1	-	1	-
Female	0.88	0.08-10.06	1.24	0.06-26.96
Smoking				
Never	1	-	-	-
Ever smoked	1.49	0.21-10.67	-	-
Smoking Status				
Never	1	-	-	-
Current	0.83	0 .07-9.78	-	-
Ex-smoker	2.22	0.24-20.62	-	-
Packs per year				
Never	1	-	1	-
0-10 packs year	0.68	0 .11-4.48	0.96	0.27-3.33
≥10 packs years	3.78±	0 .51-28.23	2.09	0.10-45.59
Years of education	1*	0.88-0.98	1	0.94-1.05
Reported Hypertension				
No	1	-	1	-
Yes	2.51±	0.82-7.61	1.07	0.13-8.48

Reported Diabetes				
No	1	-	1	-
Yes	1.54	0.06-43.10	-	-
BMI (kg/m2)				
Underweight (BMI<18.5)	1.07	0.33-3.46	-	-
Normal (BMI 18-25)	1	-	1	-
Overweight (BMI 25-30)	0.94	0.37-2.38	-	-
Obese (BMI >30)	1.29	0.21-7.98	-	-
Number of people living in house	1	0.62-1.60	-	-
Any biomass fuel exposure				
No	1	-	1	-
Yes	1.32±	0.74-2.36	0.69	0.25-1.87
Occupation group 1	1.62	0.20-13.22	-	-
>5 years of exposure in group 1	1.63±	0.88- 3.01	-	-
Occupation group 2	0.68	0.14-3.40	-	-
>5 years of exposure in group 2	1.34	0.54-3.34	-	-
Occupation group 3	0.55	0.12-2.47	-	-
>5 years of exposure in group 3	2.30	0.52-10.29	-	-
Working in Farming				
No	1	-	1	-
Yes			-	-
Current Mokken scale	**OR**	**P-value**	**OR**	**P-value**
	0.95	0.536	-	-

***indicates p<0.05; ± indicates p<0.2**

Occupation group 1: Working in agriculture, textile or food industry

Occupation group 2: Working in Mining and construction industry)

Occupation group 3: Welders, firefighters, cleaners or exposed to chemicals and fumes during work

4.3.5.7 Factors associated with post-bronchodilator airway obstruction defined by LLN

Those aged 60-69 had the highest odds of having stage 2 COPD or higher using the local reference range (OR 2.07, 95% CI 1.13-3.82). Participants with a higher educational level were less likely to have stage 1 COPD or higher (OR 0.50, 95% CI 0.27-0.93), as were those who used firewood for water heating (OR 0.32, 95% CI 0.13-0.77). None of the other risk factors were associated with any obstruction defined using LLN (Table 4.17 and 4.18). Using the Mokken scale, no association was identified between participants' socioeconomic status and developing COPD using LLN and GOLD definitions. Additionally, no association was identified with occupational groups and obstruction.

Table 4.17 Bivariate and multivariable associations of risk factors with Modified Stage 1 or higher COPD defined using the NHANES III reference range (Post-BD FEV1/FVC < LLN; n=61/1320)

Variable	**Bivariate association**		**Multivariable association**	
	Odds Ratio	**95% CI**	**Odds Ratio**	**95% CI**
Age Group				
18-29	1	-	1	-
30-39	2.80±	0.57-13.86	2.07	0.59-7.35
40-49	2.70±	0.34-21.62	2.53	0.32-19.79
50-59	1.75	0.30-10.21	1.25	0.12-12.83
60-69	4.16±	0.73-23.84	3.65	0.73-18.24
70+	2.35	0.31-18.02	1.7	0.12-24.35
Gender				
Male	1	-	1	-
Female	1.58	0.21-11.96	1.52	0.26-8.67
Level of education				
None	1	-	1	-
Primary school	0.93	0.21-4.19	1.4	0.03-59.02
Middle school	0.75	0.30-1.87	1.17	0.02-56.68
High school or above	0.50*	0.27-0.93	1	0.01-157.5
Reported Hypertension				

No	1	-	1	-
Yes	1.04	0.19-5.58	-	-
Reported Diabetes				
No	1	-	1	-
Yes	1.13	0.04-30.66	-	-
BMI (kg/m2)				
Underweight (BMI<18.5)	1.81	0.37-8.86		
Normal (BMI 18-25)	1	-	1	-
Overweight (BMI 25-30)	1.2	0.60-2.38	-	-
Obese (BMI >30)	1.58	0.13-19.78	-	-
Smoking Status				
Never	1	-	1	-
Ever smoked	0.73	0.15-3.49	-	-
Smoking Status				
Never	1	-	1	-
Current	0.39	0.01-14.27	-	-
Ex-smoker	1.11	0.14-9.04	-	-
Smoking packs years				
0-10 Years	0.52	0.08-3.55	-	-
≥ 10 Years	1.16	0.23-5.92	-	-
Number of people living in house	1.04	0.94-1.14	-	-
Any biomass fuel exposure				
No	1	-	1	-
Yes	1.55	0.24-10.19	-	-
Use of firewood in cooking >6 month				
No	1	-	1	-
Yes	0.53±	0.16-1.80	0.61	0.09-3.96
Household used wood to heat water				
No	1	-	1	-
Yes	0.32*	0.13-0.77	0.47	0.12-1.83
Occupation group 1	1.16	0.12-10.95	-	-
>5 years of exposure in group1	1.35	0.76-2.40	-	-

Occupation group 2	0.56	0.13-2.41	-	-
>5 years of exposure in group2	1.02	0.38-2.72	-	-
Occupation group 3	1.06	0.16-7.23	-	-
>5 years of exposure in group3	1.72	0.39-7.62	-	-
Working in Farming				
No	1	-	1	-
Yes	1.2	0.14-10.68		
Current Mokken scale	**OR**	**P-value**	**OR**	**P-value**
	0.89	0.220	-	-

***indicates p<0.05; ± indicates p<0.2**

Occupation group 1: Working in agriculture, textile or food industry

Occupation group 2: Working in Mining and construction industry)

Occupation group 3: Welders, firefighters, cleaners or exposed to chemicals and fumes during work

Table 4.18 Bivariate and multivariable associations of risk factors with Modified Stage 2 or higher COPD defined using NHANES III reference range (Post-BD FEV1/FVC < LLN and post-BD FEV1 < 80% predicted; n=55/1320)

Variable	**Bivariate association**		**Multivariable association**	
	Odds Ratio	**95% CI**	**Odds Ratio**	**95% CI**
Age Group				
18-29	1	-	1	-
30-39	3.89±	0.53-28.58	2.99	0.57-15.74
40-49	3.18	0.18- 55.31	3.01	0.17-53.70
50-59	2.42	0.29-20.59	2.28	0.31-16.73
60-69	5.26±	0.60-46.36	4.93	0.84-28.81
70+	0.7±	0.29-36.58	2.78	0.19-40.16
Gender				
Male	1	-	1	-
Female	1.66	0.14-19.10	1.64	0.20-13.28
Level of education				
None	1	-	1	-
Primary school	0.85	0.36-2.00	1.21	0.33-4.45

Middle school	0.86	0.54-1.36	1.25	0.77-2.01
High school or above	0.54±	0.18-1.62	1.03	0.48-2.18
Reported Hypertension				
No	1	-	1	-
Yes	1.18	0.23-6.00	-	-
Reported Diabetes				
No	1	-	1	-
Yes	1.28	0.05-36.21	-	-
BMI (kg/m2)			-	-
Underweight (BMI<18.5)	1.73	0.23-12.93	-	-
Normal (BMI 18-25)	1	-	1	-
Overweight (BMI 25-30)	1.26	0.40-3.96	-	-
Obese (BMI >30)	1.67	0.13-21.67	-	-
Smoking Status				
Never	1	-	1	-
Ever smoked	0.73	0.15-3.48	-	-
Smoking Status				
Never	1	-	1	-
Current	0.31	0.02-6.50	-	-
Ex-smoker	1.25	0.14-11.37	-	-
Smoking packs years				
0-10 Years	0.59	0 .10-3.66	-	-
≥ 10 Years	1.02	0.14-7.58	-	-
Number of people living in house	1.03	0.86-1.23	-	-
Any biomass fuel exposure				
No	1	-	1	-
Yes	1.5	0.34-6.55	-	-
Use of firewood in cooking >6 months				
No	1	-	1	-
Yes	0.56±	0.23-1.33	0.64	0.17-2.38
Used wood to heat water				
No	1	-	1	-
Yes				

Occupation group 1	1.17	0.07-19.16	-	-
>5 years of exposure in group1	1.27	0.69-2.35	-	-
Occupation group 2	0.65	0.16-2.64	-	-
>5 years of exposure in group1	1.16	0.43-3.10	-	-
Occupation group 3	1.2	0.19-7.75	-	-
>5 years of exposure in group1	1.93	0.43-8.61	-	-
Working in Farming			-	-
No	1	-	1	-
Yes	1.21	0.08-19.02	-	-
Current Mokken scale	**OR**	**P-value**	**OR**	**P-value**
	0.90	0.202	-	-

***indicates p<0.05; ± indicates p<0.2**

Occupation group 1: Working in agriculture, textile or food industry

Occupation group 2: Working in Mining and construction industry)

Occupation group 3: Welders, firefighters, cleaners or exposed to chemicals and fumes during work

4.3.5.8 Factors associated with low FVC

Being underweight had the highest odds of having low FVC using NHANES III reference ranges in both bivariate and multivariate analysis (OR 3.07; 95% CI: 2.24-4.20). Being aged 60-69 was protective against low FVC using NHANES III (OR 0.80; 95% CI: 0.66-0.97) in bivariate analysis, though no association was identified after adjustment. Moreover, participants who had smoked for more than 20 pack-years were less likely to have low FVC in both bivariate and multivariate analysis (OR 0.33; 95% CI: 0.13-0.82). In bivariate analysis, using biomass fuels for cooking for more than 6 months produced higher odds of having a low FVC (OR 1.19; 95% CI: 1.01-1.39). No association was identified after adjustment. No association was identified between socioeconomic status based on the Mokken scale and spirometric restriction (Table 4.19). Using the local reference range, no association was identified between low FVC and any of the risk factors.

Table 4.19 Bivariate and multivariate associations of risk factors with low FVC, defined using NHANES III reference range (FEV1/FVC ratio >0.70 and FVC <80% predicted; n=713/1320)

Variable	Bivariate association		Multivariable association	
	Odds Ratio	95% CI	Odds Ratio	95% CI
Age Group				
18-29	1	-	1	-
30-39	1.01	0.64-1.60	1.1	0.63-1.92
40-49	1.23	0.54-2.79	1.44	0.79-2.62
50-59	0.98	0.61-1.56	1.17	0.59-2.31
60-69	0.8*	0.66-0.97	0.86	0.42-1.74
70+	0.46±	0.09-2.23	0.53	0.12- 2.54
Gender				
Male	1	-	1	-
Female	1.24	0.65-2.39	1.14	0.63- 2.05
Level of education				
None	1	-	1	-
Primary school	0.88	0.11-6.90	-	-
Middle school	1.22	0.42-3.52	-	-
High school or above	1.01	0.31-3.24	-	-
Reported Hypertension				
No	1	-	1	-
Yes	1.08	0.73-1.62	-	-
Reported Diabetes				
No	1	-	1	-
Yes	1.02	0.52-2.03	-	-
BMI (kg/m2)			-	-
Underweight (BMI<18.5)	2.95*	2.30-3.76	3.07*	2.24-4.20
Normal (BMI 18-25)	1	-	1	-
Overweight (BMI 25-30)	0.97	0.48-1.96	0.89	0.63-1.23
Obese (BMI >30)	1.14±	0.96-1.36	1.04	0.75-1.43
Smoking Status				
Never	1	-	1	-

Ever smoked	0.79±	0.37-1.38	-	-
Smoking Status				
Never	1	-	1	-
Current	0.91	0.34-2.40	-	-
Ex-smoker	0.56±	0.31-1.00	-	-
Smoking packs years				
0-10 Years	0.82	0.29-2.28	0.8	0.30-2.10
10-20 Years	0.75±	0.18-3.16	0.81	0.21-3.20
>=20 Years	0.29*	0.11-0.80	0.33*	0 .13-0.82
Number of people living in house	0.99	0.95-1.03	-	-
Any biomass fuel exposure				
No	1	-	1	-
Yes	1.19*	1.01-1.39	1.3	0.91-1.86
Occupation group 1	0.85±	0.62-1.15	2.77	0.72-10.56
>5 years of exposure in group1	0.83	0.65-1.07		
Occupation group 2	0.79	0.44-1.40	-	-
>5 years of exposure in group1	0.56±	0.39-0.89		
Occupation group 3	0.8	0.19-3.39	-	-
>5 years of exposure in group1	0.58	0.23-1.41		
Working in Farming			-	-
No	1	-	1	-
Yes	1.22±	0.85-1.76	0.34	0.06-1.91
Current Mokken scale	**OR**	**P-value**	**OR**	**P-vlaue**
	1.01	0.667	-	-

***indicates p<0.05; ± indicates p<0.2**

Occupation group 1: Working in agriculture, textile or food industry

Occupation group 2: Working in Mining and construction industry)

Occupation group 3: Welders, firefighters, cleaners or exposed to chemicals and fumes during work

4.3.5.9 Spirometry and age

Post-bronchodilator obstruction using GOLD (Stage 1 COPD) was prevalent in 7.7% [SE 1.8] of those aged ≥40 vs. 1.2% [SE 0.4] of those aged 18-39. While GOLD stage 2 or higher COPD was prevalent in 6.6% [SE 1.3] of subjects in the ≥40 group vs. 1.1% [SE 0.4] in the 18-39 group, those in the older group had higher odds of developing stage 1 and 2 COPD (OR 7.12; 95% CI: 4.38-11.58 vs. OR 6.03; 95% CI: 3.09-11.77).

Similarly, using the LLN definition, subjects in the older group had higher estimates of modified stage 1 COPD or higher (5.5% [SE 0.8] and 4.1% [0.8]) and stage 2 or higher (5% [SE 0.6] and 2.7% [SE 0.5]) using local and NHANES III reference range respectively. No association was identified between COPD and age using LLN.
Airway reversibility scores were higher in those aged ≥40 when compared with those aged 18-39 (10% [SE 0.7] vs. 4.3% [SE 0.6] respectively) in both men and women, although subjects in the younger group had a higher prevalence of low FVC (54.3% [SE 4.2] vs. 52.7% [SE0.09]) (Table 4.20).

Table 4.20 Age and gender stratified prevalence estimates for abnormal spirometry, among participants with full spirometry data (those aged ≥40 vs. those aged 18-39)

Spirometric definition (Reference range)	Age group (n= 1,307)	Male (n= 651)	Female (n=657)	Total (n=1308)
		Prevalence (SE)	Prevalence (SE)	Prevalence (SE)
Post bronchodilator obstruction FEV1/FVC Ratio <70% (NHANES)	18-39	0.7% (0.6)	1.6% (1.3)	1.2% (0.4)
	≥40	9.4% (1.8)	6% (1.9)	7.7 (1.7)
	Total	3.9% (0.4)	3% (1.5)	3.4% (0.8)
Post bronchodilator moderate to severe obstruction FEV1/FVC ratio <70% AND FEV1 <80% predicted (NHANES)	18-39	0.7% (0.6)	1.6% (1.3)	1.2% (0.4)
	≥ 40	7.6% (1.2)	5.7% (1.5)	6.6% (1.3)
	Total	3.2% (0.2)	2.8% (1.4)	3% (0.6)
Post bronchodilator moderate to severe obstruction FEV1/FVC ratio <70% AND FEV1 <80% predicted (Locally derived)	18-39	0.4% (0.3)	1.2% (1)	0.9% (0.4)
	≥40	4% (0.9)	4.5% (1.1)	4.3% (1)
	Total	1.7% (0.07)	2.3% (1.1)	2% (0.6)
Prevalence of LLN Modified Stage 1 or higher COPD (Post-BD FEV1/FVC < LLN) by age and sex (NHANES)	18-39	1.9% (0.8)	4.3% (1.7)	3.2% (0.6)
	≥40	5.1% (0.6)	6% (1.1)	5.5% (0.8)
	Total	3.1% (0.5)	4.8% (1.4)	4% (0.5)
Prevalence of LLN Modified Stage 1 or higher COPD (Post-BD FEV1/FVC < LLN) by age and sex (locally derived)	18-39	2.5% (1)	3.1% (1.6)	2.8% (0.6)
	≥40	4.9% (0.7)	3.3% (1)	4% (0.8)
	Total	3.4% (0.6)	3.1% (1.3)	3.2% (0.4)
Prevalence of LLN Modified Stage 2 or higher	18-39	1.6% (1.1)	3.8% (1.8)	2.8% (0.5)
	≥40	4.5% (0.8)	5.5% (0.6)	5% (0.6)

COPD ((Post-BD FEV1/FVC < LLN and post-BD FEV1 <80% predicted) by age and sex (NHANES)	Total	2.7% (0.7)	4.4% (1.3)	3.6% (0.4)
Prevalence of LLN Modified Stage 2 or higher COPD (Post-BD FEV1/FVC < LLN and post-BD FEV1 <80% predicted) by age and sex (locally derived)	18-39	1.3% (0.8)	1.7% (1.3)	1.5% (0.4)
	≥40	3.2% (0.4)	2.3% (0.8)	2.7% (0.5)
	Total	2% (0.5)	1.9% (1.1)	2% (0.4)
Airway reversibility FEV1 increase ≥200ml AND ≥12% following bronchodilator	18-39	5.2% (0.3)	3.6% (1)	4.3% (0.6)
	≥40	9.9% (0.8)	10% (0.6)	10% (0.7)
	Total	7.2% (2.2)	5.7% (0.5)	6.4% (0.3)
Restriction FEV1/FVC Ratio>0.7, AND FVC<80% predicted (NHANES)	18-39	55% (2.6)	53.7% (5.7)	54.3% (4.2)
	≥40	43.6% (1.8)	62.1% (0.5)	52.7% (1)
	Total	51% (1.5)	56.3% (4.3)	53.8% (2.7)
Restriction FEV1/FVC Ratio>0.7, AND FVC<80% predicted (Locally derived)	18-39	5.4% (0.8)	8.1% (2.6)	6.9% (1.2)
	≥40	5.2% (0.9)	11.1% (1.8)	8.1% (1.6)
	Total	5.3% (0.2)	9.1% (2.4)	7.3% (1.3)

4.3.5.10 Spirometry and location

Wad Medani locality had the highest estimates of airway obstruction using both GOLD and LLN definitions (4.8%) followed by Alkamleen locality (2.3% and 4.3% respectively), while Sharg-Algezira locality had the lowest estimates (2.3% and 3.4% respectively) as well as the lowest estimates of airway reversibility (4.9% [SE 0]). Alshnateer village, the only nomadic community included in this study, had the highest prevalence estimates using both LLN and GOLD definitions (25.1% [SE 0]). Subjects in Wad Medani locality had higher odds of developing stage 1 and 2 COPD using the GOLD definition when compared to Sharg-Algezira locality (OR 2.16; 95% CI: 2.16- 2.1 and OR 2.01; 95% CI: 2.01- 2.01) (Figure 4.6).

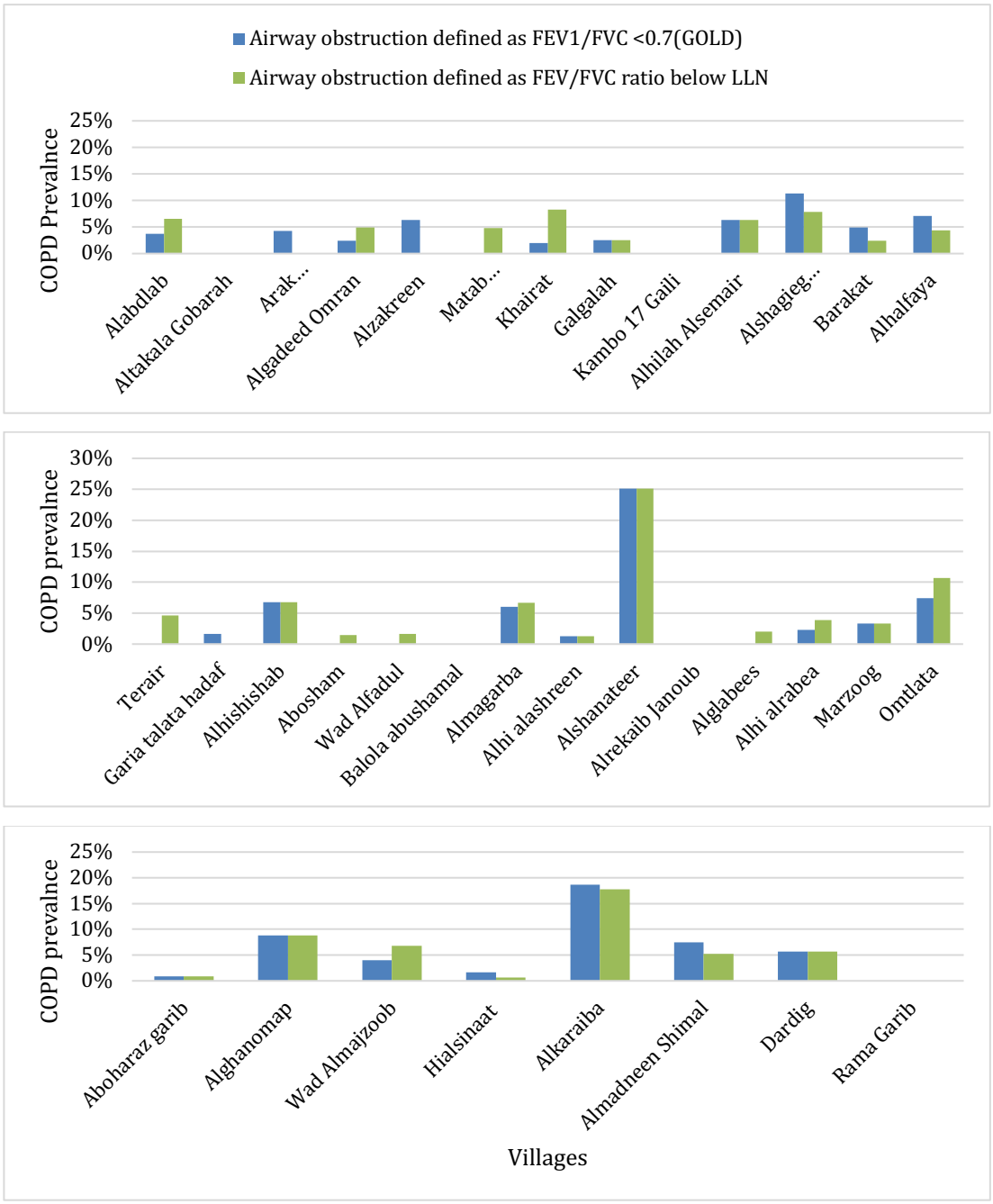


Figure 4.7 Prevalence of airway obstruction based on both GOLD and LLN by locality. The upper panel represents the villages of Alkamleen locality, followed by Sharg Algezira and Wad Medani. Prevalence of COPD by village is shown in each panel.

4.4 Discussion

This study aimed to investigate the prevalence of NCLD in rural Sudan in adults aged 18 and older. The main finding was that 3.4% of the overall study population returned results indicative of COPD using the GOLD definition, though this

percentage was slightly higher when using LLN (4.1%). In subjects aged 40 and older, the COPD prevalence estimate based on the GOLD definition was 7.7%, though this was lower when using LLN (5.5%). These findings are consistent with the urban study results discussed in the previous chapter, as well as literature suggesting that using a fixed ratio of FEV1/FVC <0.7 as a cut-off point (as in the GOLD definition) might result in an overestimation of COPD prevalence in the elderly population (185,186) while using a below-LLN ratio can mitigate the increase in COPD diagnoses related to age (6, 7).

Having 55% of the study population below 40 years will likely explain the lower prevalence of COPD in the overall population in the rural vs urban study. Previous studies in SSA reported similar findings (101).

Like the urban study, findings here suggest a high prevalence of low FVC (53.8%) in the overall population. Interestingly, higher estimates of low FVC were identified in study participants younger than 40. Overall, women tended to have a higher prevalence of low FVC when compared to men. As discussed in chapter 3, there is no justification for high prevalence estimates when using NHANES whilst having lower estimates using a local reference range derived from the healthy, non-smoking Sudanese adult population used in the previous study (188).

