
**THE 1ST INTERNATIONAL LUNG
SCIENCE SYMPOSIUM AND INSTITUTE
INAUGURATION**

**MAKERERE UNIVERSITY
LUNG INSTITUTE
SINCE 2015**



**MAKERERE UNIVERSITY LUNG INSTITUTE
COLLEGE OF HEALTH SCIENCES**

**THE 1ST INTERNATIONAL LUNG
SCIENCE SYMPOSIUM AND INSTITUTE
INAUGURATION**

**MAKERERE UNIVERSITY
LUNG INSTITUTE
SINCE 2015**



Kampala 2019



Vision

An African population with a low burden of lung diseases

Mission

Lung health research that integrates disease prevention, clinical care and training in sub-Saharan Africa

Core values

- Innovation
- Excellence
- Integrity
- Care
- Effort norm

Back cover Photo: The Front elevation of the Makerere University Lung Institute.

Photo credit, Editorial Design & Layout: Department of Medical Illustration, Makerere University

Published by Makerere University Lung Institute

Copyright: Makerere University Lung Institute (MLI), 2019

Table of Contents

Foreword	vii
Foreword from Vice Chancellor, Makerere University.	viii
Foreword from the Principal, Makerere University College of Health Sciences	ix
Foreword from the Director, Makerere University Lung Institute.	x
Welcome Remarks - Chair 1st Makerere University Lung Science Symposium & Inauguration organising Committee	xi
The MLI Governance and Management Structure	xii
Board of Directors, Makerere University Lung Institute.	xiii
MLI Technical Board	xiv
Management team	xv
Current status of the MLI.	xvi
SYMPOSIUM KEYNOTE.	xix
PANEL DISCUSSION	xxii
SYMPOSIUM SCIENTIFIC PROGRAM	xxiii
SYMPOSIUM INAUGURATION PROGRAM	xxiv
Symposium abstracts.	1
SYMPOSIUM ABSTRACTS	2
Exploring local beliefs and behaviours regarding chronic lung diseases in rural Uganda – a mixed-method FRESH AIR study.	3
Feasibility of conducting an internet-based Spirometry training for health care workers in Uganda: The Fresh Air H2020 experience.	4
Mortality and associated factors among patients with Chronic Obstructive Pulmonary Disease (COPD) in Uganda.	6
Prevalence of tuberculosis risk factors among bacteriologically negative and bacteriologically confirmed tuberculosis patients from five regional referral hospitals in Uganda	7
Health seeking behavior among individuals presenting with chronic cough symptoms at regional referral hospitals in Uganda; missed opportunity for early tuberculosis diagnosis	8
Feasibility and acceptability of a midwife-led health education strategy to reduce exposure to biomass smoke among pregnant women in Uganda	9
Household air pollution effects on cardio-respiratory health of urban slum dwellers in Kampala (HAPCRUSH)	10
Geographic patterns of referral for TB evaluation with introduction of Xpert MTB/RIF at regional referral hospitals in Uganda: Evidence for country wide roll out.	11
“Johns Hopkins and Makerere University collaboration: Four years of research and training.	

Qualitative insights into COPD management in Uganda and Nepal: field experiences and preliminary results.”	12
Burden of fungal asthma in Africa	13
Maternal and socioeconomic determinants of lung function among infants in Uganda: a birth cohort study	14
Chest X-ray performs better than the WHO symptoms in screening for tuberculosis in Uganda	15
Proportion of Tuberculosis affected households experiencing catastrophic costs due to TB in Uganda: main cost drivers	16
The silent economic impact of chronic lung diseases in low-resource settings in Africa, Asia and Europe – a FRESH AIR study	17

A COMPEDIUM OF RESEARCH CONDUCTED AT MAKERERE UNIVERSITY LUNG INSTITUTE (MLI) SINCE 2015 19

Improving inpatient medication adherence using attendant education in a tertiary care hospital in Uganda	21
Effectiveness-implementation of COPD case finding and self-management action plans in low- and middle-income countries: global excellence in COPD outcomes (GECO) study protocol.	22
Prednisolone and <i>Mycobacterium indicus pranii</i> in Tuberculous Pericarditis	24
Socio-economic factors, gender and smoking as determinants of COPD in a low-income country of sub-Saharan Africa: FRESH AIR Uganda.	25
Electric scooters: batteries in the battle against ambient air pollution?	26
Predictors for MTB Culture-Positivity among HIV-Infected Smear-Negative Presumptive Tuberculosis Patients in Uganda: Application of New Tuberculosis Diagnostic Technology	28
Association between Household Air Pollution Exposure and Chronic Obstructive Pulmonary Disease Outcomes in 13 Low- and Middle-Income Country Settings	30
Evaluation of Automated Molecular Testing Rollout for Tuberculosis Diagnosis Using Routinely Collected Surveillance Data — Uganda, 2012–2015	31
Tuberculosis risk factors among tuberculosis patients in Kampala, Uganda: implications for tuberculosis control	35
Patient satisfaction with TB care clinical consultations in Kampala: a cross sectional study.	36
ADVANCES IN THE DIAGNOSIS, TREATMENT AND CONTROL OF HIV ASSOCIATED TUBERCULOSIS	37
The State of Ambient Air Quality in Two Ugandan Cities: A Pilot Cross-Sectional Spatial Assessment	38
Access to affordable medicines and diagnostic tests for asthma and COPD insub Saharan Africa: the Ugandan perspective.	40
A pre–post intervention study of pulmonary rehabilitation for adults with post-tuberculosis lung disease in Uganda	42