The finding that participants aged 40 and older had COPD prevalence of 7.7% when using a GOLD definition and 5.5% when using LLN is higher when compared to other studies conducted in rural SSA, such as in Rwanda (101). These prevalence rates were however far lower when compared with those found in Uganda (97), though this study reported high levels of exposure to cigarette smoke and biomass fuels. The COPD estimates in our study are higher when compared to a recent study from a major city in central Africa which reported the LLN-COPD prevalence at 2.4%, and the GOLD-COPD prevalence at 0.5% (189). As with the previous study discussed in chapter 3, BOLD studies from countries in SSA such as South Africa (36) and Nigeria (167) reported higher prevalence estimates than those found in this study. However, similar studies from MENA countries such as Saudi Arabia, Abu Dhabi, Tunisia (103) and Morocco (165) reported lower prevalence estimates, with the exception of Algeria (175).

Age was the main risk factor associated with COPD using LLN and GOLD definitions in this study. This is consistent with the previous study (discussed in chapter 3) and literature demonstrating that population aging is one of the primary COPD risk factors, especially in developing countries with lower levels of smoking (18, 19). The finding that years of education was associated with COPD when using the GOLD definition and that higher educational level was shown to be protective against COPD when using LLN is compatible with previous studies asserting that lower educational level is associated with COPD (18, 20, 21).

No association was observed between airway obstruction and increased numbers of inhabitants per household, or between airway obstruction and low socioeconomic status using the Mokken scale. This contrasts with other studies suggesting that crowded housing and low socioeconomic status may be associated with a progression of airflow limitation (22, 23). Having large houses and therefore additional space within the household may reduce the intensity of exposure to cigarette smoke and biomass fuels in this setting. However, the Mokken scale was used to assess the socioeconomic status of study participants and an association was found between airway obstruction and some socioeconomic status markers including home ownership and access to a private source of drinking water. This is consistent with previous studies asserting that poor education, low socioeconomic status and being underweight are COPD risk factors in developing countries (9, 18, 24, 25).

Reasons behind the high prevalence of low FVC were not explored in this study but previous research has reported similar findings (166). Literature suggested that unknown environmental factors, genetics, race, low birth weight, early exposure to biomass fuels and air pollution and poor diet are common factors associated with low FVC in developing countries (8, 10). These factors might also contribute to the high estimates of low FVC in this study, as the strongest risk factor for low FVC was being under weight.

The negative association found between biomass exposure and moderate to severe obstruction using local reference range as well as a negative association between the use of firewood for water heating and any obstruction using LLN is contrasting

previous studies. Conversely, this might be a random association as only 0.02% of participants with moderate to severe obstruction using local reference range were exposed to biomass fuel and only 0.04% of participants with any obstruction used firewood for water heating.

On the other hand, no association was identified between the use of biomass fuels and low FVC. However, the high prevalence of respiratory symptoms and the high occurrence of low FVC found in this study might be explained by the high percentage of subjects (48%) who had exposure to biomass fuels for 6 months or more (181), as well as exposure to other environmental factors as a result of a living in poor communities (nine of 35 villages were "Cambos" – a rural, mixed-composition, displaced community – while one was nomadic). In addition, childhood respiratory infections might possibly contribute to this high prevalence having pneumonia ranked as the second cause of hospitalisation in Sudan (26). The association between being female and shortness of breath might be a result of exposure to biomass fuels in these poor settings. There were associations between sputum production and low socioeconomic status, and between cough and poor educational level, while higher socioeconomic status was a factor in preventing lung restriction. This is consistent with previous studies (36,166,188).

Asthma and other respiratory diseases might be prevalent in Gezira state as medically diagnosed asthma was reported by 6.4% of the study population, the prevalence of airway reversibility was 6.4% and a high prevalence of a cough, shortness of breath and functional limitations was reported by younger age groups of (18-39). The previous study conducted in Gezira state suggested that asthma prevalence in school children aged 13-14 was 9-12% (190) and the ISAAC study reported a prevalence of 5% in rural and 12% in urban Sudan(191). Other studies in SSA, from rural Tanzania and Cameroon, reported a higher prevalence (192), though these studies targeted children rather than adults.

In this study, an association was observed between airflow obstruction defined by GOLD and occupational exposure for more than 5 years only for those working in agriculture, textile and food industry. As found in the urban study from Khartoum, farming was the most frequently reported occupation.

Having the highest prevalence estimates of obstruction, low FVC and airway reversibility in one locality might be due to the more urban settings of the locality when compared to other study localities and because 40.2% of the total current smokers studied lived in this locality (94). However, a high prevalence of COPD in Alshnateer village might be explained by the factors associated to nomadic life and poverty (151). In this village, 75% of participating subjects reported an exposure to biomass fuels for 6 months or more. Though no association was identified with either obstruction or low FVC, long-term exposure to allergens and various irritants (as a consequence of living with animals), having no private source of drinking water and no flush toilets or bathrooms might explain the high prevalence of airway obstruction (11, 30).

4.4.1 Comparison with Khartoum study

Overall, COPD was more prevalent in the urban vs rural study using both LLN and GOLD estimates for participants aged ≥40. This contrasts with published literature suggesting that people living in more rural settings tend to have more exposure to environmental risk factors such as indoor air pollution, biomass fuels and allergen irritants. However, this study found that exposure to biomass fuels, especially firewood and coal occurred more in urban (82.4%) than rural settings (48%). Having higher exposure to biomass fuel in Khartoum is unexpected but could be explained by the high levels of migration from rural Sudan to Khartoum State over the last decade as a consequence of conflict. As a result, participants might not have lived in urban settings their whole lives and therefore continue to use more traditional methods for cooking and heating. Furthermore, although Gezira State has been officially classified a rural state, it is relatively wealthy as it has the largest agriculture project in the country(184). Moreover, the high prevalence of COPD in Khartoum might be due to the exposure to air pollutants coming from the large number of factories and millions of cars in the State.

In the Gezira study, 92% of participants owned their own houses and 85% had access to a private indoor or outdoor water supply, while these percentages were 70% and 66.2% respectively in the urban study. A higher educational level was also reported in Gezira State when compared to Khartoum (44% vs. 32%) as the state was the

pioneer in education in Sudan. These factors might contribute to the lower levels of post-bronchodilator obstruction observed in Gezira state (18, 20, 21).

The prevalence of reported previous TB was lower in this study than rates reported by the National Tuberculosis program in Khartoum and Gezira states. As discussed in chapter 3, the stigma around TB in Gezira State (193) and generally in Sudan might explain the small number of reported TB cases in both studies, and given the high prevalence of low FVC, TB might be more prevalent in this area than reported. The lack of the association between TB and COPD or low FVC in either study can be justified by the few self-reported TB cases.

The findings regarding airway reversibility in both rural and urban studies highlight the need for further investigation of asthma in the area.

Rurally based participants returned a higher low FVC prevalence estimate, especially in the group aged <40, while the prevalence of respiratory symptoms in the overall population was higher in rural populations compared to urban populations (42% vs. 23% respectively). The finding of having higher prevalence of respiratory symptoms in those with low FVC in both studies is tangible suggestion that the burden of low FVC requires more attention and investigation.

Despite a relatively high smoking prevalence, cigarette smoking was only associated with post-bronchodilator obstruction in the urban study using the GOLD definition. Therefore, the obstruction reported in both studies might not be the result of heavy smoking, given that 50% and 94% of the smokers reported a smoking history of fewer than 10 pack-years in urban and rural studies respectively.

No association was identified between airway obstruction and body mass index in the rural study. However, having a higher BMI was found to be protective against airway obstruction in the urban study. A higher BMI generally in the urban population might explain this finding as a higher percentage of the rural population are a normal weight.

4.4.2 Strength, limitations and challenges

This study is the first of its kind in rural Sudan and including a younger age group of 18 years and above allowed research to explore different types of condition and lung abnormalities. Results were based on spirometry tests conducted to ATS standards with careful quality control. The followed sampling technique allowed the estimation of a population weighted prevalence and associated risk factor. Moreover, the findings suggested a high prevalence of low FVC in younger subjects, which should be explored further in future research. Using the BOLD standardised method also allowed comparability with other findings from the continent and worldwide.

The study also had limitations. A response rate of 59% occurred because 22% of initial sampled participants left the area and it was not possible to locate them. In addition, 17% of recruited participants had inadequate spirometry readings mostly due to refusal to complete the post-test and taking the inhaler. Yet we included a sample size > 600. This reduced the sample size and limited the exploration of associations between location and airway obstruction and low FVC having some villages with small number of participants.

Moreover, there was of a high refusal rate in different study villages, particularly amongst those more rural. There was no record of the number of refusals on those villages, though reasons for refusal varied across different villages and ethnic groups. Participants declining to take part in spirometric testing was the most common reason for incomplete data. This may have been because of local beliefs that blowing into a machine and taking an inhaler might transmit asthma. Additionally, working in a challenging rural environment and traveling for long distances reduced the amount of time that data collectors could spend in villages and recruit participants.

4.5 Conclusions

Finding COPD prevalence rates of 5.5% and 7.7% (using the GOLD definition and LLN respectively) in subjects aged ≥40, an airway reversibility of 6% and a high prevalence of low FVC suggest that NCLDs, especially COPD and perhaps asthma, are serious public health problems in adults in rural Sudan and emphasise the need for more investment in prevention and management of chronic respiratory disease.

Similarly, the high prevalence of respiratory symptoms across different age groups, especially in younger age groups, needs further investigation and consideration from public health authorities and researchers

The gap between medically diagnosed COPD reported in this study and prevalence identified by spirometric testing suggests that COPD is under-diagnosed in rural areas of Sudan. This might be due to a lack of availability of proper diagnostic tools such as spirometry as well as a lack knowledge and consideration of this disease and its associated risk factors other than cigarette smoking

Taken together these findings, serious actions and calls for smoking cessation programmes, provision of diagnosis and treatment options for chronic respiratory disease with a focus on COPD and asthma as well as changes to the use of biomass fuels in the country is highly needed.

Chapter 5 A comparison of smartphone and paper data-collection tools in the Burden of Obstructive Lung Disease (BOLD) study in Gezira state, Sudan

5.1 Introduction

Advances in information technology have opened exciting new avenues for how research is conducted and data collected, however, traditionally paper-based data collection has been the mainstay of data gathering for the Burden of Obstructive Lung Disease (BOLD) study. As highlighted in chapter 2, section 5.2.1, BOLD is an internationally recognized study that uses standardised methods to measure the burden of chronic obstructive lung disease (68). However, automated data collection and processing methods are becoming more widespread in healthcare research (31,194) and they have many advantages (195–197). There are studies investigating the use of automated data collection via smartphones as a research tool in developing countries though there are fewer of these studies than in the developed world and fewer still exploring smartphone usage in large-scale and complex surveys, such as BOLD (197). Experience with smartphone-based data collection in challenging rural environments where internet connection is problematic, as in Sudan, is particularly limited.

Paper-based data collection is often convenient for researchers and data collectors. Paper questionnaires have several potential advantages over automated methods. Paper questionnaires are often easier to produce, modify, manipulate, and implement, and data extraction is not restricted to a specific place. Additionally, paper-based data collection provides a long-lasting record of all modifications and evaluations of completed questionnaires can be completed by different reviewers instantly (32,198).

However, studies from developing countries have found that using a paper-based method tends to result in incomplete records more, frequently increases the potential for human error and requires more time to organise the data (32,199,200). This is because labour-intensive data entry is necessary and this may reduce time available for analysis (200).

In the last decade, the number of mobile phone users in Africa has dramatically

increased, with mobile users representing 83% of total telephone users in the continent. South Africa boasts the highest rates of mobile phone ownership with 36.4 mobile phones per 100 people. They are no longer considered a luxury (196,197).

Smartphones is deliberated to be the combination of the traditional Personal Digital Assistant (PDA) and mobile phone, with an improved focus on the mobile phone part. These handheld devices incorporates mobile phone capabilities with the more common features of a handheld computer or PDA. As information communication technologies grow, with software supporting 'Android' platforms and the development of many open-source applications, researchers in the health sector have begun using smartphones as a tool in patient data collection, disease surveillance, clinical research and national surveys (31,32). However, paper-based questionnaires continue to be the main data collection tool in many countries, especially in SSA (32) .

Using smartphone technology-based tools for data collection has many potential advantages, providing a broad range of options. It facilitates faster reporting, more accuracy and greater efficiency, reduce cost, condense survey procedures, and improve data quality (199,201,202). Data collection and entry can be combined into a single step (31), tools can be developed to ensure that data supplied on forms is reliable and complete, and additional features, such as the Global Positioning System (GPS), can be deployed. Additionally, time stamps, alarms, automatic completions and reminders can help to monitor work-rate and validate data (195,198,203). Moreover, Smart phones showed that, it has a great potential when considering capacities of messages and alert system as has been used by the UNICEF in Sudan to provide real-time and cost effective abilities for local health personnel to trace absentee; and for central disease control authorities to track disease (204). Smartphones also allow supervisors to keep better track of the gathered data, which in turn enhances performance, enables the identification of potential problems, and reveals interesting lines of inquiry while they can still be addressed, as well as improves accountability of the various actors (205).

However, data security and connectivity can be a concern, and data collectors need to be comfortable using an automated tool (195). Accidental loss of data, battery life,

loss or theft of the device, security of the device and network connectivity in rural areas are also major concerns (201,205,206).

In Sudan, both the government and civil society frequently use smartphones to gather data. There is, however, very little published research regarding this. Therefore, this study aims to compare accuracy, completeness and the quality of data collected using smartphone-based versus paper-based methodologies for the BOLD study in Gezira State, Sudan. The present study in this chapter explored whether BOLD survey data collection might be expedited by conducting this work as a one-step process 'in the field' (smartphone-based data collection), improving the speed with which questionnaire data could be processed and improving responsiveness to new data. Furthermore, this study aimed to provide evidence that will inform the selection of data collection methodologies in future BOLD surveys in rural Sudan and wider SSA and MENA region.

5.2 Methods

5.2.1 Study design and setting

The parent BOLD study discussed in chapter 4, is a cross-sectional household survey with a multi-stage random sampling plan, conducted in 35 villages in Gezira state, Sudan. This exploratory cross-sectional household survey piloted within the same setting of the rural BOLD survey following the same study design and targeted the same population with identical inclusion criteria: all participants were non-institutionalised adults, aged 18 and older and lived in Gezira state.

Convenience sampling of 100 accessible participants from 3 randomised villages was conducted between August and September 2016. Each of these villages was composed of 30 households, which were similar in all study characteristics including population density, educational level, geographic area, sex distribution, ethnic groups and infrastructure.

The method of data collection was randomized separately from the main BOLD survey. A total of eight participants were randomized daily (four to be administered by smartphone and four by paper) prior to the start of data collection. The data

collector administering the questionnaires for the BOLD team was then also randomized. The collection of the BOLD survey core questionnaire data and this pilot study of concurrent data collection methods ran simultaneously. (Figure 5.1).

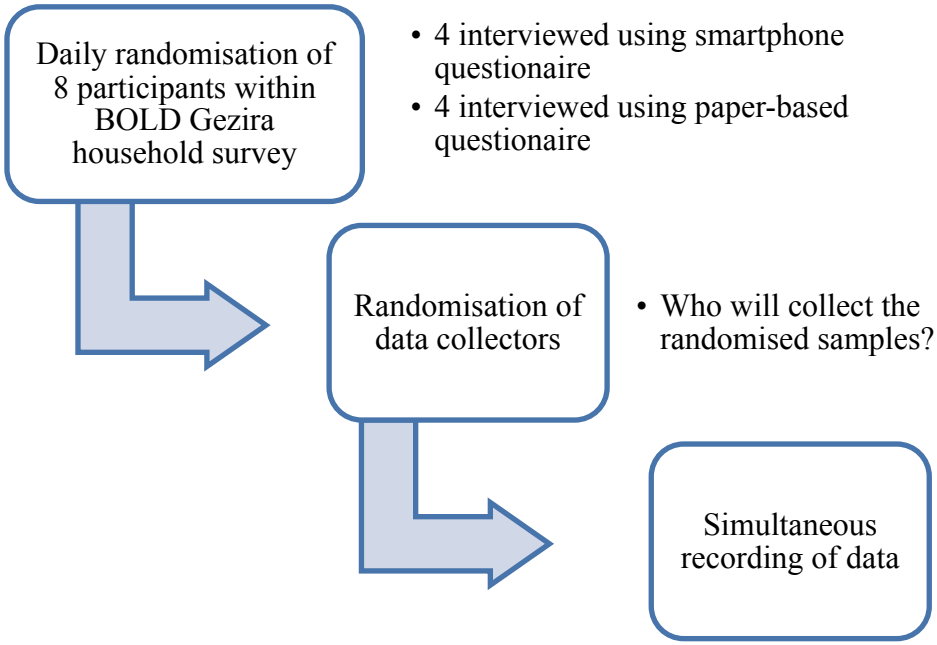


Figure 5.1 Data collection methodology of smartphone and paper-based questionnaires

5.2.2 Need assessment

Prior to the start of this study, a needs assessment was conducted with the aim of increasing data collection efficiency and of avoiding errors that are common in household surveys. This assessment was based on discussions with different experts including a software engineer, an epidemiologist and an expert public health surveyor. This exercise identified requirements essential to the development and implementation of the electronic data collection forms and system. A wide range of available software was explored. The Open Data Kit (ODK) was selected based on its affordability, its evidence-based use in developing countries and its offline data entry facility. Standard operating procedures (SOPs) in line with ethical approval were developed prior to the start of data collection (Appendix (7)).

5.2.3 Open Data Kit (ODK) questionnaire development

The ODK (207) was used by the study's principal investigator to develop an electronic version of the BOLD core questionnaire for the Samsung S3 smartphone, which included seven main sections: demographic information, respiratory symptoms and disorders (cough, sputum, wheezing, and shortness of breath), use of medication, cigarette smoking, occupational exposure, economic impact and activity limitation. The questionnaire was composed of 26 pages with 44 questions (with multiple sub-questions and different skip patterns). Each questionnaire consisted of 204 fields, including 48 keyed-in, open-ended questions and 105 multiple-choice questions. A unique six-digit study ID was manually assigned to the participant (following the BOLD study protocol) and all questionnaires were labelled with a serial number (i.e. 1–100) (See Appendix (3) for BOLD core questionnaire).

Initially the ODK questionnaire was designed using Microsoft excel and then, using guidance from the ODK instructions and xlsform.org, an XLSForm was developed. To avoid errors, validation check boxes, reliability rules, alerts, skip patterns, and fields requiring data were programmed into the ODK. The form included three sheets. The first was a 'survey sheet', which included all collectable data in Arabic, the GPS location, survey start and finish times and notes to guide data collectors, including hints and data constraints. The second was a 'choices sheet', which contained a comprehensive list of all answer options with labels in Arabic and English. The third sheet, of 'settings', contained the form title in the mobile interface and the form ID.

Questions were grouped and answers programed based on whether they were open ended or single/multiple choice questions. The excel file was then uploaded into http://opendatakit.org/xiframe/ and the fully functioning form was previewed in "Enketo" (provided by the ODK). XML forms were then uploaded into ODK Aggregate. To use the forms on mobile devices, the ODK Collect application for android was used (See appendix (8) for mobile interface snapshots).

After development, the tool was tested and validated in one village independent of the two study villages. The study's principal investigator and another trained data

collector from the BOLD team carried out data collection via smartphone-based forms. Six data collectors collected paper-based forms.

As Internet connectivity was very limited in the study area, it was essential that ODKs could be used offline. Data were entered into smartphones during collection, saved, and later uploaded to the server once reliable internet connectivity could be secured.

5.2.4 Data collection and entry

Data collection involved recording participants' information simultaneously on both paper and electronic forms. Both smartphone and paper questionnaires were administered in local Arabic language. Two data collectors concurrently completed the core questionnaire alternately in a random order (i.e. if one data collector asked the questions and completed data entry using the paper-based method, the smartphone data collector listened and entered data on the smartphone, and vice versa) to ensure no additional burden on participants. The order of administration of the paper questionnaire and the smartphone questionnaire was randomized each day. Study SOPs were agreed between the two data collectors before the start of data collection.

The paper-based questionnaire data were double-entered in a predesigned SPSS (IBM Corp. Released 2015. IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp) spreadsheet. Data were entered into two different spreadsheets, where crosschecking and cleaning were performed before analysis. Smartphone forms were submitted to the ODK aggregate server and then retrieved using Briefcase, saved as a CVS file, compiled, and then translated into SPSS format. All data collectors were graduates and had been extensively trained in BOLD questionnaire administration, research methods and ethics by senior researchers, data managers and IT specialists. The mobile data collectors were also trained in how to use the ODK and how to administer the BOLD core questionnaire using Samsung S3 mobile phones.

5.2.5 Ethical considerations

Ethical approval from Liverpool School of Tropical Medicine research Ethics Committee was obtained prior to the start of this study (Ref. 11.03RS). Additionally, for the main BOLD study, ethical approval was obtained from the ethics committee at Imperial College London and the research department at the Ministry of Health in Gezira state, Sudan (Appendix (5). During the data collection stage, all data were anonymised. All participants received information sheets concerning the details of the study and written consent was obtained prior to participation.

5.2.6 Statistical analysis

Descriptive statistics for the main variables in the questionnaire were produced alongside frequency distributions in order to test for data completeness. A chi squared test was used to examine the association between the percentage of forms with errors and form type (smartphone-based/paper-based), for collection order (first versus second) and possible interaction of form type by order.

Intraclass correlation coefficient tests were used to test consistency and agreement between continuous variables, while percentage agreement and Cohen's Kappa statistics were used to test the agreement between categorical variables. P-values of less than 0.05 were used to report the significance of the results. Kappa ranges are described in Table 5.1 (208).

Table 5.1 Kappa range and level of agreement

Kappa range	**Level of agreement**
0	Less than chance
0.01–0.20	Slight
0.21–0.40	Fair
0.41–0.60	Moderate
0.61–0.80	Substantial
0.81–0.99	Almost perfect

5.3 Result

Data collected via paper forms took approximately 15 days from the initial collection to be double entered in SPSS software and cleaned, whereas electronic data were rapidly accessible and retrieval took one day.

5.3.1 Study population demographics

Of the 100 participants (median age = 41.5 ± 16.4 years), 63% were women. Perfect agreement (inter-rater measurement agreement = 0.929) was shown between the two methods in the age variable (Table 5.2).

Table 5.2 Characteristics and demographic information of study participants

Variable	**Smartphone Frequency (%) (N = 100)**	**Paper Frequency (%) (N = 100)**
Age (years)		
18–30	28 (28.0%)	28 (28.0%)
31–40	21 (21.0%)	21 (21.0%)
41–50	15 (15.0%)	15 (15.0%)
51–60	19 (19.0%)	19 (19.0%)
60–70	15 (15.0%)	13 (13.0%)
> 70	2 (2.0%)	4 (4.0%)
Sex		
Male	37 (37.0%)	38 (38.0%)
Female	63 (63.0%)	62 (62.0%)
Educational level		
Primary school	26 (26.0%)	26 (26.0%)
Middle school	11 (11.0%)	11 (11.0%)
High school	28 (28.0%)	28 (28.0%)
College (trade/professional/ community)	6 (6.0%)	6 (6.0%)
Four-year college/university	22 (22.0%)	19 (19.0%)
None	6 (6.0%)	6 (6.0%)
Unknown	1 (1.0)	1 (1.0)
Father's educational level		

Primary school	15 (15.0%)	15 (15.0%)
Middle school	7 (7.0%)	7 (7.0%)
High school	6 (6.0%)	7 (6.0%)
College (trade/professional/ community)	4 (4.0%)	1 (1.0%)
Four-year college/university	9 (9.0%)	9 (9.0%)
None	28 (28.0%)	33 (33.0%)
Unknown	31 (31.0%)	28 (28.0%)
Mother's educational level		
Primary school	26 (26.0%)	29 (29.0%)
Middle school	6 (6.0%)	5 (5.0%)
High school	12 (12.0%)	11 (11.0%)
College (trade/professional/ community)	2 (2.0%)	2 (2.0%)
Four-year college/university)	2 (2.0%)	3 (3.0%)
None	36 (36.0%)	37 (37.0%)
Unknown	16 (16.0%)	13 (13.0%)

Two ethnic groups were dominant in the studied population: Halaween represented 42% while Jaalia represented 17%, though other ethnic groups were also represented. Kappa statistics showed substantial agreement between the two methodologies (Kappa = 0.630). Date of birth also represented a strong agreement. Generally, the two methodologies agreed on all demographic information on the questionnaire.

In 'higher education level achieved', two records were missing in the paper-based data collection and inconsistencies in the values collected using both methods were seen. However, the Kappa statistics showed strong to substantial agreement.

5.3.2 BOLD questionnaire results

The BOLD questionnaire results are summarised in Table 5.3. The results are from both paper and smartphone collected data. Where disagreement occurred both percentages are reported with an asterisk.

Table 5.3 Respiratory symptoms, smoking status, occupational exposure and economic impact in BOLD questionnaire (n=100)

Variable	Paper-based Number (%)		Smartphone based Number (%)	
	Yes	No	Yes	No
Cough often, without viral illness	24%	75%*	24%	76%*
Productive cough, without viral illness	15%	85%	15%	85%
Wheeze in the last 12 months	13%*	5%*	11%*	7%*
Shortness of breath	18%*	81%*	16%*	84%*
Took respiratory medicine in last 12 months	19%	81%	19%	81%
Ever smoked Cigarette	20%	78%*	20%	80%
Current smoker	40%	60%	40%	60%
Ex-smoker	60%	40%	60%	40%
Think smoking can cause serious illness	97% *	3%*	99%*	1%*
Worked in an occupation that has dust	23% *	76%*	20%*	80%*
Work for income generation	38% *	62%*	40%*	60%*
Unemployed	60% *	40%*	62%*	38%*
Unemployed because of respiratory problems	2%	60%	2%	60%
Unemployed because of other health problems	19%*	41%*	23%*	37%*
*** Indicates a disagreement in reported percentage**				

5.3.3 Areas of strongest agreement

Several BOLD questionnaire areas showed almost perfect agreement between the two data collection methods. The major questions relating to cough had a 99% agreement, with one record missing in the data collected using the paper-based methodology, and major questions relating to phlegm demonstrated 100% agreement between the two methods. Questions relating to emphysema, asthma, and chronic

bronchitis all showed strong to perfect agreement.

Strong to perfect agreement was also seen in the smoking section, as shown in Table 5.4. No significant differences were found on smoking questions such as smoking *shisha*, cigars, *canapés*, and special substances. All other smoking related questions had a strong level of agreement between results yielded through smartphone and paper collection, and substantial agreement was also found in questions regarding smoking at work (kappa = 0.77, $p < .05$).

Significantly low inter-rater agreement was found on questions related to the number of cigarettes smoked weekly (Interclass coefficient = 0.552, $p < .05$) (Table 5.4). The mobile variable was calculated automatically for results in the smartphone-based collection and calculated manually in the paper-based collection.

Table 5.4 Smoking

Variable	Interclass coefficient	P-value	Skip required
How old were you when you started smoking?	1.000[1]	$p < .001$	No
How old were you when you quit smoking?	1.000[1]	$p < .001$	No
How many cigarettes do you smoke daily?	0.976[1]	$p < .001$	No
How many cigarettes do you smoke weekly?	0.552[2]	0.025	No

1 = High inter-rater agreement, 2 = Low inter-rater agreement.

Absolute agreement was demonstrated in most of the questions regarding medication use (Table 5.5). The timeframe of taking the medication should have been specified in days and weeks in both methods of data collection. In smartphone-based questionnaires, there were specifications for this timeframe (days/weeks) but in the paper-based questionnaires there were not. Of the ten participants taking medication,

only two had the timeframe of medication duration specified. Kappa values cannot be calculated for this variable, though there was an 11% agreement between them.

Table 5.5 Medication

Variable	Kappa statistic	p-value	Skip required
If medication had been taken in the past 12 months	0.935[2]	p < .001	No
Type of medication	0.696[3]	p < .001	No
When the medication was taken	0.833[2]	p < .001	No
Period in months	1.000[1]	p < .001	No

1 = perfect agreement, 2 = almost perfect agreement, 3 = substantial agreement.

Occupational exposure showed strong agreement (kappa = 0.88) and the inter-rater class statistic showed absolute agreement between the two variables for a question related to 'number of years of exposure'. Similarly, questions concerning participant comorbidities also had a strong level of agreement between the two versions of the data, apart from questions regarding heart disease, which had fair agreement (kappa= 0.393).

Moderate to substantial agreement was found in questions regarding participant's knowledge of smoking related disease (see Table 5.6).

Table 5.6 Knowledge, opinions, and attitudes

Variable	Kappa statistic	p-value	Skip required
Smoking causes stroke	0.421[4]	< 0.05	No
Smoking causes heart attack	0.550[4]	< 0.05	No
Smoking causes lung cancer	0.487[4]	< 0.05	No
Smoking causes chronic bronchitis	0.663[3]	< 0.05	No
Smoking causes emphysema/COPD	0.563[4]	< 0.05	No

3 = substantial agreement, 4 = moderate agreement.

Sections regarding participants' views of their health, how they feel, and how well they can do their usual activities showed almost perfect agreement using Kappa statistics with values of 0.927 and 0.818. The only exception was a particular question regarding physical health and emotional problems. In this question, substantial agreement was shown (kappa = 0.795).

In follow-up questions concerning phlegm, a slight inconsistency was shown in the skipping patterns between the two methods. Fair level of agreement (kappa = 0.23, $p < .05$) was seen in skip-pattern questions relating to 'hearing wheeze' (Table 5.7).

5.3.4 Areas of weakest agreement

The main areas of disagreement were in questions with skip patterns. In the 'shortness of breath' questions demonstrating disagreement, 15 of the paper-based questionnaires showed incorrect usage of the skip pattern (e.g. 'if the answer is no, then the next two questions should be skipped'). Kappa statistics showed no agreement in results from the two different methods in this area (Table 5.7). Where the skip instructions were properly followed strong agreement was found (kappa =0.839).

Table 5.7 Respiratory symptoms and disorder

Variable	Kappa statistic	p-value	Skip required
Cough most days	1.000[1]	< .001	Yes
Phlegm most days	0.867[2]	0.001	Yes
Wheeze in the past 12 month	0.895[2]	< .001	No
Wheeze only with cold	0.239[5]	0.309	Yes
Wheeze with shortness of breath	1.000[1]	< .001	Yes
Cannot walk because of shortness of breath	0.858[2]	< 0.001	No
Shortness of breath when going uphill	-0.013[7]	0.895	Yes
Walk slower because of shortness of breath	0.040 [6]	0.674	Yes
Stop walking to breath better	0.111[6]	0.439	Yes
Stop for breath after walking 100 yards	0.149[6]	0.170	Yes

1 = perfect agreement, 2 = almost perfect agreement, 5 = fair agreement, 6 = slight agreement, 7 = less than chance agreement.

The skip pattern was also not adhered to in questions related to ex-smokers. Four of 11 did not appropriately follow the skip pattern in the paper-based collection group, while it was appropriately followed during the same questions in the smartphone-based collection group. Substantial agreement was found in these variables (kappa = 0.770, $p < .05$).

Similarly, questions in the economic impact section exhibited variation in the level of agreement. The 'skip pattern' questions showed moderate to substantial agreement, while the remainder showed strong agreement (Tables 5.8 and 5.9).

Table 5.8 Economic impact -1

Variable	Kappa statistic	P-value	Skip required
Work days lost			
Did you work for income?	0.985[2]	< 0.05	No
Did you not work for income mainly due to breathing problems?	0.492[4]	< 0.05	Yes
Did you not work for income because you were a full-time homemaker or caregiver?	0.803[3]	< 0.05	Yes
Did your health problems stop you from performing your usual homemaking/caregiving tasks?	0.576[4]	< 0.05	Yes
During the past 12 months, did health problems stop you from working for income?	1.000[1]	< 0.05	No
Non-work activities missed			
Did health problems prevent you from participating in one or more non-work related activities?	0.758[3]	< 0.05	No
How many days did you not participate in non-work related activities due to your health problems?	1.000[1]	< 0.05	Yes

1 = perfect agreement, 2 = almost perfect agreement, 3 = substantial agreement, 4 = moderate agreement.

Table 5.9 Economic impact-2

Variable	Interclass coefficient	P-value	Skip required
How many days were you unable to perform your homemaking/caregiving tasks due to your health problems?	1.000[1]	< 0.05	Yes
During the past 12 months, how many days were you unable to perform your homemaking/caregiving tasks specifically due to breathing problems?	1.000[1]	<0 .05	Yes
How often during the past 12 months did you work for income?	0.997[2]	< 0.05	Yes
How many days were you unable to work for income due to your health problems?	-0.115[5]	0.559	Yes

1 = perfect agreement, 2 = almost perfect agreement, 3 = substantial agreement, 4 = moderate agreement, 5= Less than chance agreement

5.3.5 Incomplete records

Missing records were seen in paper questionnaires across different questions (as shown in Table 5.10).

Table 5.10 Incomplete records in 100 questionnaires

Questionnaire section	Number of missing records in paper-based forms	Number of missing records in mobile-based forms
Demographics	13	0
Respiratory symptoms and disorders	11	0
Medications	5	0
Smoking	12	2
Knowledge attitude and perception	5	0
Occupational exposure	2	0
Additional comorbidities	9	0
Views about own health	1	0
Economic	13	0

5.3.6 Forms with errors

Errors originated from three sources: (1) an erroneous form, (2) erroneous collection methodology, and (3) error on the part of the data collector. Errors were defined as questions with no answers or wrong use of the 'skip pattern'. In smartphone-based forms, most of the errors found were due to having different answer options (Table 5.11). A chi Square test demonstrated that paper forms were significantly more likely to contain errors (82.5% of the total). In comparison, 10.5% of smartphone-based questionnaires contained errors and 7% occurred in both formats (X^2 (3, n = 100) = 64, $p < .001$). There was no significant association between erroneous forms and the order of questionnaire administration with respect to using the smartphone or paper-based first ($p = .686$).

Table 5.11 Forms with returned errors

Variable		Frequency (Percentage)	p-value (Pearson Chi-Square)	Correlation (Pearson's R)
Error type	Error in paper forms	47 (82.5%)	<0 .05	-0.995
	Error in mobile forms	5 (10.5%)		
	Error in both	4 (7.0%)		
Administration method	Mobile-based	27 (47.4%)	0.686	0.061
	Paper-based	30 (52.6)		
Data Collector	1	9 (15.8%)	0.496	-0.038
	2	16 (28.1%)		
	3	2 (3.5%)		
	4	8 (14.0%)		
	5	8 (14.0%)		
	6	14 (24.6%)		

There was no statistically significant association between the occurrence of errors in forms and the data collector ($p = 0.50$) and weak negative correlation between these variables (Pearson's $R = -0.038$).

Furthermore, a multiple linear regression was calculated to predict the errors on forms based on who did the data collection and in what order the questionnaire was administered; however, no significant association was found ($F(2,97) = 0.299$, $p > .05$, $R^2 = 0$).

5.4 Discussion

Data collection is one of the most important steps in conducting health research and having consistent, complete, and accurate data is essential to this process. This study found that the use of a smartphone-based data collection method in rural Sudan was feasible and provided timely and quality data with a lower number of errors and inconsistencies when compared with data collected using paper-based methods.

These findings are in line with other studies conducted in similar settings (194,199,203,208,209). A recent study of routine influenza sentinel surveillance in Kenya and southern India both reported similar results, with fewer errors and inconsistencies in smartphone-collected data (31,199).

Smartphone data collection allowed data to be gathered more quickly for analysis in comparison to the paper-based forms. A collection date, start time and end time of each questionnaire could also be electronically logged when using smartphones, whereas this information was not routinely available for data obtained using the paper-based method. Furthermore, even though both methodologies were administered simultaneously, filing electronic forms was quicker compared to paper-based forms.

Although no cost-specific data were collected or evaluated in this study, electronic data collection was relatively cheap as Epi-Lab organisation already possesses some of the building blocks for smartphone data collection. Therefore, it was possible to use two existing smartphones (Samsung Galaxy S3). Nevertheless, buying smartphones is often expensive, previous studies reported that this cost was compensate by fewer people needed for data entry, computer devices for database entry and printing cost (194,202).

Moreover, using an open source application, such as ODK, also decreased the software cost of this study.

Inadequacies in the data mainly occurred on questions with complicated skip patterns on mobile-based forms. However, the use of automated checks and validations on electronic forms prevented the occurrence of these errors, which was also found in a Kenyan influenza surveillance study (199). Using the wrong skip pattern on such surveys can affect the quality of collected data and may lead to misleading results.

Variables without mandatory data entry requirements on mobile-based forms and open-ended questions caused 8 (80%) of the errors from a total of 10 returned errors on mobile-based forms. Other studies reported similar findings with the limitation of unrestricted questions using mobile data collection(199). The remaining 20% were due to technical programming problems.

Some of the reported data inadequacies may not have been caused by the data collection method used, but because the participant provided unclear answers. During data collection, the researcher was required to select the option he/she deemed to be most accurate. Therefore, problematic responses to questions (views about the paticipants' own health—how they feel and how well they can do their usual activities) may not have been caused by the collection method used. Similarly, when assessing the level of education, there were differences in the 'unknown' and 'none' classifications as this was dependent on the researcher's personal assessment.

5.4.1 Challenges, limitations, and lessons learnt

One of the main limitations of this study was the use of a convenience sampling plan and a sample size of 100 participants. The sample size was selected based on the number of previously recruited participants within the main survey each month as well as time and budgetary constraints. Additionally, because of the length of the BOLD questionnaires the interviews could only be performed once per individual. Ideally the questionnaires would be taken using both methodologies simultaneously by the same data collector to allow more comparisons with respect to administration time and the efficiency of data collectors.

Although the ODK tool is an open source application, there were some obstacles during the development and data extraction stages, as well as during retrieval. Firstly, accessibility of the aggregate website in Sudan was difficult. Occasionally, during data collection, the ODK application would unpredictably close and the researcher would need to restart the application. As internet connectivity and network coverage are very limited in the three rural villages, the availability of offline data collection facility in ODK makes it a viable tool in rural settings.

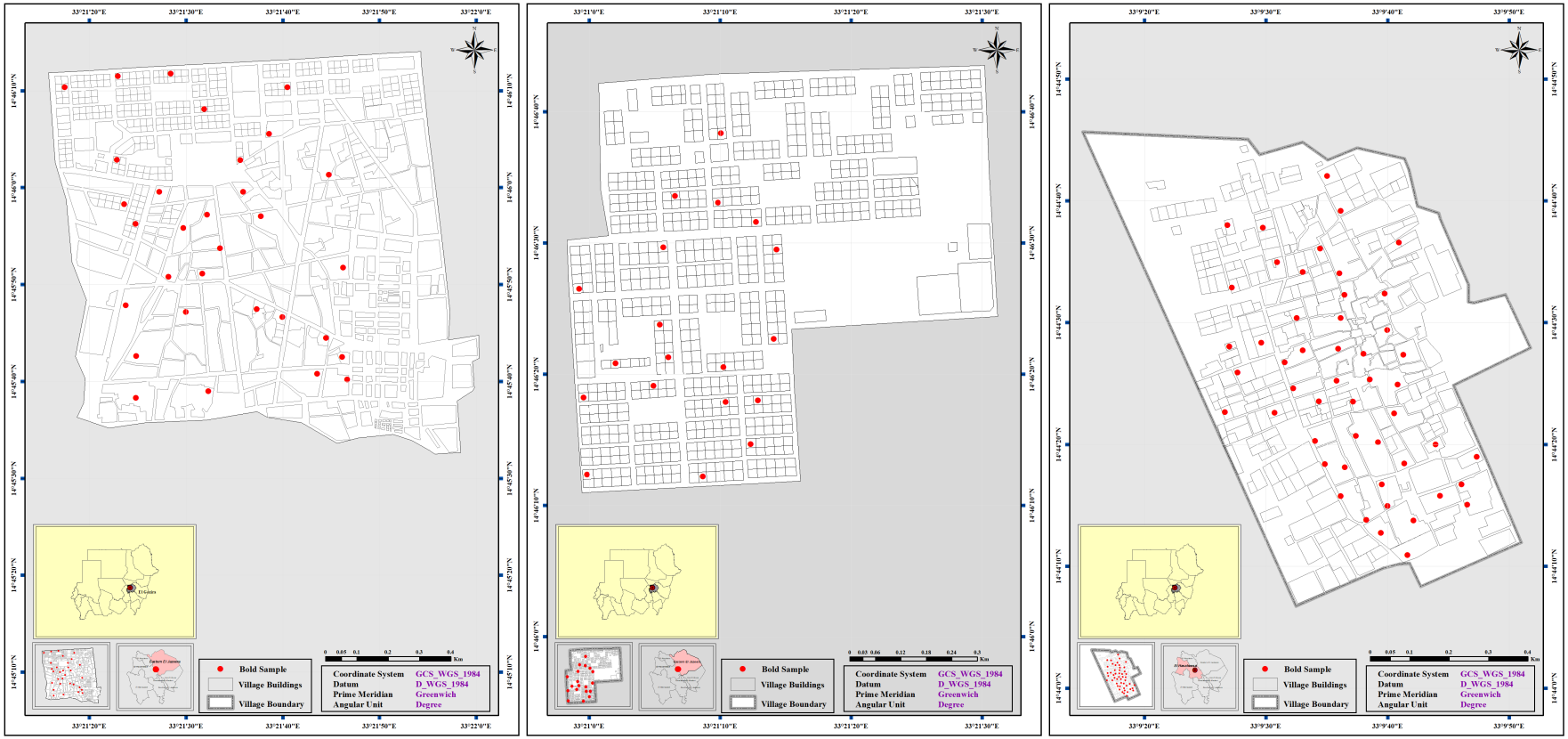
Secondly, using Arabic on the ODK software was challenging during questionnaire development and data retrieval, particularly with regards to open-ended questions. Importing the CVS files from ODK into Excel was also an issue as Excel was not able to correctly interpret Arabic content of incoming CVS files. However, other platforms and software exist, but unlike the ODK they need a subscription and payment.

One skip pattern in the smoking section had a programming error, which resulted in errors in two of the mobile forms and options were incorrectly skipped.

The main challenge with respect to both the paper and electronic forms was the length of the BOLD core questionnaire and the frequent skip patterns. Long questionnaire completion time affected the programming time, collection, data entry and analysis in the electronic version as providing a challenge for the data collectors. These collectors were experts in administering the paper-based core questionnaire and were sometimes faster than the smartphone-based data collectors when explaining questions to participants. In future studies, increased data collector experience may accelerate smartphone-based data collection (31).

The electronic format allows, in theory, GPS coordinates to be easily obtained during the interview process and therefore accurate mapping of participants' locations, even in rural areas. However, in practice the GPS coordinates were inconsistent, especially in the first village, and there was a delay in obtaining data. If fully functional, this system does hold an advantage over traditional paper-based data collection (Figure 5.1–5.2). See Appendix (9) for maps permission letter.
The overall economic cost of using this mobile data-collection method, including software development, mobile/electronic devices, network connection and internet accessibility, requires further investigation. The use of local rather than the current cloud servers provided by the ODK platform also needs evaluating.

Lastly, for large questionnaires with many nested questions and multiple skip patterns such as the BOLD core questionnaire, having either mobile-friendly questionnaires with strict validation checks or minimising the skip patterns on paper-based forms may improve the data collection process and improve data quality.



(A) (B) (C)

Figure 5.2 Maps showing geographical locations of study participants in in included villages in Gezira state, Sudan. (A) Rufaa Alhai 4 village. (B) Rufaa Alhai 20 village. (C) Altakala Joubara village

5.5 Conclusions

This study demonstrates that electronic data collection via smartphones for the BOLD study is an effective and efficient method in the challenging environment of rural Sudan. It provides timely and accurate data that are comparable with traditional method of paper-based formats, with lower levels of user error. When inconsistencies between the two formats did occur, this was primarily due to the inappropriate completion of the BOLD skip-format questions in paper-based questionnaires. While the smartphone-based technique is not without challenges, this study adds to the growing body of evidence supporting electronic data collection as a feasible method of obtaining data for health surveys in similar rural environments.

Chapter 6 : Summary, implications and conclusions

6.1 Summaries and implications

This thesis describes three related studies that were designed to shed light on the burden of chronic non-communicable respiratory disease in SSA and MENA with a focus on Sudan and as well as to examine potential methods for improving data collection in large health surveys. The overall aim was to improve our understanding of the burden, prevalence and factors associated with the development of chronic non-communicable lung diseases, as they are a major public health concern which receives little investigation in SSA and MENA region. This chapter summarises these studies with an emphasis on their rationale, main findings and their implications, concluding with suggestions for further research.

Globally, 3.9 millions of NCDs deaths are due to CRDs and COPD in particular (1). COPD is now the third most common cause of death globally; 90% of these deaths occur in Low and Middle-Income Countries (LMICs) (35–37,210). In 2016, COPD affected 251 million people, and its related deaths represented almost 5% of all deaths (74). On the other hand, asthma currently affects 235 million people, and causing substantial mortality, there were 383,000 deaths due to asthma in 2015 (76). Limited literature is published on the epidemiology of COPD and Asthma from SSA and MENA. Both diseases are under-diagnosed and underestimated in both SSA and MENA. Furthermore, the burden of COPD in SSA is disputed and reports offer variable prevalence estimates, ranging from 4.1% to almost 22.2% (92). SSA and MENA countries reported similar COPD mortality rates of 18 per 100,000 population (47). WHO estimates that there are 250,000 deaths per year from asthma. Although asthma is a less common cause of death compared to COPD it is a major cause of morbidity; for example it is in the top twenty causes of disability in children globally. Risk factors for CRDs are genetic and environmental; the latter primarily from air pollution exposure including tobacco smoke (129), household air pollution (88,124), outdoor air pollution and occupational exposure (136).

Data on COPD prevalence from both SSA and MENA regions are limited and when available are often based on varied definitions and lacking standardisation. In Sudan particularly, there are no national estimates for COPD while available reports

regarding CRDs are of high degree of uncertainty (24). Similar to the broader regions, the priority has been always given to communicable disease with a little focus on non-communicable disease in the country. The studies that do exist are limited to specific populations such as miners and previously treated TB patients(27,143). In addition, good quality post-bronchodilator spirometry is lacking in Sudan health system and diagnosis generally depends on clinical decision, and knowledge about COPD is often limited.

The reported prevalence rates in both SSA and MENA regions propose a similar rate of diseases burden in Sudan. This study is the first, to our knowledge, to provide prevalence estimates of COPD in Sudanese adults using internationally accepted methods and procedures as well as an appropriate sampling technique. Through the use of the BOLD study protocol, estimates can be straightforwardly compared with other BOLD studies.

The BOLD study described in Chapter 3 set out to estimate the prevalence of chronic obstructive pulmonary disease through spirometric testing in urban Khartoum and identify the impact of risk factors on the prevalence of the disease. COPD prevalence was 10.3% and 14.8%, using the LLN, and GOLD definitions, respectively. The main risk factor for COPD was older age, primarily the age group 60-69 years old. Smoking was also identified as a risk factor using the GOLD definition. Using the NHANES III reference range, the prevalence of moderate to severe obstruction was 9.2% and 12.6% using LLN and GOLD definitions respectively. Using local reference ranges, the prevalence of COPD was far lower than when using both LLN and GOLD definitions. Low forced vital capacity (FVC) prevalence estimates were 58.1% using NHANES. Airway reversibility was found in 6.1% of the total study population while airway obstruction persisted after use of a bronchodilator in 10.5% of subjects with reversibility using GOLD and 18.5% using LLN. This study suggested that COPD is prevalent and a considerably under-diagnosed public health problem in urban Sudan. In addition, with over 50% of the sampled population having low FVC and a large variance in prevalence using NHANES and locally derived ranges, there is a need for prioritisation of CRDs and investment in improving diagnostic tools as well as research to investigate the reasons behind these high estimates.

To explore whether the high burden of non-communicable lung disease that was seen in the urban Sudan setting of Khartoum would also be seen in a rural setting, a second study was conducted incorporating the same core BOLD Study protocol in the rural state of Gezira. We were particularly interested in the extent to which the burden of disease would be similar in younger as well as older (aged 40 years and older) adults included in the BOLD study. Therefore, the scope of work was expanded to include a second age stratum (age 18-39). This study replicated findings from the previous urban study and reported a higher prevalence in respiratory symptoms, which were reported by 41% participants (19% reported a cough, 14% reported sputum production, 19% reported shortness of breath and 5% reported a wheeze). However, the prevalence of post-bronchodilator obstruction in the overall population was lower compared to the urban study findings (4% using both LLN and GOLD definitions). Amongst participants aged 40 years and older the prevalence was 5.5% and 7.7% using LLN and GOLD definitions respectively. Similarly, low FVC was seen in 52.7% of those aged 40 years and older group using NHANES. Factors associated with obstruction and low FVC included age, lower level of education, being underweight and living in a particular locality called Wad Medani. Airway reversibility was 6.4% while airway obstruction persisted after use of a bronchodilator in 18.5% of subjects with reversibility using LLN and 15% using GOLD. This finding along with findings from the urban study might suggest a high prevalence of asthma in both study areas.

Overall, COPD was more prevalent in the urban area than in the rural area using both LLN and GOLD estimates in participants aged ≥40 years. This contrasts with the published literature suggesting that people who live in more rural settings tend to have more exposure to environmental risk factors such as indoor air pollution, biomass fuels and allergen irritants. Findings from both studies were consistent with published literature suggesting that using a fixed ratio <0.7 with the GOLD definition might overestimate the COPD prevalence in elderly populations (185,186) while using the below LLN ratio can reduce the increase in COPD diagnoses related to age (48,187). However, advocates of GOLD argue that using a fixed ratio can detect patients with substantial pulmonary pathology and respiratory morbidity, while advocates of LLN claim that the use of <0.7 as a cut-off point is more likely to return false positives (48,172).

The prevalence of low FVC was high in both studies. The rural population tended to be more symptomatic than the urban population (40% vs. 23% respectively) with a higher prevalence of respiratory symptoms occurring in the younger group <40 years. The reasons behind this high prevalence are not known and were not investigated in these studies. Having higher prevalence of respiratory symptoms in participants with low FVC suggests that this phenomena carries a real burden. No association was identified between either airway obstruction or low FVC and known risk factors such as smoking, biomass fuels and occupational exposure in both present studies in the multivariate analysis. A possible reason of high prevalence of respiratory symptoms and reduced lung capacity might be previous respiratory infections (59,211) as in Sudan, childhood respiratory infections; particularly pneumonia has been reported as the second cause of hospitalisation in 2007 (18). This is consistent with previous studies in low smoking exposure settings such as Malawi (166), and other studies, that suggest that unknown environmental factors such as genetics, race, low birth weight, early exposure to biomass fuels and air pollution and poor diet are common factors associated with a low FVC in developing countries (36,166,188).
In both rural and urban studies, no association was identified between occupation and airflow obstruction except in rural study for those who had an occupational exposure for >5 years working in agriculture, textile and food industry, and farming was the primary reported occupation.

Exposure to biomass fuels, especially firewood and coal, was reported in urban settings (82.4%) more than in rural settings (48%). This contrasts with findings in previous studies that higher exposure to biomass fuels tended to occur in rural settings.

However, high levels of migration from rural Sudan to Khartoum state in the last decade due to conflict, inflation and lack of work means that participants in the urban study might not have been living in urban areas for their whole life. Moreover, although Gezira state has been officially classified as rural, the socioeconomic status of the state's population is higher than in other areas of Sudan as the state was home to the biggest agriculture project in Africa until a decade ago. In the rural study, 92% of participants owned their houses and 85% had access to a private supply of drinking water, while in the urban study these figures were 70% and 66.2% respectively.

Moreover, a higher average educational level was reported in Gezira State more than in Khartoum (44% vs. 32%). These factors might contribute to the lower level of post-bronchodilator obstruction in Gezira State (66,69,79).
Though the case finding of tuberculosis was high according to the National Tuberculosis program in both Khartoum and Gezira states, the prevalence of reported TB history was low in our study. Therefore, we had limited power to explore associations between TB and spirometric abnormalities.

In both studies, there were no comorbidities identified with airway obstruction, except for having hypertension which was found to be associated with GOLD stage 2 COPD using the local reference range in the rural study. In both studies, only hypertension and diabetes were frequently reported by the participants and few cases reported TB, heart disease and lung cancer. This contrasts with work suggesting that COPD is associated with one or more comorbidities (48). However, this might be due to the stigma linked with TB which is known to be a major public health concern in Sudan (212), though studies showed that there is a low prevalence of other diseases: lung cancer is less common in Sudan (213), and prevalence of cardiovascular disease is only 2.5% (214).

Taken together with the findings of the Khartoum study, there is a strong evidence that NCLDs are a serious concern in rural Sudan and deserve consideration with respect to public health. While estimates reported by WHO are highly uncertain because of the unavailability of national estimates, this study confirmed that CRD is highly prevalent in both urban and rural Sudan. Our findings suggest that AFO are underestimated and under-diagnosed, with only 12 (2.1%) and 31 (1.5%) participants reporting medically diagnosed COPD and 39 (6.4%) and 117 (6.4%) reporting medically diagnosed asthma in Khartoum and Gezira states respectively. Prioritisation of chronic lung diseases and inclusion of proper diagnostic tools such as spirometry in Sudan's health system would improve the diagnoses of these diseases and therefore provide a clearer representation of the disease burden.

The use of paper-based questionnaires was stipulated by the BOLD Study protocol and as such, they were used in both the Khartoum and Gezira state studies. However, this approach provided some challenges in the field and in the data entry office, as it

was time-consuming. Moreover, poor data accessibility affected data accuracy, completeness and information quality. The opportunity was therefore taken to explore the possibility of administering the BOLD study questionnaires using a digital format alongside the required paper-based questionnaire approach while conducting the Gezira state study by selecting 100 participants from three rural villages. The ODK was used to programme questionnaires in Arabic into smartphones and questionnaire data were collected using both paper-based and smartphone-based methods simultaneously. Agreement between the two methodologies was tested using the Kohen's Kappa statistics and inter-rater class coefficient. The two data collection methods varied from perfect to slight agreement across the 204 variables evaluated (Kappa varied between 1.00 and 0.02 and had an inter-rater coefficient between 1.00 and -0.12). Errors, incomplete and inconsistent records were most commonly seen with paper questionnaires on questions with complex skip-patterns, which were a major source of errors. Compared to paper-based data collection, smartphone technology worked well for data collection in the challenging rural setting. This approach provided timely, quality data with fewer errors and inconsistencies than paper-based data collection. Based on this research, this method is recommended for future BOLD studies and other population-based studies in similar settings.

6.2 Pathways to impact

The implementation of the two BOLD studies by the Epi-Lab organisation came as a continuation of the previous work by the organisation as pathfinder, that led the work on Lung Health in Sudan and become a recognised WHO/EMRO lung health collaborating centre as well as the union collaborative centre following on its achievement on Tobacco cessation, standard Asthma, and Pneumonia case management among others (215).

In order to disseminate study findings and find a way to shape and influence health policy regarding chronic non-communicable lung diseases in Sudan, we carried out a dissemination meeting on April 24th 2018 in Khartoum, Sudan under the title "Evidence to promote Lung Health in Sudan". The study findings were presented together with other studies concerning lung health. The main objective of the meeting

was to shape national policy and practice response to a body of local research evidence on CRD (meeting minutes in appendix 10).

The meeting organised by the Epi-Lab and was well attended, with participation from Under Secretary for Health, pioneering chest physicians, public health consultants, Non-governmental Organisation (NGO) representatives, WHO and United Nation Development Program (UNDP) representatives and researchers and academics from different fields including the environments, pharmacy sectors and development partners.

During the dissemination of the study's results, it was suggested by the researcher that CRD, particularly COPD and asthma are underestimated and underdiagnosed. Gaps in Sudan health system and shortage in diagnostic tools, as well as lack of national estimates, were highlighted as a priority unmet need in order to estimate disease burden and prevalence as well as to provide better disease management and treatments. This was prompted by the findings of a high prevalence of spirometric abnormality, particularly COPD, airway reversibility and a higher prevalence of low FVC and respiratory symptoms in rural population.

The researcher stressed on the importance of including spirometry in the diagnosis of chronic lung disease particularly COPD and asthma. Knowing that spirometry is not routinely available in either the private or public sectors, discussion around the possibility of introducing spirometry in the Sudan health system and scaling up provision took place. This discussion has been picked up by health system representative and reinforced that spirometry is crucial for the diagnosis of COPD and highlighted the deficiency in diagnostic tools in Sudan. This representative went on to state that works is being done to provide spirometric testing in secondary health care, however, training of doctors in spirometry is still needed and efficacy assessments must be carried out before spirometry can become commonplace across other levels of health care, including in primary health care. An area he deemed important for future collaboration with the Epi-Lab.

The discussion around study findings and implications highlighted the magnitude of the CRDs burden while potential interventions in Sudan health system and policy

might be emphasised by these research findings, specifically what can be done by community health workers in health education as well as on prevention, management and referral for emerging cases. Having a higher prevalence in Khartoum state with weak association with smoking that only associated with GOLD definition highlighted the need for authorities to address the issue of a high pollutant State in order to decrease air pollution. Having proactive health prevention policies will possibly manage these conditions sustainably. In addition, anti-smoking campaigns should be prioritised by the policymakers to help smokers quit and to initiate smoking cessation programs. This should be coupled with non-pharmacological modalities such as rehabilitation and nicotine patches (though these are available in the country, they are however expensive). There is a need to provide psychological support in smoking cessation programs as well as effectively treating existing co-morbidities.

Overall, this meeting highlighted gaps in the Sudanese health system with regard to chronic lung health and the deficiency in the diagnosis of COPD and asthma as well as investigating the reasons behind these findings. The meeting also highlighted the need for research to strengthen existing services and introduce new interventions for these diseases. Additionally, the results of this study has provided evidence-based estimates using standardised recognised BOLD study protocol and possibly have a potential impact in Sudan health system and policy with regard to chronic lung diseases having the undersecretary of the Federal Ministry of Health strongly emphasized that these were the first data on COPD to be presented, owing to the lack of research and surveillance data regarding chronic lung disease in Sudan while highlighted the need for Sudan to prioritise these diseases.

6.3 Conclusions

In conclusion, the prevalence of COPD in Sudan was relatively high compared to other neighbouring countries in SSA and MENA regions, especially in the urban survey. The high prevalence of low FVC and high prevalence of reported respiratory symptoms in urban and rural settings needs further investigation and research. Moreover, the findings regarding airway reversibility in both rural and urban studies suggest that asthma may be underdiagnosed and highlight the need for future research to assess disease prevalence and burden. The findings of no association with the known risk factors to lung abnormality such as smoking and use of biomass fuels

suggest that other environmental or racial factors may contribute to the burden of lung diseases in Sudan. Sudanese health care institutions need to invest in training, diagnosis and service delivery and prioritise non-communicable and chronic lung disease. There is a serious need for primary and secondary interventions initiated by Sudanese health policymakers and the government to prioritise the development and implementation of chronic lung disease policies.

6.4 Recommendations

1) Prioritisation of airflow obstruction in the Sudanese healthcare system and investment in healthcare training and service delivery with regard to COPD, asthma and other chronic lung diseases based on this study.
2) Integration of respiratory health into Primary Health Care (PHC), scale up of the existing asthma strategy and development of a management strategy and guidelines for clinicians and public health experts for better diagnosis of COPD and other CRDs and an improved understanding of the disease burden.
3) Consideration of the use of spirometry alongside clinical diagnosis, following international guidelines for better diagnosis and assessment to help reduce the burden of chronic lung disease in Sudan by early detection of disease and prompt prevention and management of NCLDs. This can include prioritisation and establishment of smoking cessation programs and interventions as a key preventive method for airflow obstruction. However, weak association with smoking was identified in this study but smoking is known globally as biggest risk factor for COPD.
4) Consider including specific statistics about COPD, asthma and other NCLDs in health annual reports of Sudan to help policymakers, practitioner and researchers as well as inform decision making regarding disease care, management, distribution and required services.
5) Adopt automated methods such ODK software in data collection for future health surveys in Sudan to enhance data quality and accessibility in wider studies and surveys and strengthen mHealth programmes for CRDs.

6.5 Further work

Several areas were not addressed by this study and some questions remained unanswered. This research highlighted the need for further work regarding non-communicable lung disease in Sudan, including work to:

1) Investigate the reasons behind the high prevalence of low FVC in urban and rural Sudan.
2) Investigate the reasons behind the high prevalence of respiratory symptoms in rural Sudan.
3) Investigate the association between exposure to air pollution and COPD in urban Sudan.
4) Understand possible contributing risk factors to the prevalence of COPD in Sudan.
5) Assess asthma prevalence and associated risk factors in adults in Sudan.
6) Understand possible health system and social responses to the burden of CRD delineated in this research.
7) Investigate the use of mobile health and digital technologies in a wide range of health surveys and surveillance systems in Sudan.

APPENDICES

Appendix (1): Literature review Search strategy

A search for all published studies, available in English, and meeting the study scope and criteria as below:

1. The initial stage included a limited search using DISCOVER, that pulls out results from PubMed and Medline databases. To carry out this search, boolean "AND/OR/NOT" were used to combine keywords and phrases included in the study topic. This preliminary search allowed us to identify relevant keywords contained in the title, abstract and subject descriptors (Table 1).
2. Terms identified in the previous step and the synonyms used by respective databases were used in an extensive search of the literature using Medical Subjects Headings (MeSH) approach.
3. Reference lists and bibliographies of the articles collected from those identified in stage two above were then searched.

Papers indexed in following databases were searched: PubMed, Science direct, Global health, and BOLD website. Grey literature databases were also used and these included Google scholar as well as data banks from WHO and World Bank.

Table 1. Terms used for online databases search

Search terms	"NCDs" OR "Non communicable disease " OR "non-communicable disease" "COPD" OR "Burden" , "Chronic Obstructive Pulmonary Disease burden " OR "global", "Pulmonary disease chronic obstructive" OR prevalence" OR "Africa" , "Global burden of COPD" "Global initiatives for COPD" OR "GOLD" OR "Lower limit of normal", "Disease definition" OR "COPD definition", "Chronic Obstructive Pulmonary Disease" OR "European Respiratory Society" OR "American Thoracic Society" OR "British Thoracic Society" **"**Asthma definition" OR "GINA", "global initiative for asthma" OR "Global Asthma network**"** OR "asthma standardised definition" "COPD prevalence*" OR "Sub Saharan Africa*", OR "COPD in Africa" OR "Asthma in Africa" **,** " Respiratory disease" OR "Africa" OR "SSA" OR "MENA" OR " Middle east and North Africa" OR "Middle East" OR "North Africa" OR "Sudan" OR "Khartoum" OR Gezira" OR "Gazeera" OR "Algazira" "Less developed countr*" OR "developing countr*"OR "low to middle income countr*" OR low resource OR setting" OR "underdeveloped countr*" OR "low income countries" OR "underserved "COPD" OR "Risk factors" OR "associated factor" OR "exposure" OR "related factor" OR "older age" OR "aging" OR "smoking" OR "smoke" OR "biomass" OR "fuel" OR "occupational exposure" OR "work exposure", "Chronic respiratory risk factor" OR "global" OR "Africa" OR "developing countr*" "COPD burden" OR "rural" OR "urban", "COPD prevalence in country " , "COPD" or "industrialised" OR "developed"

	"COPD Comorbidities ", " COPD" OR "other disease", "CRD" OR "TB" OR "hypertension" OR "Diabetes " OR "lung cancer" OR "cardiovascular disease" "CRD" OR "adult" OR " 40 years" OR "18 years" OR "forty" OR "eighteen"
Databases searched	PubMed, Science direct, Global health, and BOLD website, Google scholar , data banks from WHO and World Bank
Part of journals searched	European Respiratory Journal, American Thoracic Society journal, AIMS, International Journal of Tuberculosis and Lung Disease, Chest Journal, Allergy, American Journal of Respiratory and Critical Care Medicine, COPD: Journal of Chronic Obstructive Pulmonary Disease, Global Health Action, International journal of chronic obstructive pulmonary disease, Journal of Allergy and Clinical Immunology, The Journal of asthma : official journal of the Association for the Care of Asthma, The Lancet, Plos Medicine, Plos One, Respiratory Medicine, Respirology, Thorax
Years of search	There were no time limits. However, most recent publications within the period of 5 years were included.
Language	English
Inclusion criteria	All published articles/reviews in a peer reviewed journal from the globe with the focus on SSA and MENA regions for chronic respiratory diseases, COPD and asthma

Appendix (2) Participant information sheets and consent

The Epidemiological Laboratory

A survey on Chronic Obstructive Pulmonary Diseases in Gezira State

Participant information sheet and consent

Study title: Survey of the burden of lung diseases and disability in Gezira State

Participant's address……..
Participant's Phone number……..

You have been selected to participate in this survey about chronic obstructive pulmonary disease. Please read the information below for detailed information on the study and ask the researcher about any parts of the study that are unclear to you. We would like you to participate after being fully aware of the study and how you were selected to participate in it. Your participation is fully voluntary, and you have the right of refusal to participate in this study. No ill consequences regarding the current or future health service provided will result from refusing to participate in the study. You may drop out from the study at any time even after providing initial consent.

- ✓ This study has been approved by **the Gezira Ministry of Health, Imperial college London and Liverpool School of Tropical Medicine** and will be conducted according to ethical guides of the Declaration of Helsinki and local ethical guides for conducting research.
- ✓ This study is an investigation of chronic lung diseases in Gezira state and will involve:

1. Filling of questionnaires
2. Conducting a lung function test using a spirometer
3. Random selection of participants
4. Participants are requested to give information on the following:

a) Socioeconomic status
b) Health status

c) Conducting a lung function test using a spirometer before and after giving a safe dose of bronchodilator
d) Waist and hip circumference and pulse which are important for the lung function test

- ✓ You might also be randomly selected as part of another sub study aims to compare two data collection methods. Two researchers will fill part of the questionnaires at the same time using both mobile-based forms and paper-based forms for the sake of testing the two different methodologies of the data collection. However, only one of them will ask you the questions.
- ✓ Participants will benefit from conducting the lung function test of which they may have a copy of the results. No payments will be given in return for participation in the study.
- ✓ There are no risks to participating in this study which has been conducted in many other countries around the world where no risks have been reported.
- ✓ The information obtained from questionnaires is strictly confidential. No names will be written on questionnaires or lung function tests. The participant's address and phone number will be written only after consent.
- ✓ Do you have any questions or enquiries now? If you have questions at any other time please contact the researcher……. Phone number……

Participant's consent

I …….agree to participate in the survey about chronic obstructive pulmonary disease and declare the following:

1. I have read and understood the information in the participant information sheet above
2. I have been given the opportunity to ask questions and all my questions have been answered to my satisfaction
3. I have understood that participation in this study is voluntary and I have not been persuaded in any way to be part of it
4. I have been given the option of dropping out of the study at any point without ill consequences

Participant's signature……..

Witness's signature……...

I ……..declare the following:

1. I have informed the participant of the above information
2. I have encouraged the participant and gave him/her ample time to answer their questions
3. I am convinced that the participant has understood all parts of the study outlined above

Researcher's signature……..

Witness's signature……

Appendix (3): BOLD study Data collection tools

BOLD questionnaires are listed below:

1) Participant tracking questionnaire

Country's code:

City's code:

ID:

Date: year/month/day:

Participant tracking

1.Age___ ____ ____ years

2 Gender Male □1

Female □2

3. Data Collected:

	Yes 1	**No**2
Core Questionnaire	□	□
Cigarette Smokers Questionnaire	□	□
Biomass Questionnaire	□	□
Spirometry (including Questionnaire)	□	□
Minimal Data/Refusal Questionnaire	□	□
Occupational Questionnaire	□	□
Additional Questionnaire	□	□

4. Non-Response: [For Participants with no data (all 'No') in Question 3.]

Refused/No data collected□4□

Known to have permanently left area□5

Temporarily out of area□6

Dead□7

Age ineligible□8

Institutionalized □9

Untraceable (e.g.

bad address and phone)□10

Unreachable (e.g.

never returns mail or answers phone) □11

5. The following questions 5.1 and 5.2 are optional

5.1. Record Geographical Information Data (e.g. geographical coordinates

postcode

zip code) _____

5.2. Record Geographical Information Data

_____

Compulsory question

6. For centres that have performed multistage sampling techniques kindly enter cluster identifier numbers here

6.1 locality Number_ __ __

6.2. Number given to village __ __ __

6.3. Number for house (if applicable) _ __ __

If you have performed a simple random sampling

enter 000 for 6.1 to 6.3

Done by ……..

2) Core questionnaire

Country's code:

City's code:

ID:

Date: year/month/day:

Phone number

Family member phone number

BOLD core questionnaire

Demographic data:

- What is the participant's gender?

- What is the participant's ethnic group?

- What is your date of birth ___/___ /___
  Day/month/year

- What is the highest educational level you have reached?
  - Primary School ☐
  - Middle School ☐
  - High School ☐
  - Some College (Trade/ Professional/ Community) ☐
  - Four Year College/ University) ☐
  - None ☐
  - Unknown ☐

- What is the highest educational level your father has reached?
  - Primary School ☐
  - Middle School ☐
  - High School ☐
  - Some College (Trade/ Professional/ Community) ☐

	Four Year College/ University)	
	None	
	Unknown	
- 1-What is the highest educational level your mother has reached?	Primary School	
	Middle School	
	High School	☐
	Some College	☐
	(Trade/	☐
	Professional/	☐
	Community)	☐
	Four Year College/	☐
	University)	☐
	None	
	Unknown	

6-2- does one of these things exist at home or one of the home residents own it? Read them all:	Yes	No	Do not know
- Electricity	☐	☐	☐
- Siphoning-toilet	☐	☐	☐
- Home telephone	☐	☐	☐
- Television	☐	☐	☐
- Radio	☐	☐	☐
- A fridge	☐	☐	☐
- A car	☐	☐	☐
- Scooter/bike	☐	☐	☐
- Washing machine	☐	☐	☐
- Do you own the house?	☐	☐	☐
- Internal bathroom			

- Water tabs inside the house n- Water tabs outside the house - Internet - Mobile phone	☐ ☐ ☐ ☐ ☐	☐ ☐ ☐ ☐ ☐	☐ ☐ ☐ ☐ ☐
- Have you-or one of your family members- ever felt hunger, because you do not have money?	Most of the days Most of the weeks Most of the months Several times a year occasionally never		☐ ☐ ☐ ☐ ☐ ☐
6-3- when you were 5 years old, was there any one in your home who owns one of these things? Read them all: - Electricity - Siphoning-toilet - Home telephone - Television - Radio - A fridge - A car - Scooter/bike - Washing machine - Do you own the house? - Internal bathroom - Water source outside the house	Yes ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐	No ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐	Don't know ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐

n- Water tabs inside the house - Internet - Mobile phone	☐ ☐ ☐	☐ ☐ ☐	☐ ☐ ☐
- Have you ever felt hunger, because you don't have money?	Most of the days Most of the weeks Most of the months Several times a year occasionally never		☐ ☐ ☐ ☐ ☐ ☐
6-4-howmany people live with you in the same house? (including you)	……		
6-5- how many rooms are there in your house? (without the kitchen and the bathroom)	……..		

Respiratory symptoms and disorders:

The following questions will be about, if possible please answer with Yes or No, if you are not sure please answer No.		
Cough:		
- Do you cough often, when you don't have cold?	Yes No	☐ ☐
If the answer was yes, continue to question 7a, if it was No move to question 8.		
7 a- are there some months in which you cough most of the days?	Yes No	☐ ☐
If the answer was yes, ask question 7b, 7c if it was No move to question 8.		
7 b- do you cough most of the days for 3 months a year?		

7 c- for how many years do you have the cough?	More than 5 years	☐
phlegm:		
7- Usually, do you expel the phlegm from your chest or it stays in the chest and doesn't get out when you don't have cold?	Yes No	☐ ☐
If the answer was yes, continue to question 8a, if it was No move to question 9.		
8 a- are there some months in which you have phlegm most of the days?	Yes No	☐ ☐
If the answer was yes, ask question 8b, 8c if it was No move to question 9.		
8 b- do you expel phlegm from the chest most of the days for 3 months a year?	Yes No	☐ ☐
8 c- for how many years do you expel phlegm?	Less than 2 years 2-5 years More than 5 years	 ☐ ☐ ☐
Wheeze:		
9- In the last 12 months, do you hear wheeze in your chest?	Yes No	☐ ☐
If the answer was Yes asking question 9a and 9b, if it is No, move to question 10.		
9a- do you hear wheeze in your chest, in the last 12 months, only when you have cold?	Yes No	☐ ☐
9b- in the last 12 months did you have wheezing that led to shortness of breath?	Yes No	☐ ☐
Shortness of breath:		
10- Are you unable to walk for any reasons other than breath shortness?	Yes No	☐ ☐

If the answer for question 10 was Yes, describe the reasons in the line below and move to question 12. If it was No or you were not sure, go ahead to question 11. Type of condition or cause…… ……		
1- *Do you* get short of *breath* as *you are hurrying on level ground, or* uphill?	Yes No	☐ ☐
If the answer was Yes, ask the questions 11A-11D, if it was No move to question 12.		
11a- do you walk slower than your peers on level ground because of shortness of breath?	Yes No	☐ ☐
11b- do you stop for breathing when walking with a normal speed on level ground?	Yes No Not applicable	☐ ☐ ☐
11c-have you stopped for breathing after a 100 yards' walk or a minutes' walk on level ground?	Yes No Not applicable	☐ ☐ ☐
11d- did you have an attack of breath shortness that kept you from going out, or putting on your clothes?	Yes No Not applicable	☐ ☐ ☐
2- Have you been told before by a doctor or a health care provider that you have emphysema?	Yes No	☐ ☐
3- Have you been told before by a doctor that you have asthma, chronic bronchitis, or allergy? If the answer was Yes, move to question 13A, if it was No move to question 14.	Yes No	☐ ☐
13 a- do you still have the asthma, chronic bronchitis, or allergy?	Yes No	☐ ☐

4- Have you been told before by a doctor or a health worker that you have chronic bronchitis? If the answer was Yes, move to question 14A, if it was No move to question 15	Yes No	☐ ☐
14a- do you still have the chronic bronchitis?	Yes No	☐ ☐
5- Have you been told before by a doctor or a health worker that you have chronic obstructive pulmonary disease?	Yes No	☐ ☐

Section management

Now I will ask you some questions about your medications that you take to help your breath, medication you are taking regularly and those you take when you have symptoms, we want to know your medications, their form, and the frequency of taking them monthly.

1- In the last 12 months did you take medications to help your breath (including nasal congestion medications)? Yes ☐ No☐

If the participant didn't take any medication to help him breath,move to next question

16b-drug code														
16c-dosage form	Tablets Inhaler Nebulizer Liquid Suppositories Injections Other forms	☐ ☐ ☐ ☐ ☐ ☐ ☐	Tablets Inhaler Nebulizer Liquid Suppositories Injections Other forms	☐ ☐ ☐ ☐ ☐ ☐ ☐	Tablets Inhaler Nebulizer Liquid Suppositories Injections Other forms	☐ ☐ ☐ ☐ ☐ ☐ ☐	Tablets Inhaler Nebualizer Liquid Suppositories Injections Other forms	☐ ☐ ☐ ☐ ☐ ☐ ☐	Tablets Inhaler Nebulizer Liquid Suppositories Injections Other forms	☐ ☐ ☐ ☐ ☐ ☐ ☐	Tablets Inhaler Nebuliz er Liquid Supposit orie Injectio ns Other forms	☐ ☐ ☐ ☐ ☐ ☐	Tablets Inhaler Nebulizer Liquid Suppositori es Injections Other forms	☐ ☐ ☐ ☐ ☐ ☐ ☐
16D-do you usually take the drug most of the days,	Most of the days With symptoms Both other	☐ ☐ ☐ ☐	Most of the days With symptoms Both other	☐ ☐ ☐ ☐	Most of the days With symptoms Both other	☐ ☐ ☐ ☐	Most of the days With symptoms Both other	☐ ☐ ☐ ☐	Most of the days With symptoms Both other	☐ ☐ ☐ ☐	Most of the days With sympto ms Both other	☐ ☐ ☐ ☐	Most of the days With symptoms Both other	☐ ☐ ☐ ☐

or when you have symptoms, or in both cases?														
If it was taken most of the days, ask question 16E, if it was for symptoms ask the questions 16E and 16F.														
16E- When you take the drug, for how many days or weeks do you take it?	Days/weeks ...../.....		Days/weeks ...../.....		Days/weeks ...../.....		Days/weeks ...../.....		Days/ weeks ...../.....		Days/weeks ...../.....		Days/weeks ...../.....	
16F- taking the drug, for how many months of the last 12 months?	3-0 6-4 9 -7 12-10	☐ ☐ ☐ ☐	3-0 6-4 9 -7 12-10	☐ ☐ ☐ ☐	3-0 6-4 9 -7 12-10	☐ ☐ ☐ ☐	3-0 6-4 9 -7 12-10	☐ ☐ ☐ ☐	3-0 6-4 9 -7 12-10	☐ ☐ ☐ ☐	3-0 6-4 9 -7 12-10	☐ ☐ ☐ ☐	3-0 6-4 9 -7 12-10	☐ ☐ ☐ ☐

2- Please, do you take any other medication or do activities that help your breath?

Medicine or activity	code

- Have you ever measured your breathing rate by a doctor or health worker with the spirometer? Yes ☐ No ☐
  if the answer was Yes, ask question 18A, if it was No move to question 19.
  18A- did you use the spirometer during the last 12 months? Yes ☐ No ☐
- Have you had an attack of breath shortness that kept you from doing your daily activities or going to work? Yes ☐ No ☐
  if the answer was Yes asking question 19A, if it was No, move to question 20.
  19A-How many times have you had this attack in the last 12 months? ____times ____
  if the answer for 19A>0 ask question 19B and 19C if it was not moving to question 20.
  19B-How many times have you had this attack and needed to see a doctor or health worker, in the last 12 months? ____times ____
  19C-How many times have you had this attack and have been admitted to the hospital for a whole night, in the last 12 months? ____times ____
  if the answer for 19C>0 ask question $19C_1$ if it was not; move to question 20.
  $19C_1$-how many times have you spent the whole night admitted to the hospital because of these attacks, during the last 12 months? ____days ____

Cigarette smoking

Whither the participant concerns the following questions is currently or formerly smoking, and the type of cigarette smoked

20-1- have you ever smoked in your life?	Yes	☐
	No	☐

The answer Yes means more than 20 boxes in your life, or more than 1 cigarette every day for a year.
if the answer was Yes asking question 20A-20D, if it was No move to question 20.2

A- How old were you when you started smoking regularly?	____ ____years	
B- If you have quitted smoking before, how old were you when you did that for the last time (if the participant is still smoking, record the number 999)	____ ____years	
C- How many cigarettes do you smoke daily /weekly?	……. cigarette/day ……cigarette/week	
D- During ……. , were you smoking a manufactured or handmade cigarette?	manufactured handmade	☐ ☐
20.4- have you ever smoked pipe in your life?	Yes No	☐ ☐

if the answer was Yes asking the questions 20.4A-20.4D, if it was No move to question 20.5

A-How old were you when you started smoking pipe regularly?	____ ____years	
B-If you have quitted smoking pipe before, how old were you at that time?	____ ____years	
(if the participant is still smoking, record the number 999)		
C-how many pipe tobaccos do you smoke daily /weekly? ……. gram/day ……gram/week	……. pipes/day ……pipes/week	
20.5-have you ever smoked cigars, cheroots, or cigarillos in your life? if the answer was Yes asking the questions A-C, if not move to question 20.6	Yes No	☐ ☐
A-How old were you when you started smoking cigar regularly?	____ ____years	
B-how old were you when you quitted smoking cigar?	____ ____years	
(if the participant is still smoking, record the number 999)		
C-Averagely, in the whole period during which you were smoking, how many cigars, cheroots, or cigarillos were you smoking daily /weekly?	……. cigars/day ……cigars/week	
20.6-have you ever smoked water pipe (shisha) in your life? if the answer was Yes asking the questions A-C, if not move to question 20.7	Yes No	☐ ☐

A-How old were you when you started smoking shisha regularly?	____ ____years	
B-how old were you the last time you quitted smoking shisha? (if the participant is still smoking, record the number 999)	____ ____years	
C-Averagely, in the whole period during which you were smoking shisha, how many shishas were you smoking daily /weekly?	……. shishas/day ……shishas/week	
Note: you have the choice to be asked the questions 20.7 and 20.8 or not		
20.7-have you ever smoked hashish in your life? if the answer was Yes asking the questions A-C, if not move to question 20.8	Yes No	☐ ☐
A-How old were you when you started smoking hashish regularly?	____ ____years	
B-how old were you the last time you quitted smoking hashish? (if the participant is still smoking, record the number 999)	____ ____years	
C- Averagely, in the whole period during which you were smoking, how many times were you smoking daily /weekly?	…….Juan's/day ……Juan's/week	

20.8-have you ever smoked or sniffed any other substance in your life? (e.g. local, recreational smoked substances)	Yes No	☐ ☐
20.8.1 Specify the type: ……		
20.8.2 What is the unit?		
if the answer was Yes asking the questions A-C, if not move to question 21		
A-How old were you when you started smoking ……. regularly?	____ ____years	
B-how old were you the last time you quitted smoking or sniffing …….? (if the participant is still smoking or sniffing, record the number 999)	____ ____years	
C-Averagely, in the whole period during which you were smoking, how much was the quantity were you consuming daily /weekly?	……. units / day ……units/week	
(if the participant is still smoking (question 20B is 999) ask the questions 21A and 21B, if not, move to question **23**		
21A- during the past year, how many times have you quitted smoking for at least 24 hours?	____ ____times	
21B- are you seriously considering quitting smoking?	Yes, during the coming 30 days ☐	

	Yes, during the coming 6 months ☐ No, I am not considering it ☐	
If the participant never smoked (answered No for all the questions 20.1-20.5), move to question 24.1, if not answer question 23. (there is no question No. 22)		
23- have you been recommended before, by a doctor or a health worker to quit smoking?	Yes No	☐ ☐
If it was yes asking the questions 23A and 23B, if it was No, move to question 24		
23A- have you received a medical advice to quit smoking, during the last 12 months?	Yes No	☐ ☐
23B- have you used any nicotine having medication (prescription or non-prescription) to help you quit smoking?	Yes No	☐ ☐
If it was Yes asking question $23A_1$, then 24, if it was No move directly to question 24.		
23B-1- What is the type of medication you were using to help you quit smoking?	Nicotine Replacement Bupropion Tofranil Other	☐ ☐ ☐ ☐
24- have you used or done anything to help you quit smoking?	Yes No	☐ ☐

If the answer was Yes, ask question 24A, if it was No, move to question 24.1		
24A- what have you done?	Hypnosis	☐
	Acupuncture	☐
	Biofeedback l	☐
	Other	☐
24.1 excluding you, how many regular smokers are there in your house?	……	
24.2 do people smoke regularly in your work place?	Yes	☐
	No	☐
	You don't work	☐
24.3 how many hours per day are you exposed to cigarette smoke from others?		
24.3.1 at home	…….. hours	
24.3.2 at work	…….. hours	
24.3.3 in the cinema, bar, café, restaurant, or any public place	…….. hours	
24.3.4 in any other place	…….. hours	
24.4 was your father a regular smoker in your childhood?	Yes	☐
	No	☐
24.5 was your mother a regular smoker in your childhood?	Yes	☐
	No	☐

Knowledge, opinions, and attitude:

Introduction		
The following questions are about cigarette and tobacco.		
24.6 as to your knowledge belief and faith, does smoking cause serious illnesses?	Yes	☐
	No	☐

If the answer was Yes asking question 24.7,
if not, move to question 25.

24.7 as to your knowledge belief and faith, does smoking cause any of the following? Read them all:	Yes	No	Don't know
- cerebral thrombosis (a clot in the brain, which causes paralysis)	☐	☐	☐
- Heart attack	☐	☐	☐
- lung cancer	☐	☐	☐
- chronic inflammation of lungs	☐	☐	☐
- emphysema/ chronic narrowing of airways	☐	☐	☐
	☐	☐	☐

Occupational exposure:

25 have you ever worked in an occupation that has dust?	Yes	☐
	No	☐
25A how many years have you worked in occupations that expose you to dust?	……years	
26 have you been told before, by a doctor or a health worker, that you have:		
26A heart disease	Yes	☐
	No	☐
26B hypertension	Yes	☐
	No	☐
26C diabetes	Yes	☐
	No	☐
26D lung cancer	Yes	☐
	No	☐
26E cerebral embolism	Yes	☐
	No	☐
26F tuberculosis	Yes	☐
	No	☐

If the answer for 26F was Yes, ask questions
26f1 AND 26F2, if not move to question 27

26F1 are you on anti-tuberculosis drugs now?	Yes No	☐ ☐
26F 2 have you ever taken anti tuberculosis drugs in your life?	Yes No	☐ ☐
27 have you have surgery in your chest in which part of your lung was removed?	Yes No	☐ ☐
28 have you been admitted to the hospital for a whole night because of breathing problems, when you were no older than 10 years?	Yes No Don't know	☐ ☐ ☐
29 during the last 12 months, did you take medications for influenza?	Yes No Don't know	☐ ☐ ☐
30 did a doctor or a health worker say that your father, mother, sister, or brother has lung enlargement (emphysema), chronic lung inflammation or swelling lung/ chronic bronchial obstruction.	Yes No	☐ ☐
31 in the last two weeks, is there a cigarette/ pipe/ cigar smoker living with you in the house?	Yes No	☐ ☐

12SF:

The following questions are about your health and the health problems that you feel, chose the answer that describes your condition the best:

32- Generally, do you consider your health:

Excellent ☐

Very good ☐

Good ☐

Average ☐

Bad ☐

33- the following questions are about the activities that you can do in a normal day. Does <u>your current health status hinder</u> you from doing the following activities? if this is the case, to what extent?

33A medium effort activities, such as moving a table, pushing a sweeping machine, swimming, or cycling.

Yes, a lot ☐

Yes, a little bit ☐

No, not at all ☐

33B walking up several flights of stairs:

Yes, a lot ☐

Yes, a little bit ☐

No, not at all ☐

34- During the <u>last 4 weeks</u>, how many times did you meet any of these difficulties, when you are doing your work or your daily activities, because of <u>your physical health</u>?

34A- achieved less than what you want

Always ☐

Often ☐

Sometimes ☐

Seldom ☐

Never ☐

34B- your achievement was limited to a specific <u>type</u> of work or other activity

Always ☐

Often ☐

Sometimes ☐

Seldom ☐

Never ☐

35- During the <u>last 4 weeks</u>, how many times did you meet any of the following difficulties, when you are doing your work or any other normal daily activities, because of <u>any emotionally related problems</u> (such as feeling depression or anxiety)?

35A- achieved less than what you want

Always ☐

Often ☐

Sometimes ☐

Seldom ☐

Never ☐

35B- achieved your work or other activity with less attention than usual

Always ☐

Often ☐

Sometimes ☐

Seldom ☐

Never ☐

36 during the last 4 weeks, to what extent does pain hinder your normal work (including your work at home and outside)?

None ☐

A little bit ☐

Averagely ☐

A lot ☐

So much ☐

37 the following questions are about your feeling and dealing with things during the last 4 weeks, for each question. please give the answer that expresses you're feeling the most.

During the last 4 weeks, how often have you

37A- felt calm and peaceful

Always ☐

Often ☐

Sometimes ☐

Seldom ☐

Never ☐

37B- been active and energetic

Always ☐

Often ☐

Sometimes ☐

Seldom ☐

Never ☐

37C- felt sadness and depression

Always ☐

Often ☐

Sometimes ☐

Seldom ☐

Never ☐

38- During the last 4 weeks, how often did your physical health or emotion related problem hinder your social activities (such as visiting friends and relatives, etc.….)?

All the time ☐

Most of the time ☐

For Some time ☐

For little time ☐

Never ☐

 (SF-12 Standard U.S. Version 2.0)

Economic Impact

Lost days of work

The following questions are about work and the time lost because of health problems

39- any time during last 12 months, have you worked for income generation?

If the answer was No, continue with question 39A, if it was Yes, move to question 40

39A during last 12 months, you were not working in a paid job because of breathing problems?	Yes	☐
	No	☐
39B during last 12 months, you were not able to work because you	Yes	☐
	No	☐

were all day busy at home, or busy with your health issues? If the answer was Yes, continue with question 39C, if it was No, move to question 44		
39C during last 12 months, is there a health problem that keeps you from doing your domestic work or care about your health? If the answer was Yes, continue with question 39D and E, if it was No, move to question 44	Yes No	☐ ☐
39D during last 12 months, for how many days were you not able to do your domestic work or care about your health because of a health problem?	……days	
39E during last 12 months, for how many days were you not able to do your domestic work or care about your health because of a respiratory problem?	……days	
40-before how many months, during the last 12 months, were you in a paid job?	……. months	
41- in the months during which you were working, how many paid days per week did you work?	……. days	
42-how many paid hours a day did you work?	……hours	
43- During last 12 months, were there health problems that prevented you to work?	Yes No	☐ ☐

If the answer was Yes,
continue with question 43A and
43B, if it was No, move to
question44.

43A- during the last 12 months,
what is the sum of the paid days you
were not able to work because of
health problems? ……days

43B- during the last 12 months,
what is the sum of the paid days you
were not able to work because of
respiratory problems? ……days

Lost activities other than work

The following questions are
about the time in which you can't do
your normal activities (shopping,
visiting friends and family, going to
the mosque or any other activity)

44- During last 12 months,
were there health problems that keep you from doing any activity other than work?

Yes ☐
No ☐

If the answer was Yes
continuing with question 44A and
44B, if it was No, move to done by
at the end of the questionnaire.

44A- During last 12 months, for how many
days you were not taking part in public activities
because of health problems? ……. days

44B- During last 12 months, what is the
sum of the days in which you were not taking
part in non-job-related activities particularly
because of respiratory problems? ……. days

Done by…….

3) Spirometry questionnaire

Country's code:

City's code:

ID:

Date: year/month/day:

spirometry questionnaire

Security questions

- In the last 3 months, have you had a surgery in your chest or abdomen? Yes ☐ No ☐
- In the last 3 months, have you had a cardiovascular event? Yes ☐ No ☐
- have you had ……or did a surgery in your eye? Yes ☐ No ☐
- Have you been admitted to the hospital for any other problem during the last month? Yes ☐ No ☐
- Are you in the last trimester of pregnancy? Yes ☐ No ☐

- Does the participants heart rate exceed 120 bpm at rest? Yes ☐ No ☐

- Are you currently on anti-tuberculosis medications? Yes ☐ No ☐

- Are there any reasons that prevent the participants from undergoing spirometry? Yes ☐ No ☐

If the answer for any of the questions from 1-8 is yes, the test should not be performed, move to the test results, and answer the questions 11A and 11B with "No", and chose the second option "the participant was medically excluded" for question 11c. Yes ☐ No ☐

- In the last 3 weeks, have you had a respiratory infection (cold)? Yes ☐ No ☐

0- 1-Did you take any respiratory medication in the last 24 hours? Yes ☐ No ☐

If the answer for 10-1 was yes record the name and type of medicine(s).

……
……...

if the answer for 10-1 was yes and the medicine used is in this table,

TYPE OF MEDICATION	Examples	
Short-acting beta-2 agonist	albuterol, salbutamol	6 hours prior to clinic visit
Anticholinergic inhaler	Atrovent, ipratropium	6 hours prior to clinic visit
Long-acting beta-2 agonist (including combination preparations that have a LABA)	Serevent, Advair, formoterol, Symbicort	12 hours prior to clinic visit
Oral beta-2 agonist	Albuterol	12 hours prior to clinic visit
Oral theophylline	Theodur	12-24 hours prior to clinic visit, depending upon preparation
Long-acting anticholinergic	Spiriva, tiotropium	24 hours prior to clinic visit

answer the question 10-2, if not, answer question 10-5.

0-2- did the *participant take short acting beta agonist or anticholinergic inhaler alone or combined with something else in the last 6 hours?* Yes ☐ No ☐

10-3- did the *participant take long acting Beta agonist and selective Beta2agonist alone or combined with something else in the last 12 hours?* Yes ☐ No ☐

10-4- did the *participant take* an oral theophyllin or long acting anticholinergic *alone or combined with something else in the last 24 hours?* Yes ☐ No ☐

10-5- when was your last cigarette? …….. day(s) ago

…….. hour(s) ago

Write 999 if non-smoker or ex-smoker (doesn't smoke last month).

10-6- optional

Record carbon monoxide …….

(before performing spirometry)

(before performing spirometry)	Bpm
10-7- heart rate	……
10-8- height	Cm
10-9-weight	….
10-10-A primary measure for the hip circumference.	Kg
10-10-B secondary measure for the hip circumference.	…cm
10-11-A primary measure for the waist circumference.	…cm
10-11-B secondary measure for the waist circumference.	…cm
	….c
	m

Spirometry Outcome

11A. Acceptable pre-bronchodilator test completed?

□ Yes □ N

11B. Acceptable post-bronchodilator test completed?

□ Ye

□No

11C. Unable to obtain satisfactory spirometry (check one)

The participant did not understand instructions □

The participant was medically excluded □

The participant was unable to physically cooperate □

The participant refused □

12-has the test performer seen any side effects due to spirometry?

If the answer was yes, please described these effects.

……

…….

13- does the participant have any conditions that can affect spirometry results (e.g. amputated limp, a hunchback……etc.) record this condition here.

……

……..

Done by:

4) Cigarette smoking questionnaire

Country's code: City's code: ID: Date: year/month/day: **Cigarette smokers' questionnaire**

Please, ask this question to all the participants who are still smoking:

Nicotine addiction questionnaire

- When do you smoke the first cigarette after getting up?	0-5 minutes	☐
	6-30 minutes	☐
	31-60 minutes	☐
	More than 60 minutes	☐
- Do you find it difficult to stop smoking in places where smoking is banned?	yes	☐
	no	☐
- Which kind of smoking is the most difficult to stop?	The first cigarette in the morning	☐
	Any other cigarette	☐
- how many cigarettes do you smoke daily?	10 or less	☐
	11-20	☐
	21-30	☐
	More than 31	☐
- Do you usually smoke immediately after getting up in the morning or during the day?	Yes	☐
	no	☐
- Do You smoke when you are sick, and bed ridden?	Yes	☐
	no	☐

Cigarette economy: In the following, we are going to ask you about the last time you bought cigarette for yourself.

- Have you ever bought cigarettes for yourself?
  If the answer is yes, ask the questions from6-1 to 6-6, if the answer is NO, move to question 7.

  Yes ☐
  no ☐

6-1- the last time you bought cigarettes for yourself, you bought?
(for……, enter the group and the number, chose one answer a, b, c, or d):

- A Cigarette ☐
- I- Box ☐
  ii-How many cigarettes were in the box? …….
- I-Box ☐
  ii-How many cigarettes were in the box? …….
- I-Something else: specify…….
  ii- How many cigarettes were in each?

6-2- how much did you spend for buying cigarettes?
(for the ……. if s/he doesn't know, enter 0)
Specify the country's currency… the Pound…

…….Pounds

6-3-what was the trademark of the cigarette you bought?
(consult the list of country specific answers by entering the code). The code……

……

6-4- the last cigarette you bought for yourself, where did you get it from?

Selling machine ☐
A store ☐

	A	☐
	Army store	☐
	Free duty markets	☐
	Abroad	☐
	Koisec	☐
	internet	☐
	From any other person	☐
	Other: specify ……..	☐
	I don't remember	
6-5- are the cigarettes you buy filtered or not?	With filter	☐
	Without filter	☐
6-6- are the cigarettes you smoke light, medium or heavy? **(change to country specific categories)**	Light	☐
	Medium	☐
	Heavy	☐
	Nothing of the above was written on it, we don't know	☐
- In which of these places do you smoke?		
	Cinema	☐
	Restaurant	☐
	School	☐
	Office	☐
	Bus	☐
	Airplane	☐
	None of the above	☐
- Is smoking allowed in the workplace?	Yes	☐
	No	☐
	I don't work	☐

In the following question is about your exposure to media in the last 30 days.

10- In the last 30 days, was there any type of the following smoke advertisement?

	yes	no	I don't know
- Cigarette free sample			
- Cigarette discounts			
- cigarette			
- Gifts or special deals for any other products to buy cigarettes			
- Clothes, cars, or any other things with the trade mark on it or the shape of a cigarette.			
- Cigarette deals in the mail.			
- A cigarette trade mark supporting any sport event. Done by:…….			

5) Occupational questionnaire

Country's code:
City's code:
ID:
Date: year/month/day:
BOLD occupational questionnaire

1-have you worked in one or more of the following occupations for 3 months or more? Chose Yes or No for each case Work years: (if less than one year write 00)	Yes ☐ No ☐	
a- In solid rock mines	Yes ☐ No ☐	___ ___years
b-in coal mines	Yes ☐ No ☐	___ ___years
c- Cleaning or enamelling stones or glass using the *sandblasting machine*	Yes ☐ No ☐	___ ___years
d- in asbestos (rock silk)	Yes ☐ No ☐	___ ___years
e-in plastics and petrochemical industry	Yes ☐ No ☐	___ ___years
f-in a mill	Yes ☐ No ☐	___ ___years

g- In cotton and fibre industry	Yes ☐ No ☐	___ ___years
h-In iron and steel melting	Yes ☐ No ☐	___ ___years
I- In welding.	Yes ☐ No ☐	___ ___years
j- In fire control	Yes ☐ No ☐	___ ___years
k- In agriculture	Yes ☐ No ☐	___ ___years

Questions from L-O concern some occupations that are known for being a risk factor for COPD

If you need to use these questions please contact: boldcentreuk@imperial.ac.uk

Chose Yes or No for each case		Number of working years (unless it is less than one year, write 00)
l- building	Yes ☐ No ☐	___ ___years
m-cleaning: domestic and industry detergents, working with detergents and antiseptics or other chemicals	Yes ☐ No ☐	___ ___years
n- textile	Yes ☐ No ☐	___ ___years

o-cement industry	Yes ☐ No ☐	___ ___years
2- are you regularly exposed to dust in your current occupation?	Yes No Not working currently	☐ ☐ ☐
3-are you regularly exposed to smoke in your current occupation?	Yes No Not working currently	☐ ☐ ☐
4- do you use any protective (such as mask) in your current work to protect your chest?	Yes No Not working currently	☐ ☐ ☐

4-1- currently you are: (chose one answer only)

Working (including military work)	
Working, free work.	
Unemployed, looking for work.	☐
Not working, for health reasons.	☐
At home all the time	☐
Student	☐
Retired.	☐
Other	☐
	☐

5-what is the job you have occupied for the longest time? (name the job)

.....if the participant has never worked (e.g. all the time at home) answer “never worked” and move to question 6.

5-A-what exactly the work you do in your job? (describe)

5B- What is the industry you are working in now?

5C-how many years have you been working in this job? ___ ___years

5D-do you work as:

- Administrative? Yes ☐ No ☐
- Supervisor? Yes ☐ No ☐
- Worker and not administrative or supervisor? Yes ☐ No ☐
- free worker Yes ☐ No ☐

5E- enter ISCO code

6- Have you ever decided to leave your job because it causes respiratory problems to you? Yes ☐ No ☐

If the answer is yes, ask the questions from6 A to 6E, if the answer is NO, move to the next question.

6A-what is this job? (name it)

6B-what do you do exactly in this job? (describe)

..... ___

6c- how many years do you have in this job? ___years

6D-at that time, what is the industry you were working in?

Yes ☐

No ☐

6E-do you work now as:

Yes ☐

- Administrative? No ☐

- Supervisor? Yes ☐

No ☐

- Worker and not administrative or supervisor?

Yes ☐

d- free worker? No ☐

6E- enter ISCO code --------

Done by……

6) Biomass fuel questionnaire

Country's code:

City's code:

ID:

Date: year/month/day:

the resident's questionnaire about her daily use of fuel

1- have you ever used charcoal as a major cooking fuel in your house for more than 6 months? Yes ☐

If the answer to question 1 is yes, ask the questions from A1 to D1, if the answer is NO, move to question 2. no ☐

A1-how many years have you been using charcoal for cooking in your house? ..... years

B1- in average, how many hours daily do you personally spend cooking with charcoal? ..... hours

C1-Do you still use charcoal for cooking in your house? Yes ☐ No ☐

D1- does the smoke go outside through a chimney or a window? Yes ☐ No ☐

2- have you ever used wood, straw, crop residues or animal wastes as a major cooking fuel in your house for more than 6 months? yes ☐ no ☐

If the answer to question 1 is yes, ask the questions from A2 to D2, if the answer is No, move to question 3.

A2-how many years have you been using wood, straw, crop residues or animal wastes for cooking in your house? ..... years

B2- in average, how many hours daily do you personally spend cooking with wood, straw, crop residues or animal wastes? ..... hours

C2-Do you still use wood, straw, crop residues or animal wastes for cooking in your house? Yes ☐ No ☐

D2- does the smoke goes outside through a chimney or a window? Yes ☐ No ☐

3- have you ever used charcoal as a major way for warming/heating in your house for more than 6 months? yes ☐ no ☐

If the answer to question 3 is yes, ask the questions from A3 to B3, if the answer is No, move to question 4.

A3-how many years have you been using charcoal as a major way for warming/heating your house? ..... years

B3-Do you still use charcoal as a major way for warming /heating your house? Yes ☐ No ☐

4- Have you ever used wood, straw, crop residues or animal wastes as a major way for warming/heating in your house for more than 6 months? yes ☐ no ☐

If the answer to question 4 is yes, ask the questions from A4 to B4, if the answer is No, move to question 4-1.

A4-how many years have you been using wood, straw, crop residues or animal wastes as a major way for warming/heating your house? ..... years

B4-Do you still use wood, straw, crop residues or animal wastes as a major way for warming /heating your house?	Yes No	☐ ☐
4-1 have you ever used wood, straw, crop residues or animal wastes as a major way for heating water in your house for more than 6 months? If the answer to question 4-1 is yes, ask the questions from A4-1 to B4-1, if the answer is No, move to question 4-2.	yes no	☐ ☐
A4-1 how many years have you been using wood, straw, crop residues or animal wastes as a major way for heating water in your house?	..... years	
B4-1 Do you still use wood, straw, crop residues or animal wastes as a major way for heating water in your house?	Yes No	☐ ☐
4-2 have you ever used Kerosene as a major cooking fuel in your house for more than 6 months? If the answer to question 4-2 is yes, ask the questions from A4-2 to D4-2, if the answer is No, move to question 5.	yes no	☐ ☐
A4-2 how many years have you been using Kerosene for cooking in your house?	..... years	
B1- in average, how many hours daily do you personally spend cooking with Kerosene?	..... hours	
C1-Do you still use Kerosene for cooking in your house?	Yes No	☐ ☐

D1- does the smoke go outside through a chimney or a window? Yes ☐ No ☐

5- what is the fuel that is used the most in your house for cooking: (you can choose more than one answer)

- Electricity □
- Gas □ (liquefied petroleum gas LPG)
- Kerosene □
- Charcoal □
- Wood □
- Hay □
- Crop residue □
- Other □ …… specify:

6- how many hours do you spend cooking every day?

……..hours

6-1- Do your eyes get teary or itch when you are cooking?

☐No, never

☐ yes, sometimes

☐yes, always

7- in your house, where most of the cooking is done?

(chose one answer only)

- Outside, in the plain air.
- Outside, in an isolate room.
- Inside, in the kitchen.
- Inside, in the living room.

If the answer is yes to question 7b,7c, or 7d continue to question 8 otherwise move to question 12.

8- is there a chimney in the house? Yes ☐ No ☐

9-is there an extractor hood in the house? Yes ☐ No ☐

10-are there open doors and windows in the room? Yes ☐ No ☐

11- How many hours do you spend in this room daily? ……..hours

12- do you heat your house? Yes ☐ No ☐

If the answer is yes continuing to question 13 if No move to the next question.

13- How many months in the year do you heat your house most of the time? …….. months

14- Is there a heater or stove in the house? Yes ☐ No ☐

If the answer is yes answer question 14-A, if it is No answer question 14-B.

14-A- in case the answer was yes: does the smoke go outside through a chimney? Yes ☐ No ☐

14-B-- in case the answer was no: are there open doors or windows? Yes ☐ No ☐

15- what is the fuel that is used the most for warming the house? (you can choose more than one answer)

- Electricity □
- B- gas □ (liquefied petroleum gas LPG)
-) Kerosene □
-) Charcoal □
-) Wood □
-) Hay □
-) Crop residue □
-) Other □ …… specify:

Done by……

7) Minimal data and refusal questionnaire

Country's code:

City's code:

ID:

Date: year/month/day:

Minimal data/ refusal questionnaire

Demographic data:

1-What is the participant's gender? Male ☐ Female ☐

2-Date of birth? ____ ____ /____ ____ /____ ____ ____ ____

Respiratory symptoms and disorders:

3-Have you ever been told by a doctor that you have: emphysema, asthma , asthmatic bronchitis, chronic bronchitis, or chronic obstructive pulmonary disease Yes ☐ No ☐

Co morbidities:

4-Have you ever been told by a doctor that you have: Cardiovascular disease, hypertension, diabetes, lung cancer, stroke, or tuberculosis? Yes ☐ No ☐

Cigarette smoking:

The following questions are about smoking

5-Have you ever smoked cigarette or water pipe or used tumbac? Yes ☐ No ☐

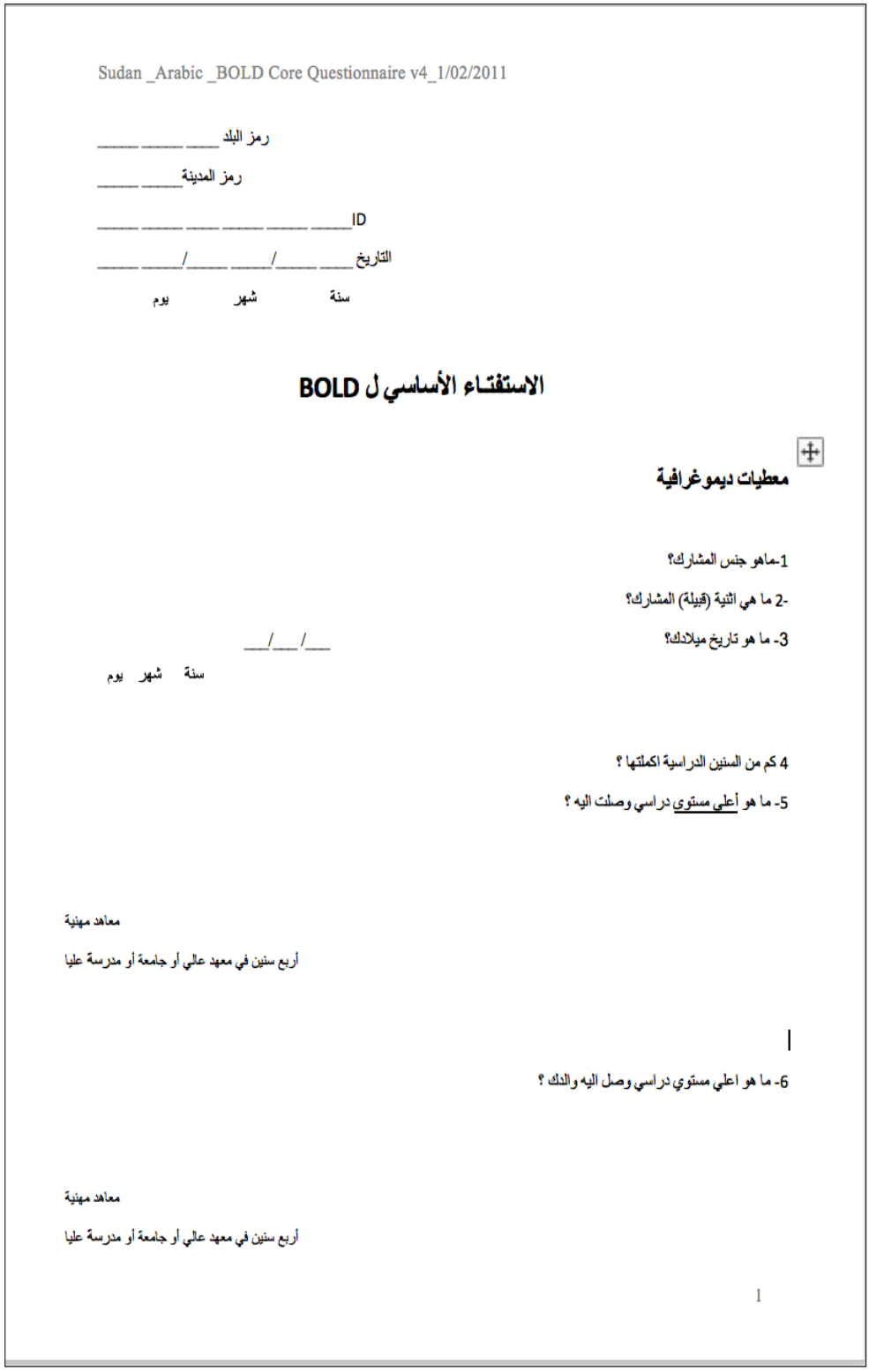
(yes, about more than 20 boxes of cigarette, water pipe or tumbac in my life, or more than one cigarette, water pipe or tumbac sniff every day for an year)

If the answer was Yes, ask question 5-A and 5-B

5-A- do you still smoke cigarette or water pipe or used tumbac? Yes ☐ No ☐

What is the rate in which you are smoking cigarette or water pipe or using tumbac?	____ ____cigarettes/day ____ ____water pipes/day ____ ___sniffs/day
Done by:……	

8) Snapshot of Arabic version of core questionnaires



Sudan _Arabic _BOLD Core Questionnaire v4_1/02/2011

رمز البلد _____ _____ _____

رمز المدينة_____ _____

ID_____ _____ _____ _____ _____ _____

التاريخ ____/_____/_____ _____/_____

سنة شهر يوم

الاستفتـاء الأساسي ل BOLD

معطيات ديموغرافية

1-ماهو جنس المشارك؟

2- ما هي اثنية (قبيلة) المشارك؟

3- ما هو تاريخ ميلادك؟ ___/___/___

سنة شهر يوم

4 كم من السنين الدراسية اكملتها ؟

5- ما هو أعلى مستوي دراسي وصلت اليه ؟

معاهد مهنية

أربع سنين في معهد عالي أو جامعة أو مدرسة عليا

6- ما هو اعلي مستوي دراسي وصل اليه والدك ؟

معاهد مهنية

أربع سنين في معهد عالي أو جامعة أو مدرسة عليا

1

Appendix (4) Khartoum and Gezira sampling plans

a) BOLD Khartoum sample plan

BOLD Sampling Plan

Centre name: Khartoum - Sudan

Contact for queries about sampling: name: Nada Bakri and Bandar
email: nano1b2000@yahoo.com
bnhome66@yahoo.com
phone: +249912251949

POPULATION

What is your population of interest? (Note, this should be defined by meaningful administrative boundaries)

The target population will be every person 40 years and above, who is living in Khartoum State. Khartoum State constitutes of 7 localities with different population size per each one. Three localities were randomly selected :

1. Jabal Awlia
2. Omdurman
3. Sharg Al Nile

- The distribution of 40years and above population will be determined according to the following equation:

(a = POP/HH,
a: average
pop: Population older than and equal 40 years
HH: Number of household
a= 1,008,659/871,142 = 1.16)
in other word for each house hold there will be 1.16 person of age 40 or more
According to the above the number of HHs have to be surveyed will be = 800/1.16 = 690.

Give a brief, general background on the population (if possible, include information that might be relevant for studies of COPD, e.g. air quality measurements, key industries)

Khartoum state population are urban, sub-urban, rural, and IDPS (Internal Displaced persons), the 3 mentioned localities are contained of all these population type. There are many industries in Khartoum such as leathers, soap, paint. Regarding other related factors to COPD, until now there is no previous study conducted to address the prevalence of COPD.

What is the total population **of all ages**? (if not known precisely, give an approximate figure)

The total population of Khartoum state: 5,274,321

The total of the three selected localities: 661,617

If figures are available *e.g.* from census data, tabulate the total population **aged 40 or over**, by sex, age-group, or other relevant grouping

State / Age	Total			Urban			Rural		
	Total	Male	Female	Total	Male	Female	Total	Male	Female
Total	**5,181,186**	**2,725,185**	**2,456,002**	**4,194,719**	**2,219,026**	**1,975,694**	**986,467**	**506,159**	**480,308**
00 - 04	650,463	332,424	318,039	505,999	258,809	247,190	144,464	73,615	70,849
05 - 09	586,309	297,985	288,324	454,584	230,264	224,320	131,725	67,721	64,004
10 - 14	559,694	288,776	270,917	438,313	225,452	212,860	121,381	63,324	58,057
15 - 19	554,527	290,609	263,918	449,562	236,254	213,308	104,965	54,355	50,610
20 - 24	593,343	317,152	276,191	496,443	268,852	227,591	96,900	48,300	48,600
25 - 29	496,553	261,664	234,889	414,011	221,878	192,133	82,542	39,786	42,756
30 - 34	375,256	199,249	176,007	310,738	167,043	143,695	64,518	32,206	32,312
35 - 39	356,383	184,869	171,514	293,114	153,365	139,749	63,269	31,504	31,765
40 - 44	262,427	140,635	121,791	216,936	117,262	99,673	45,491	23,373	22,118
45 - 49	206,490	112,590	93,900	170,421	93,249	77,172	36,069	19,341	16,728
50 - 54	167,596	91,912	75,684	139,838	76,973	62,865	27,758	14,939	12,819
55 - 59	100,207	55,819	44,388	83,526	46,790	36,736	16,681	9,029	7,652
60 - 64	95,994	54,428	41,566	79,573	45,272	34,301	16,421	9,156	7,265
65 - 69	59,102	33,997	25,105	48,574	28,029	20,545	10,528	5,968	4,560
70 - 74	55,045	29,576	25,469	44,473	23,620	20,853	10,572	5,956	4,616
75 +	61,798	33,498	28,300	48,615	25,912	22,703	13,183	7,586	5,597

SAMPLING

For simple or stratified random sampling:

How will participants be selected, and how many people will be contacted? Describe any stratification.

See below.

Tabulate the total numbers of people in your sampling frame, by age, sex or other relevant grouping.

See above.

For multi-stage designs:

List the sampling stages (there is space on the form for describing up to three stages – if you are planning more than three you should discuss the practicality of this with the Coordinating Centre):

Stage 1: Locality
Stage 2: Area
Stage 3: Household

Stage 1 : Locality

How will sampling units be selected, and how many sampling units will be chosen? Describe any stratification.

Three localities out of the seven were selected randomly.
The sample size per each locality will come out as the result of the calculation of locality population and the total number of the sample and it will be:
280 in Jabal Awalia
258 in Sharg Al Nile
153 in Omdurman.

How will sampling units be identified or coded in the database?

The localities were coded as:

Jabal Awlia	1
Omdurman	2
Sharg Al Nile	3

How will you determine and record the total number of sampling units available to be sampled? If numbers of sampling units are already known, tabulate them here.

These are already known (see above)

Stage 2: Area

How will sampling units be selected, and how many sampling units will be chosen? Describe any stratification.

- Clusters will be formed, by the following;

Total number of HHS in each locality / 15(No of HHS in each cluster):
280/15 = 19 cluster in Jabaj Awlia
258/15 = 17 cluster in Sharg Alnile
158/15 = 11 cluster in Omdurman

- The sample interval is determined in each locality as following:

TOT of cumulative HHS/ Total number of clusters in each locality, which calculated as following:
* Jabal Awlia:
154993/19 = 8157.5
The random start calculated as following:
Random start = interval + First start
First start = interval * RAND (0- 1)
First start = 1742.60
Random start = interval + first start
Then 19 Areas selected randomly as following:

- Table (1)

#	Select Area	HHS	POP
1	Alfitaih Alagaleen block west	705	4244
2	Alshigalab Alhasania	1287	8382
3	Aldwha	310	1922
4	Darelsalam block 8	1217	7224
5	Alazhary block 21/22	734	4560
6	Alazhary block 18	505	3138
7	Soba Alarady	15251	83951
8	Soba Alarady	15251	83951
9	Alfardos	563	3561
10	Alnasir west block 14 B	794	4981
11	Almansora block 3	987	5920
12	Alwihda west block 2	2087	13087
13	Alwihda west block 6	1529	7615
14	Maio AL Salam / G	808	4293
15	Al farooq 2,4,11	1224	7326
16	Al goba North 3,5	1525	10003
17	Al klakla Sangat west	1960	12073
18	Al wihda block 1	932	5964
19	Abu ayob Alansary block 5	557	3257
	Total	32975	

* Sharq Alnile:
145177/17 = 8539.8 which is the sample interval in this locality.
First start = interval * RAND (0 – 1) = 2665.14
Random start = interval + first start.

The 17 Areas selected as following:

- Table (2)

#	Selected Area	HHS	POP
1	Alsidair	224	1204
2	Altawidat block 3/4	872	4520
3	Alkarba	138	647
4	Wadhasoona south	444	2624
5	Umdwanban south west	1201	9625
6	Alkiriab	621	3418
7	Alhofra west	95	533
8	Shigla Alsafa village	1601	10309
9	Al imtedad south east	2053	13072
10	Wadelbashir west	1855	12836
11	Dar alsalam south	5587	35951
12	Alwihda west	2949	19712
13	Alhaj Yousif Algadeema	2459	14754
14	Algigaif east block 2 west	516	2955
15	Umdom south	1295	6349
16	Aleskan Alshaby	198	1198
17	Alhaj Yousif east	2242	14186
	Total	24350	

Omdurman:
84956/ 11 = 7723.3 = sample interval
First start = interval * RAND (0 – 1)
Random strat = First start + interval
First start = 2017.29
Table (3)

11 clusters containing areas are selected as following:

#	Select Area	HHS	POP
1	Hijailija	2092	12794
2	Salha east	938	5838
3	Tirais	479	2817
4	Siraw	1309	8088
5	Aborof and Higra	643	3338
6	Shohada north	244	1289
7	Almowrada east	324	1719
8	Aldwha	1049	7611
9	Moraba 6 (Block 6) Morabat	1212	8036
10	Moraba(block) 11 (Morabat)	410	2532
11	Moraba(block) 22 Albank alagary	1197	8073
	Total	9897	

How will sampling units be identified or coded in the database? (If sampling units are individuals they will be identified using a unique 6-digit BOLD ID number.)

By digits

Jabaj Awlia 1- 19

1 (name of area 1)
2 (name of area 2)
3 (name of area 3)…
…
19 (name of area 19)
:

Sharg Alnile 1- 17

1 (name of area 1)
2 (name of area 2)
3 (name of area 3)…
…
17 (name of area 17)

Omdurman 1- 11

1 (name of area 1)
2 (name of area 2)
3 (name of area 3)…
…
11 (name of area 11)

How will you determine and record the total number of sampling units available to be sampled? If numbers of sampling units are already known, tabulate them here.

Stage 3: Household

How will sampling units be selected, and how many sampling units will be chosen? Describe any stratification.

The total number of houses in the concerned area divided by the total number of the houses in the concerned locality gives the ratio of the concerned area to the total number of houses, then this ratio will multiply by the number of the sample that was selected for the locality to give the number of houses required for the area. For example:
Alfitaih Alagaleen block (area) has 705 Houses and the total number of houses in 19 selected areas of locality of Jabal Awlia are 32975

705/32975=0.02
0.02 * 280 =6
That is mean for Alfitaih alagaleen 6 houses will be selected from 705

(See Microsoft excel as attached file for the three selected areas)

How will sampling units be identified or coded in the database? (If sampling units are individuals they will be identified using a unique 6-digit BOLD ID number.)

Within each area, we will number the households consecutively from 1 - xxx

How will you determine and record the total number of sampling units available to be sampled? If numbers of sampling units are already known, tabulate them here.

All the selected houses in each area are consecutively numbered. Within those households selected we will include all eligible adults aged 40 or above years old.

See the Microsoft excel file

b) BOLD-Plus Gezira sample plan

Centre name: Gezira State, Sudan

Contact for queries about sampling: name: Rana Atta and Rashid Osman

email: rana.atta85@gmail.com

rashildo@hotmail.com

phone: +249912927665

POPULATION

What is your population of interest? (note, this should be defined by meaningful administrative boundaries)

Adults aged 18 and above living in rural Gezira State, Sudan:

Give a brief, general background on the population (if possible, include information that might be relevant for studies of COPD, e.g. air quality measurements, key industries)

The Gezira state population is urban, rural, and nomadic. This study contrasts with the recently completed Khartoum BOLD study by a predominance of rural and nomadic populations. Farming is the most common occupation and with farming-related exposures expected to dominate. There are no previous studies of the prevalence of chronic airways disease and its risk factors in the State.

What is the total population **of all ages**? (if not known precisely, give an approximate figure)

The total population of Gezira state is 3575280

If figures are available *e.g.* from census data, tabulate the total population **aged 40 or over**, by sex, age-group, or other relevant grouping

See below table

Gezira State			Gender
	Total	**Males**	**females**
Age group	3,575,280	1,724,330	1,850,950
15 - 19	394,011	187,435	206,576
20 - 24	323,837	143,704	180,133
25 - 29	273,472	117,082	156,390
30 - 34	213,878	93,780	120,098
35 - 39	214,234	94,639	119,595
40 - 44	162,516	75,335	87,181
45 - 49	133,179	65,181	67,998
50 - 54	112,953	54,807	58,146
55 - 59	69,173	36,174	32,999
60 - 64	72,602	37,085	35,517
65 - 69	45,076	24,787	20,289
70 - 74	48,854	25,326	23,528
75 +	62,574	34,463	28,111
Total	3,575,280	1,724,330	1,850,950

SAMPLING

For multi-stage designs:

List the sampling stages (there is space on the form for describing up to three stages – if you are planning more than three you should discuss the practicality of this with the Coordinating Centre):

Stage 1: Localities

Stage 2: Villages

Stage 3: Households

Stage 1

How will sampling units be selected, and how many sampling units will be chosen? Describe any stratification.

Gezira state is divided into seven localities. We have selected three of these localities to include in this study using a simple random sampling approach using Excel:

1. Sharg Algezira
2. Wad Medani
3. Alkamleen

How will sampling units be identified or coded in the database?

Locality	Code
Sharg Algezira	1
Wad Medani	2
Alkamleen	3

How will you determine and record the total number of sampling units available to be sampled? If numbers of sampling units are already known, tabulate them here.

We have selected the three localities as above. The total population of the three selected localities is 1288947.

Stage 2

How will sampling units be selected, and how many sampling units will be chosen? Describe any stratification.

Each of the three localities is divided into several administrative units each of which is divided into villages/areas as summarised below. A simple random sample of 5% of the villages (n=35) villages will be selected.

Admin Unit	Total	HHS	Villages/area
Algazeera East	463,154	78,831	
Wad_rawah Town and Rural	85,516	15,272	61
Tambool Town and Rural	141,078	24,109	115
Alhilallia Town and Rural	91,221	14,940	39
Rufaa Town	28,374	4,701	25
Rufaa Rural	116,965	19,809	79
Alkamleen	401,930	66,814	
Alsinaat	105,788	18,318	53
Almaseed Rural	108,199	17,003	37
Alkamleen Town and Rural	88,995	14,559	54
Almiailiq Town and Rural	98,948	16,934	67
Wad Madani Alkoobra	423,863	69,326	
Alshabarga	32,330	5,066	25
Hantoob	79,574	13,286	33
Madani North-West	80,577	12,937	28
Madani Central	75,864	12,976	37
Alwaha (Madani-East)	67,074	11,031	17
Alsouq Almarkazi	88,444	14,030	19

How will sampling units be identified or coded in the database? (If sampling units are individuals they will be identified using a unique 6-digit BOLD ID number.)

Each village will be given a unique identifying number.

How will you determine and record the total number of sampling units available to be sampled? If numbers of sampling units are already known, tabulate them here.

The total number of sampling units is summarised in table above (689 villages).

Stage 3

How will sampling units be selected, and how many sampling units will be chosen? Describe any stratification.

Each household in Gezira State has on average 3 adults.

We plan to sample approximately 2000 adults in total with the aim of having complete datasets on approximately 1200 participants.
By including 1000 households we anticipate being able to sample 2000-3000 adults.
We will seek to include all eligible individuals in the households to increase the efficiency of recruitment whilst recognising the impact of household-level clustering.
Since we will include 35 villages we will sample 1000/35 = 30 (rounded up to nearest 10) households per village.
A mapping exercise will then be conducted in each village/area to count and locate all households including nomadic households present at the time of the mapping and campo (migrants from other states) residents.
Sampling of households at village level will be a simple random sample of all households in the village.

How will sampling units be identified or coded in the database? (If sampling units are individuals they will be identified using a unique 6-digit BOLD ID number.)

Sampling units will be individuals identified using a unique 6-digit BOLD ID number

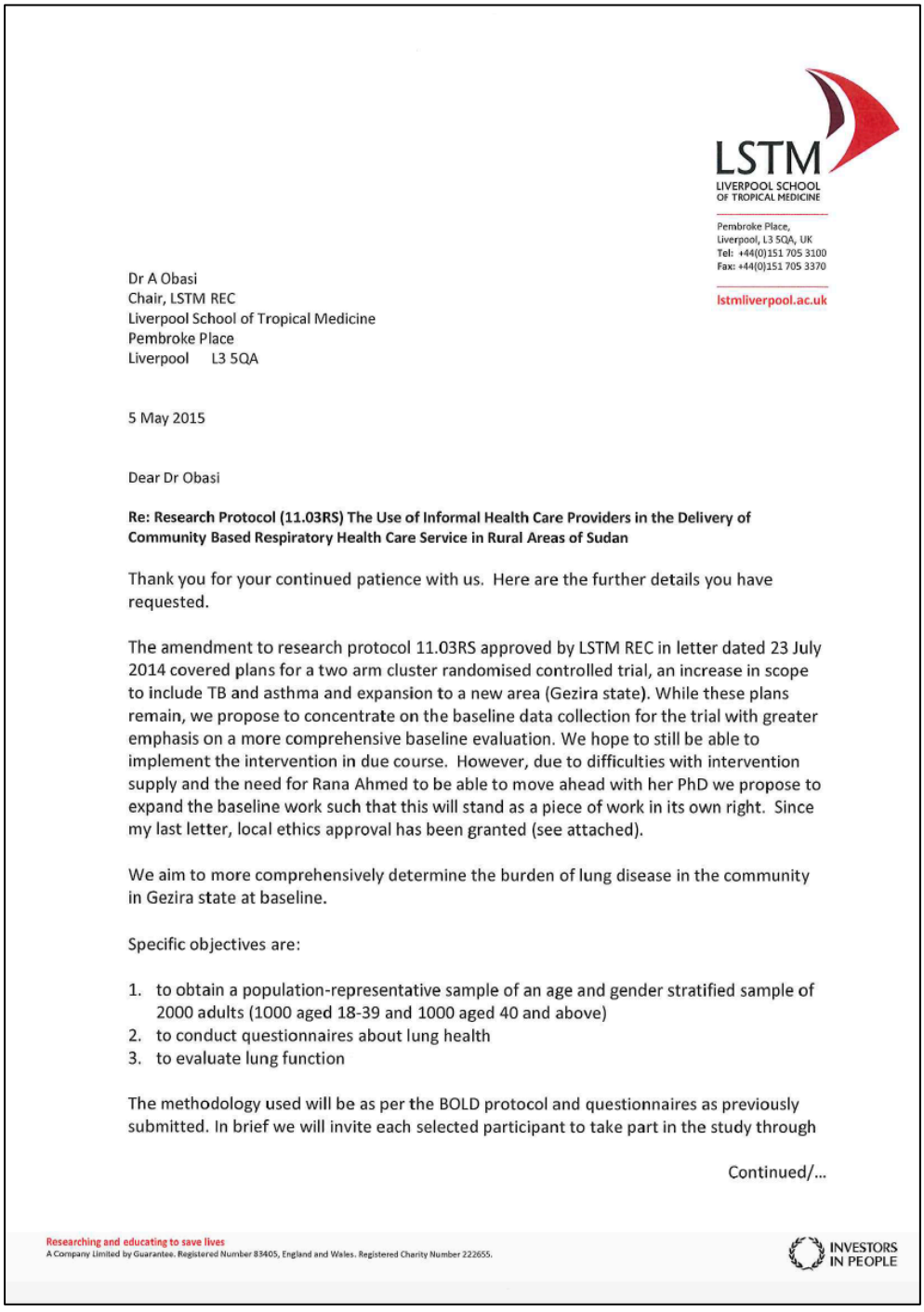
How will you determine and record the total number of sampling units available to be sampled? If numbers of sampling units are already known, tabulate them here.

At the village level we will use locally available household enumeration data.

Appendix (5) Ethics approvals

Below are ethics approval from the Ethical Review Committee of the Liverpool School of Tropical Medicine (LSTM) ,he BOLD operation centre at the Imperial collage London and the Gezira Ministry of health Wad Medani, Khartoum Ministry of Health Sudan.

a) LSTM Ethical amendment letter for BOLD Gezira study



LSTM
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lstmliverpool.ac.uk

Dr A Obasi
Chair, LSTM REC
Liverpool School of Tropical Medicine
Pembroke Place
Liverpool L3 5QA

5 May 2015

Dear Dr Obasi

Re: Research Protocol (11.03RS) The Use of Informal Health Care Providers in the Delivery of Community Based Respiratory Health Care Service in Rural Areas of Sudan

Thank you for your continued patience with us. Here are the further details you have requested.

The amendment to research protocol 11.03RS approved by LSTM REC in letter dated 23 July 2014 covered plans for a two arm cluster randomised controlled trial, an increase in scope to include TB and asthma and expansion to a new area (Gezira state). While these plans remain, we propose to concentrate on the baseline data collection for the trial with greater emphasis on a more comprehensive baseline evaluation. We hope to still be able to implement the intervention in due course. However, due to difficulties with intervention supply and the need for Rana Ahmed to be able to move ahead with her PhD we propose to expand the baseline work such that this will stand as a piece of work in its own right. Since my last letter, local ethics approval has been granted (see attached).

We aim to more comprehensively determine the burden of lung disease in the community in Gezira state at baseline.

Specific objectives are:

1. to obtain a population-representative sample of an age and gender stratified sample of 2000 adults (1000 aged 18-39 and 1000 aged 40 and above)
2. to conduct questionnaires about lung health
3. to evaluate lung function

The methodology used will be as per the BOLD protocol and questionnaires as previously submitted. In brief we will invite each selected participant to take part in the study through

Continued/...

b) LSTM Ethics approval for BOLD Gezira study

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Professor S B Squire
Liverpool School of Tropical Medicine
Pembroke Place
Liverpool
L3 5QA

Monday, 18 May 2015

Dear Professor Squire,

Re. Research Protocol (11.03RS) The Use of Informal Health Care Providers in the Delivery of Community Based Respiratory Health Care Service in Rural Areas of Sudan: Amendment 2

Thank you for your letter of 5 May 2015 providing the committee with details of amended objectives and method for the above-named study (amendment 2).

This amendment has now been reviewed, noted and accepted on the behalf of the committee. Please continue to adhere to the conditions of approval and to update us of any further changes to the study that may arise.

Yours sincerely,

Dr Angela Obasi
Chair
LSTM Research Ethics Committee

c) LSTM ethics approval for comparison between smartphone and paper-based data collection study in BOLD Gezira study

Dr. Kevin Mortimer
Liverpool School of Tropical Medicine
Pembroke Place
Liverpool
L3 5QA

LSTM
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Thursday, 25 February 2016

Dear Dr. Mortimer,

Research Protocol (11.03RS) The Use of Informal Health Care Providers in the Delivery of Community Based Respiratory Health Care Service in Rural Areas of Sudan

Thank you for your letter of 15 February 2016 providing the Committee with details of the inclusion of a comparative electronic data collection tool, in parallel with the existing paper data collection method.

This amendment has now been reviewed, noted and accepted on the behalf of the Committee. Please continue to adhere to the conditions of approval and to update us of any further changes to the study that may arise.

Yours sincerely,

Dr Angela Obasi
Chair
LSTM Research Ethics Committee

Researching and educating to save lives
A Company Limited by Guarantee. Registered Number 83405, England and Wales. Registered Charity Number 222655.

Athena SWAN Bronze Award
INVESTORS IN PEOPLE

d) Ethics approval, Gezira Ministry of Health

بسم الله الرحمن الرحيم

GEZIRA STATE
MINISTRY of HEALTH

ولاية الجزيرة
وزارة الصحة
تلفون : 0511-844666

الإدارة العامة للتخطيط والتنمية

النمرة 44/ت/خ/ا
التاريخ 5 /2015/3

السلام عليكم ورحمة الله وبركاته ،،،،،،،،،،

الموضوع: Ethical approval

جمعية البحوث العلمية للصحة العامة(المعمل الوبائي)

Project title;
Burden of Lung DiseasesBOLD- (Chronic Obstructive Pulmonary Disease COPD). Within the projeeet(Triage plus phase 2).The use of in formal health care providers in the delivery of community based respiratory health care services in rural areas of sudan .

دراسة عن امراض الرئة ضمن مشروع التقصي المبكر للاصابة بالسعال المزمن مرضي (الازمة ,الدرن) خلال العام 2015م

بهذا توافق وزارة الصحة علي إجراء البحث بولاية الجزيرة.

وزارة الصحة ولاية الجزيرة
الإدارة العامة للتخطيط والتنمية
د. عبدى جعفر حاجوب
مدير الادارة

صوره الى:
- الملف

Appendix (6) Data management strategic plan for BOLD Gezira

Project Title: BOLD Plus -Gezira State -Sudan
Data Owners: Epi-Lab BOLD Team/LHL LSTM Consultants/Imperial College
Data Managers: Rana Ahmed
Other Contributors and Roles: Rashid Kamal, Co-investigator

Data Management Plan-BOLD-Plus project
May 2015

Overview:

This plan is designed to define the procedures that are performed in flow monitoring and/or other aspects of the BOLD-Plus project as part of Epi-Lab database to ensure the accuracy and usability of the data after the raw data has been collected.
The Principal investigator who is responsible for the management of data for the study should:
o Develop instructions in the case where data management is performed directly within the Epi-Lab.
o Manage authorizations for access to data
o Ensure the protection and security of data
o Ensure confidentiality of the identity of subjects

1. Field data management:

Filed data management means the first step in the collection of data as follow:

1- Design the data collection tools (when needed) which are the responsibility of project researchers
2- Data collection tools to be revised by Data management unit of the Epi-Lab and approved by the project consultants (LSTM and LHL).
3- Piloting and Testing of data collection tool at the field by the data collectors.

4- Collection of data: The collection of the data will be daily during the project life cycle except for weekends and national holidays.

3 Project Data Types and Structure

- BOLD plus project has seven types of questionnaires, they contain quantitative data and each of them covered a special area of the study.
- Data will be interred directly from collected paper's questionnaires using imperial college online data entry system.
- One questionnaire will be designed by Epi-Lab researchers and entered in BOLD Plus data entry designed form in Epi-info data format.
- In addition readings from spirometer will be stored.

4 Data Acquisition, Integrity and Quality

- Trained data collectors/researchers will collect data.
- The training of the team will cover Overview on the project, data collection tools and techniques, practical work on filling questionnaires and data ethics.
- The team will be divided into small teams and they will have a field supervisor.
- Field supervisor is responsible for ensuring data accuracy, integrity, and completeness.
- The field supervisor will carry out daily onsite field verifications and any incorrect questionnaire will be terminated.
- Data will then be stored in a separate and locked cabinet.
- Daily and a weekly Backup plan will be followed.
- Two data entry personnel will be assigned to use the online entry system. They will ensure that entry is up to date will the collection.

5 Procedure for Compiling and Managing Field notes/checklist

- Site Data and field notes

At least every 7 days, the field supervisor shall provide notes about data collection and field experience, all data should be looked at thoroughly and any noticeable problems with the data or site will be recorded in the field notes.

- Upon returning to the office after site visits, the field notes entries should be placed in the project desktop computers and saved to the server/backup PC.

5. Data management:

- The coordinator of the project with statistician must supervise the submission/verification of the collected data from the data collectors.
- The Collected data to be handled by the coordinator of the project to the Data entry personnel and entered daily on the BOLD study platform.
- The cleaning of data it's the responsibility of the project statistician and to be on monthly basis.

6. Procedures for data backup:

- Data backup is the responsibility of the field supervisor and project statistician in addition to close supervision from the project coordinator.
- Frequent backup to ensure the safety of data will be carried out.

- Following Epi-Lab SOP: Data backup should be also conducted at least once every month in the backup server.

7. Confidentiality and Ethical Procedures:

- All data should be anonymous, no names or other personal identification of study participants should be kept nor collected.
- Complete datasets should be placed in the backup pc and no editing /changes is allowed after the backup.
- A restricted data use form should be provided by a person (other than data owners) authorized to access the data and signed by the management and data management unit responsible person.

- No complete data set should be provided to anyone(other than data owners), only aggregated data.
- Accessibility to the final dataset of the project from The BOLD operation centre to Epi-Lab researchers shall be provided as in the agreement.
- No personal information or data of a secret nature regarding project interviewee will be stored or shared.
- Data will then be stored in a separate and locked cabinet only accessible by project researchers and data entry personnel.

8. Security:

- No USB disk should be used on the entry PC, only the backup external hard disk
- Only the entry personnel, project coordinator and project statistician should know the restricted complex password of the entry pc.
- Antivirus software should be installed and updated frequently

9. Publications: Following the Epi-Lab SOP

- All data obtained in the project within the Epi-Lab is the property of the Epi-Lab
- All researchers who wish to use the Epi-Lab data for publication purpose are required to follow the Epi-Lab publications SOP and sign the data use agreement form.
- Epi-Lab (Director / PIs of any project/Section/research) will be included as an author in all publications that used the organization data.
- Epi-Lab researchers who are working in the BOLD project should agree on authorship orders before starting the paper/article drafting.
- All published papers/Articles that used the Epi-Lab data must be given back to the Epi-Lab to link it with the database with a purpose of research continuation and follow-ups.

Appendix (7) Standard operating procedures for data collection using both paper-based and mobile based methodology

The two collection methods will run in parallel during the data collection. Randomization on which methodology will be used to administer the questionnaire will be conducted prior to start the data collection. Below are SOPs to be followed in conducting this part of the study.

- **Pre-field preparation**
  - Make sure mobile phones are fully charged.
  - Take your spare batteries.
  - Make sure you took the field diary to record all events during data collection.
- **On-field procedures**
  - Selection of the participant should follow the overall BOLD study. This should be done daily before data collection starts to follow BOLD-Plus survey samples selection.
  - the participant should be consented before starting the data collection and be aware by using the mobile technology in parallel with the paper-based questionnaire.
  - Randomization of using which method to administer the questionnaire should be done before starting data collection.
  - Survey completion can take place offline, and no network coverage is necessary.
  - If there is no mobile network coverage, completed surveys will be stored securely until a signal is found at which time completed surveys are uploaded.
  - the data collector can incorporate multiple choice, free text, numeric, date, time, and other question types. In addition, data collector should follow the flow of the designed questionnaire with all skips pattern and don't edit or interfere with the skips pattern.
  - in case of questions administered by the paper-based data collectors, mobile data collector should follow the paper-based data collector in answering the questions. In case of asking the different/wrong question, the mobile data collector should fill out the questions he/she thinks correct and vice versa.

o in the opposite situation, paper-based data collector should follow the mobile-based data collector in filling out the questionnaire with no interference of questions asking during the collection time. However, in case of asking different or wrong question the above methodology should be followed.

o in both situations of administering the questionnaire, no interference should be allowed to correct or modify the other researcher work in filling out the questionnaire. However, data collector may ask the question skipped or wrongly administered at the end of the interview.

o Investigators may not collect any data from individuals who decline to Participate. In case of withdrawal, the investigator should record that on the field diary.

o in case of running out of power during the data collection, other researched should carry on and this should be recorded in the field diary.

- Investigators must not collect any data that is not explicitly approved by the research participant in the consent document.

Security consideration:

o During the field visits, mobile phones shouldn't be left unwatched on a desk, chair, or bed in the houses you visit.

o Mobile phones should be kept in researcher pocket or handbag, before and after the completion of data collection.

o Researcher should make sure he/she saves all collected forms after finishing the interview.

o No forms should be submitted after the completion of the data collection. Researcher should just save it.

o in case you accidentally closed ODK application, researcher is advised to restart the application, most of the time it will open again where left.

o If the application crashes during the data collection, researcher should restart the phone then restart the application and check if the data you were entering have been saved. You should find it back in the "Edit Saved Form" menu.

o in case of each of the above situations, researcher should continue the data collection if the form is still saved. Otherwise, the other data collector should carry on and continue in his/her own.

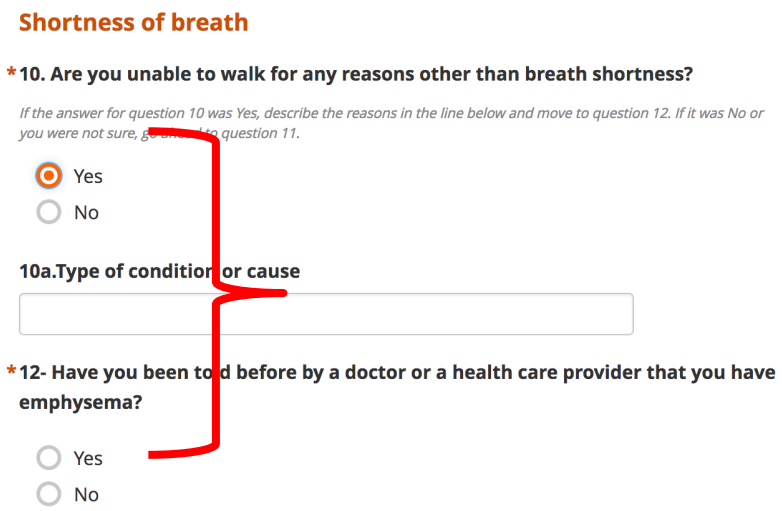
Power considerations:

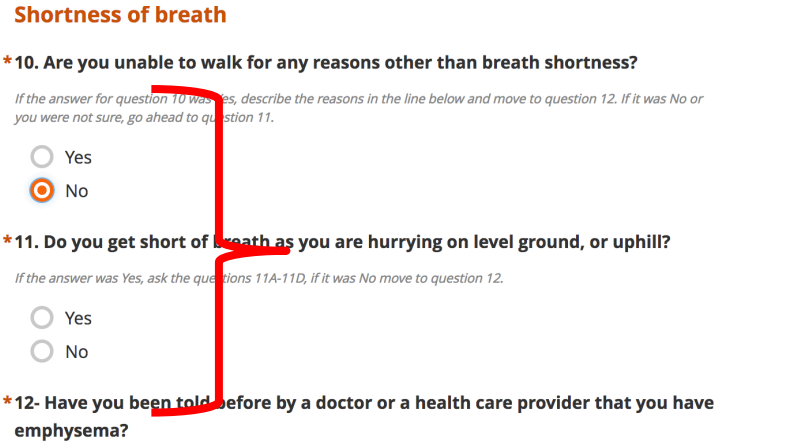
To save your mobile device power, below consideration should be taken.

- Put the phone on the flight mode
- Turn off the WIFI
- the screen's brightness must be low
- Recharge the battery and make sure it full before you go to the field
- Make sure the date is correctly set in the mobile device; you need to set up the time zone and then the date/hour.

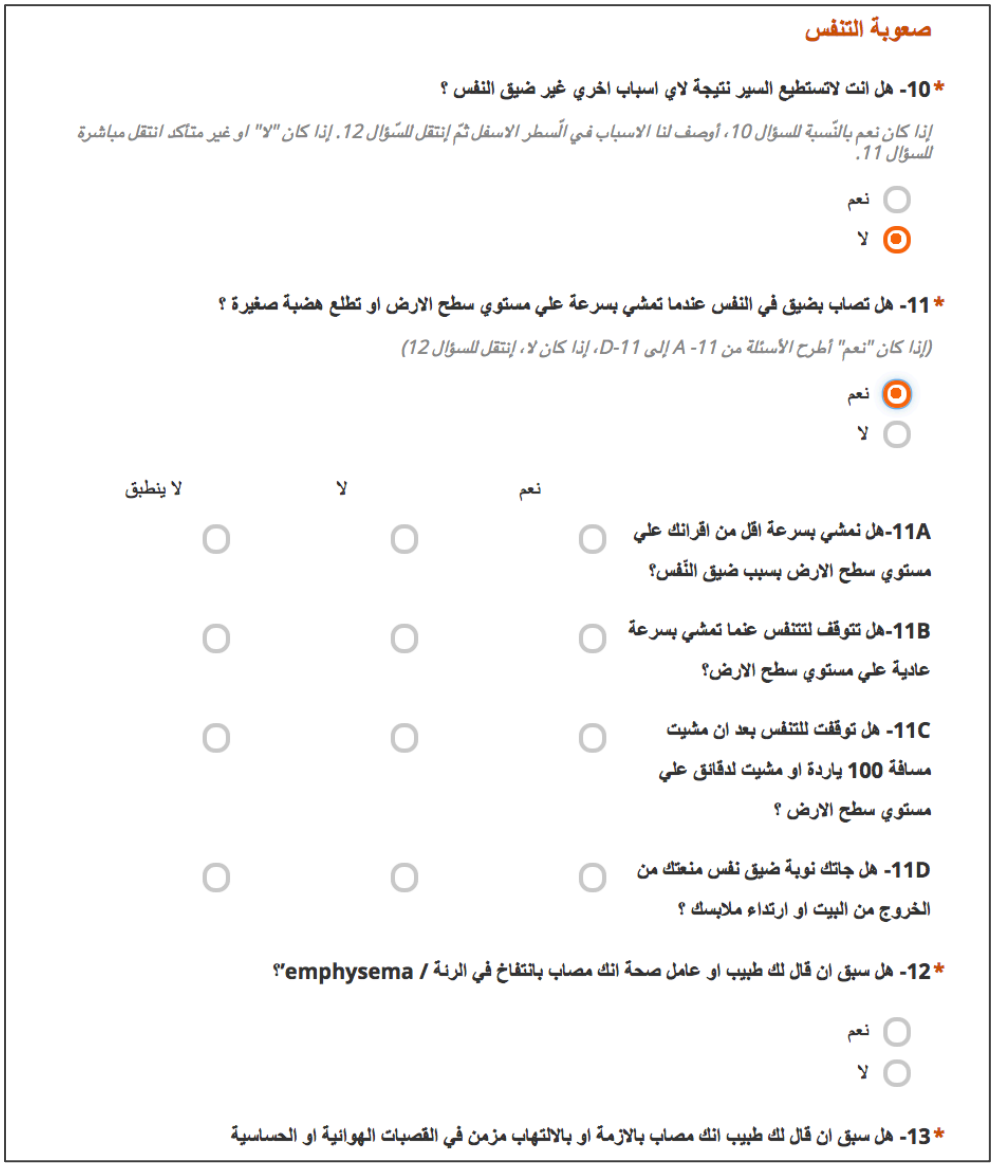
Appendix (8) Smartphone snapshots from ODK collect

a) Snapshots of automated skip pattern.





b) Snapshots of Arabic administered version of the electronic core questionnaire



صعوبة التنفس

*10- هل انت لاتستطيع السير نتيجة لاي اسباب اخري غير ضيق النفس ؟

إذا كان نعم بالنّسبة للسؤال 10، أوصف لنا الاسباب في الّسطر الاسفل ثمّ إنتقل للسّؤال 12. إذا كان "لا" او غير متأكد انتقل مباشرة للسؤال 11.

- نعم
- لا

*11- هل تصاب بضيق في النفس عندما تمشي بسرعة علي مستوي سطح الارض او تطلع هضبة صغيرة ؟

(إذا كان "نعم" أطرح الأسئلة من 11- A إلى 11-D، إذا كان لا، إنتقل للسؤال 12)

- نعم
- لا

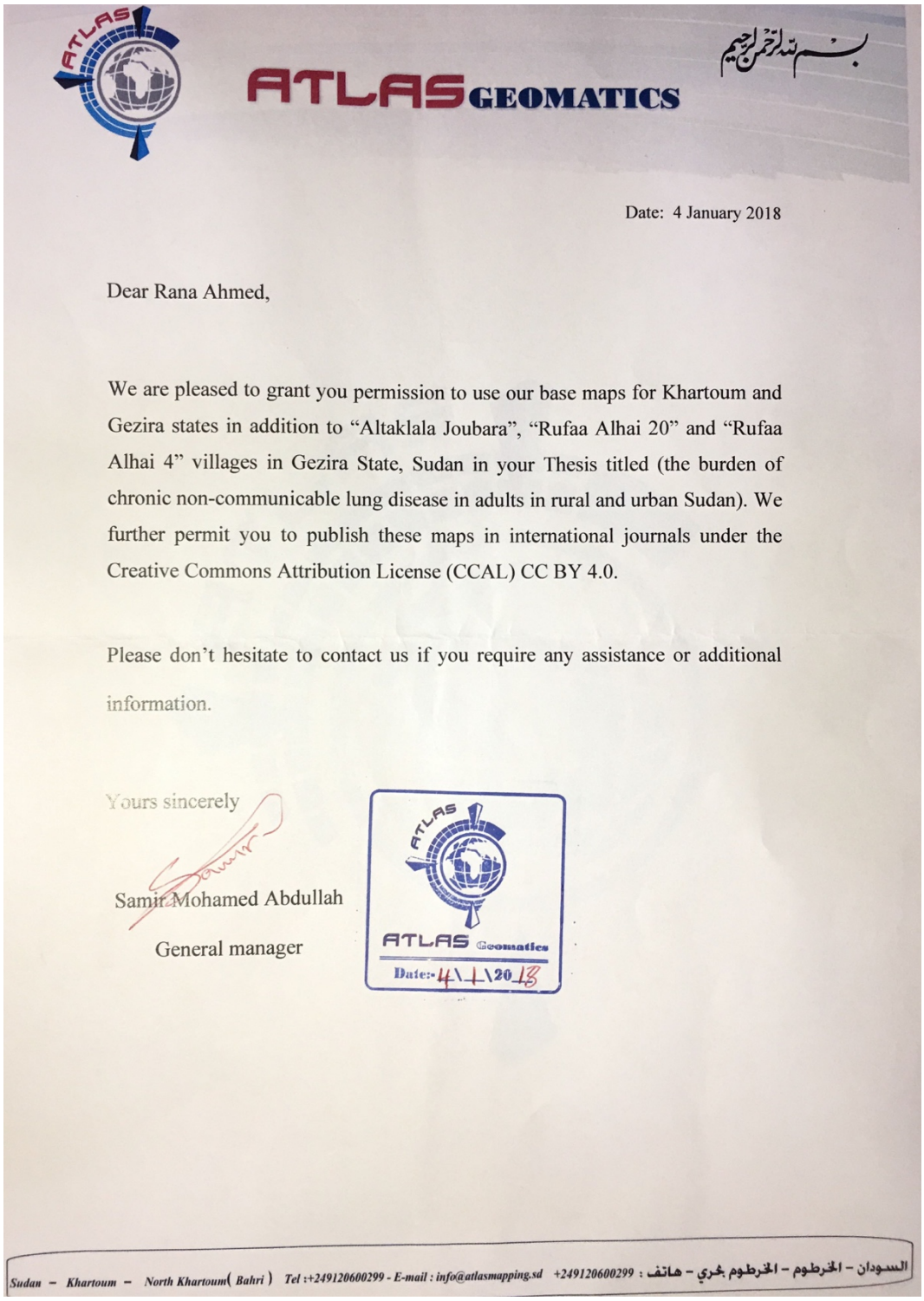
	نعم	لا	لا ينطبق
11A-هل نمشي بسرعة اقل من اقرانك علي مستوي سطح الارض بسبب ضيق النّفس؟			
11B-هل تتوقف لتتنفس عنما تمشي بسرعة عادية علي مستوي سطح الارض؟			
11C- هل توقفت للتنفس بعد ان مشيت مسافة 100 ياردة او مشيت لدقائق علي مستوي سطح الارض ؟			
11D- هل جاتك نوبة ضيق نفس منعتك من الخروج من البيت او ارتداء ملابسك ؟			

*12- هل سبق ان قال لك طبيب او عامل صحة انك مصاب بانتفاخ في الرئة / "emphysema؟

- نعم
- لا

*13- هل سبق ان قال لك طبيب انك مصاب بالازمة او بالالتهاب مزمن في القصبات الهوائية او الحساسية

Appendix (9) Maps Permission Letter



بسم الله الرحمن الرحيم

ATLAS GEOMATICS

Date: 4 January 2018

Dear Rana Ahmed,

We are pleased to grant you permission to use our base maps for Khartoum and Gezira states in addition to "Altaklala Joubara", "Rufaa Alhai 20" and "Rufaa Alhai 4" villages in Gezira State, Sudan in your Thesis titled (the burden of chronic non-communicable lung disease in adults in rural and urban Sudan). We further permit you to publish these maps in international journals under the Creative Commons Attribution License (CCAL) CC BY 4.0.

Please don't hesitate to contact us if you require any assistance or additional information.

Yours sincerely

Samir Mohamed Abdullah

General manager

ATLAS Geomatics
Date: 4\1\2018

Sudan – Khartoum – North Khartoum(Bahri) Tel :+249120600299 - E-mail : info@atlasmapping.sd +249120600299 : السودان – الخرطوم – الخرطوم بحري – هاتف

Appendix (10) Evidence to promote lung health in Sudan, dissemination meeting

a) **Meeting minutes**

The meeting was opened by the Epi-Lab director by highlighting the global burden of NCDs and stating the meeting objectives. This was followed by a talk from the federal Ministry of Health Under-secretary. As a policy maker, he highlighted the need for such research in Sudan and the importance of focussing more on NCDs and CRDs in general. He also appreciated how this research will help to see how many people at states seeking for treatment as well as how these health problems affect the wellbeing of the Sudanese population and the economy. He stated that this was an important piece of research and will complement the efforts of the Ministry of Health in Sudan and others in addressing the burden of chronic lung diseases such as COPD and asthma. He also asserted that Sudan needs to prioritise these diseases and highlighted COPD as an under-estimated disease within the country. He claimed that results provided by the present study should be included in the planning for Ministry of Health programs as they are trying to improve health services for sufferers of lung disease and integrate other stand-alone services into the NCDs program. He closed by concluding that having evidence of the burden of lung diseases in Sudan is crucial and that the integration of these findings into Ministry of Health polices and plans is paramount.

The burden of non-communicable lung diseases in adults in Sudan from both urban and rural studies were presented and the rationale, methodologies, findings, and study recommendations were discussed with the audience. Various concerns were raised and addressed during these discussions:

- The smaller sample size led to exaggerated prevalence figures in Khartoum?

  It was said that, to make sure the sample selected researchers represent all population followed a similar multistage sampling plan in both Khartoum and Gezira with a random selection at each sampling stage in both studies. Additionally, the study used weighted analysis in reported COPD prevalence and all other estimates. Consequently, choice bias was reduced, and the subjects were representative of the general populations in both Khartoum and Gezira studies.

- The study choice criteria and the justification of excluding the non-institutionalised population (e.g. prisoners). Researchers clarified that a standardised BOLD study was mimicked to assure comparability with other studies in the region and around the world. This included following the project selection and exclusion criteria. Additionally, ethical issues may have arisen from the inclusion of individuals such as prisoners. Inmates, for example, are unable to freely give consent in a manner consistent with non-institutionalised persons. They may be subjected to coercion and undue inducement. Moreover, institutionalised persons may be exposed to other risk factors with different durations and intensities when compared to those in the community.
- The investigation of known risk factors for COPD with a focus on biomass fuels, environmental factors and air pollution was raised. Discussion around the high reported burden of COPD in Khartoum state highlighting the need to explore whether air pollution is a factor in COPD prevalence in Khartoum state. These studies used standardised BOLD questionnaires and there were no specific questions about air pollution. However, there were other questions about occupational exposure to gas and smoke, as well as exposure to biomass fuels and no association found between these factors and developing COPD. Future exploration of these risk factors will strengthen these findings and clarify weather air pollution and other environmental factors contribute to the burden of COPD in Sudan.

Following the presentation, a panel discussion session conducted and chaired by Epi-Lab and LSTM. Panellists included Dr Hamad Elturabi, Associate Professor of Medicine/Consultant Physician and Pulmonologist, Soba University Hospital, University of Khartoum, Sudan and Academic Secretary, Sudan Medical Specialization Board; Dr Momen Mokhtar, Secretary General Sudanese Chest Physician Society; Dr Manal El Emam, Director of NCD Program; and Professor Sudan Suliman, Research Director at Sudan Medical Heritage Foundation.

The Panel discussion concerned primarily questions listed and addressed below:

1. *What is your reaction to the burden of chronic lung disease that has now been documented in Khartoum and Gezira in terms of overall percentage of respondents with*:
   a) *Symptoms?*

b) *Abnormal spirometry?*

Firstly, the panel responded that these were the first data on COPD to be presented, owing to the lack of research and surveillance data about this disease in Sudan. In this study, a higher prevalence of both respiratory symptoms and lung restriction were found in in Gezira while a higher prevalence of stage 1 and stage 2 COPD was found in Khartoum. Given that the prevalence of moderate to severe obstruction was 12% in Khartoum compared to 6.6% in Gezira, and that higher prevalence of moderate to severe obstruction should correspond with higher prevalence of respiratory symptoms, panellists were surprised that COPD prevalence was lower in Gezira state.

The response to this concern was that a younger age stratum (age 18-39) had been included in data for Gezira state. This group had a high prevalence of respiratory symptoms (cough and shortness of breath) and a higher prevalence of lung restriction while the older group (age 40+) had a higher prevalence of COPD. The high prevalence of respiratory symptoms in Gezira state might not be the result of COPD but other restrictive lung diseases, given the high prevalence of low FVC in this group.

Another panellist questioned whether COPD was more prevalent than asthma, even though asthma tends to be more prevalent than COPD generally.

The response was that a BOLD study was conducted which focussed on COPD rather than asthma. However, airway reversibility was assessed in both studies and estimates of airway obstruction that persisted after the use of a bronchodilator were 18.5% using LLN in both states while 15% in Gezira and 10.5% in Khartoum using GOLD. These findings show that asthma prevalence is high, even higher than COPD estimates in both states.

Further questions were asked about how biomass fuels exposure was assessed. The response to this concern was, study participants were asked if they used charcoal, kerosene, firewood for cooking for 6 months or more in their life in addition if they used this different biomass fuels for heating.

2. *We have seen that spirometry is not routinely available in either the private or public sectors. Do you think spirometry is needed in the diagnostic algorithms for chronic lung diseases and, if so, how would you go about introducing and scaling up provision?*

Panellists responded by asserting that spirometry is crucial for the diagnosis of COPD and highlighted the deficiency in diagnostic tools in Sudan. Additionally, a representative of the ministry of health said that a patient pathway should be created, so as simplify the process of diagnosis. This representative went on to state that work is being done to provide spirometric testing in secondary health care. Training of doctors in spirometry is still needed and efficacy assessments must then be carried out before spirometry can become commonplace across other levels of healthcare, including in primary health care.

Other researchers emphasised the importance of spirometry in the diagnosis of chronic lung disease. However, spirometers are expensive and need special training to carry out testing and correctly interpret results. As a solution, it was explained that the Epidemiological laboratory used peak flow meters in asthma clinics at district hospitals. Where the standard asthma case management program is provided, peak flow meters in primary healthcare would help give better diagnoses. Though results obtained are not as correct as those from spirometric testing, peak flow meters could help to ease diagnoses in most of cases where spirometric testing can be called on upon referral (at the secondary and tertiary level).

A researcher on the present study suggested that the Ministry of Health may be able to utilise the existing school health program and screen school children for asthma, whilst understanding that asthma is prevalent in adults as well as in children from this, and the earlier ISAAC study conducted in Sudan. The panellist and session chair agreed that existing programs should be made use of rather than investing new ones.

3. *What do you see as the major treatment modalities to offer patients with COPD in Sudan in terms of:*

a) *Non-pharmacological interventions e.g. (pulmonary rehabilitation / smoking cessation)?*

b) *Medicines?*

One panellist responded that, as an environmentalist, preventative strategies stand for the most sustainable way forward. Teaching individuals how to prevent and manage attacks for example can be far more effective than giving treatment modalities. In Sudan, many factories (e.g. sugar processing plants) run close to domestic areas and represent a greater risk for asthma patients. The panellist said that public authorities must address this issue to decrease air pollution. In addition, this

panellist highlighted that there is a need to encourage proactive health-protecting behaviours to manage these conditions sustainably.

Another panellist echoed the sentiment that prevention is better than cure. However, this panellist argued that, in Sudan, anti-smoking campaigns should be prioritised to help smokers quit and to start smoking cessation programs. This should be coupled with non-pharmacological modalities such as rehabilitation and nicotine patches (though these are available, they are however expensive). There is a need to give psychological support in smoking cessation programs as well as effectively treating existing co-morbidities.

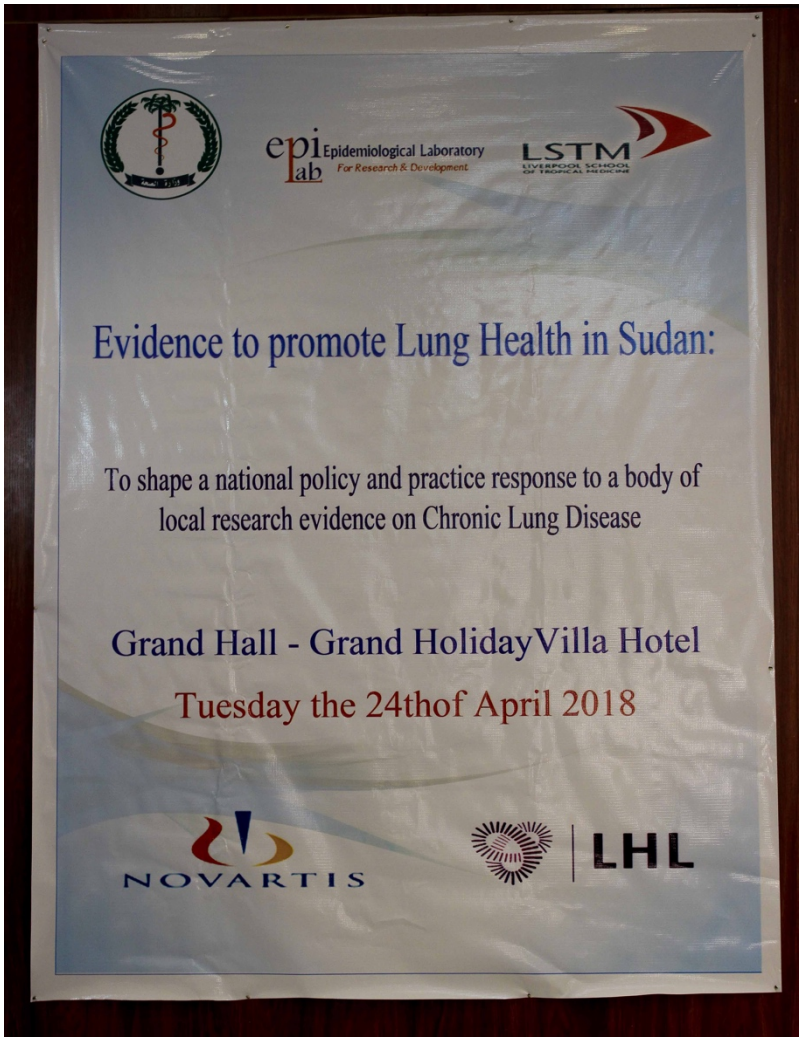
The panel chair pointed out that every urban city in the world has above acceptable levels of air pollution. Additionally, community health workers should work more in health education as well as on prevention, management, and referral for emerging cases.

Other discussions took place around the costs associated with asthma care as well as societal feelings about disability and the over-use of emergency room treatment for asthma, and how the health system policies should be changed in response. One panellist said that asthma is an under-diagnosed and under-treated disease, where stigma, encompassing the feeling of patients and people in community, plays a leading role in the lack and delay of diagnoses. This places a high demand on the health system and results in great cost to patients, The panellist added that the study revealed gaps in the Sudanese health system, that the structure of Asthma units in hospitals needs to be reformed, and that nurses must be trained to identify Asthma as a first line of defence. Additionally, the perceived cost of diagnosis and treatments (such as inhalers) may explain why patients preferentially come to emergency rooms, despite this being more expensive.

Professor Asma Elsony commented that in the standard asthma case management program, implemented by the Epidemiological Laboratory (Epi-Lab) in selected hospitals in Khartoum and Gezira States, the UNION model of standard case management is used. Most hospitals at the first referral level (district hospitals), with a catchment area of 100,000 were selected. Each hospital had an emergency room and asthma clinic with a medical officer for the clinical evaluation of asthma, a nurse or sister to give health education, and one clerk statistician or medical assistant for recording and reporting. Those clinics managed to effectively reduce the number of

hospitalizations and emergency visits, thus being a model attractive to policy makers for widespread adoption.

Overall, the policy makers, consultants, chest physicians, practitioners and researchers that took part in this meeting highlighted gaps in the Sudanese health system with regard to lung health (specifically focussed on COPD and asthma) and the need for research to strengthen existing programs and introduce new interventions. Additionally, the results provided by this study about the prevalence of COPD in urban and rural Sudan has shed light on this disease and its burden. Policy makers represented by the Undersecretary at the Ministry of Health emphasised that there will be a continuation of detailed work based on this study's results and recommendations. Additionally, there will be a focus on COPD and asthma and other chronic lung diseases, making use of these important findings.



BOLD Gezira researchers and field team

Researcher team

BOLD Khartoum- Project team in the field

BOLD Gezira-Project team in the field

Appendix (11) Academic outputs arising from this thesis

Posters and Presentations

The burden of chronic lung diseases in adults in rural and urban Sudan, Study overview, methodology and preliminary results [Poster] at LSTM postgraduate research degree student conference; May 2017, May 2016.

The prevalence and main determinant of COPD in urban Sudan [Oral presentation] at LSTM postgraduate research degree student conference; May 2017.

Rana Ahmed, Ryan Robinson, Kevin Mortimer. A comparison of smartphone and paper data-collection tools in the Burden of Obstructive Lung Disease (BOLD) study in Gezira state, Sudan[abstract]. In abstract book of the 48th World conference on Lung Health of the International Union Against Tuberculosis and Lung Disease (The union); 11-14 October 2017, Guadalajara Mexico; IJTULD; Volume 21, number 11 November 2017; Pages S1-S481; ISSN 10273719. Abstract no OA-104-12

The burden of non-communicable lung diseases in adults in rural and urban Sudan [Video presentation] LSTM postgraduate research degree student conference; May 2018.

The burden of non-communicable lung diseases in adults in rural and urban Sudan [Oral presentation] at Evidence to promote Lung Health in Sudan dissemination meeting, Khartoum, Sudan, April 2018.

Publications

Rana Ahmed, Ryan Robinson, KM. The epidemiology of noncommunicable respiratory disease in sub-Saharan Africa, the Middle East, and North Africa. Malawi Med J. 2017;29(2):203–11.

Ahmed R, Robinson R, Elsony A, Thomson R, Bertel Squire S, Malmborg R, Peter Burney, Kevin Mortimer. A comparison of smartphone and paper data-collection tools in the Burden of Obstructive Lung Disease (BOLD) study in Gezira state, Sudan. PLoS One. 2018;13(3):1–15.

Rana Ahmed[1,3], Nada Bakry[1,2], Bander Noory[1], Rashid Kamal[1], Hana Elsadig[1], Hind Eltigani[1], Rebecca Nightingale[3], Jaymini Patel[4], Peter G. Burney[4], Kevin Mortimer[3], Asma El Sony[1,2]. Prevalence and determinants of chronic obstructive pulmonary disease in Khartoum, Sudan. Pending submission.

Ahmed R, R.K. Osman, Elsony A, Thomson R, Bertel Squire S, Malmborg R, Patel J Peter Burney, Kevin Mortimer. Non-communicable chronic lung disease in adults rural Sudan. In preparation.

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