Household Air Pollution Is Associated with Chronic Cough but Not Hemoptysis after Completion of Pulmonary Tuberculosis Treatment in Adults, Rural Eastern Democratic Republic of Congo	43
Urban-Rural Disparities in Chronic Obstructive Pulmonary Disease Management and Access in Uganda.	45
International research and guidelines on post-tuberculosis chronic lung disorders: a systematic scoping review	46
Access to affordable medicines and diagnostic tests for asthma and COPD in sub Saharan Africa: the Ugandan perspective.	47
A young child with a history of wheeze	48
The “child size medicines” concept: policy provisions in Uganda	55
Clinical outcomes of children with acute asthma and pneumonia in Mulago hospital, Uganda: a prospective study.	56
Clinical outcomes of children with acute asthma and pneumonia in Mulago hospital, Uganda: a prospective study.	57
Lung Function of Children at Three Sites of Varying Ambient Air Pollution Levels in Uganda: A Cross Sectional Comparative Study	58
Availability and affordability of medicines and diagnostic tests recommended for management of asthma and chronic obstructive pulmonary disease in sub-Saharan Africa: a systematic review.	59
Prevalence and factors associated with asthma among adolescents and adults in Uganda: a general population based survey	60
The impact of HIV on the prevalence of asthma in Uganda: a general population survey	63
Does pulmonary rehabilitation alter patients’ experiences of living with chronic respiratory disease? A qualitative study	64
Predictors and short-term outcomes of recurrent pulmonary tuberculosis, Uganda: a cohort study	65
A pre–post intervention study of pulmonary rehabilitation for adults with post-tuberculosis lung disease in Uganda	67
Empiric TB treatment of severely ill patients with HIV and presumed pulmonary TB improves survival	68
A Clinical Predictor Score for 30-Day Mortality among HIV-Infected Adults Hospitalized with Pneumonia in Uganda	70
Rates of asthma exacerbations and mortality and associated factors in Uganda: a 2-year prospective cohort study.	72
Accuracy of different Xpert MTB/Rif implementation strategies in programmatic settings at the regional referral hospitals in Uganda: Evidence for country wide roll out.	73
Access to affordable medicines and diagnostic tests for asthma and COPD in sub Saharan Africa: the Ugandan perspective.	75

Association between Household Air Pollution Exposure and Chronic Obstructive Pulmonary Disease Outcomes in 13 Low- and Middle-Income Country Setting	76
Availability and affordability of medicines and diagnostic tests recommended for management of asthma and chronic obstructive pulmonary disease in sub-Saharan Africa: a systematic review	77
Prevalence and factors associated with asthma among adolescents and adults in Uganda: a general population based survey	78
Validation of the Saint George’s Respiratory Questionnaire in Uganda	79
Predictors and outcomes of mycobacteremia among HIV-infected smear- negative presumptive tuberculosis patients in Uganda.	80
Tuberculosis risk factors among tuberculosis patients in Kampala, Uganda: implications for tuberculosis control	81
Prevalence of chronic obstructive pulmonary disease and associated risk factors in Uganda (FRESH AIR Uganda): a prospective cross-sectional observational study	82
Socio-economic factors, gender and smoking as determinants of COPD in a low-income country of sub Saharan Africa: FRESH AIR Uganda.	83
Rapid assessment of the demand and supply of tobacco dependence pharmacotherapy in Uganda	84
International research and guidelines on post-tuberculosis chronic lung disorders: a systematic scoping review	86
Prevalence of chronic respiratory disease in urban and rural Uganda.	87
Guidance on the diagnosis and management of asthma among adults in resource limited settings	88
Treating tobacco dependence: guidance for primary care on life-saving interventions. Position statement of the IPCRG.	89
Prevalence of Tuberculosis Risk Factors among Bacteriologically Negative and Bacteriologically Confirmed Tuberculosis Patients from Five Regional Referral Hospitals in Uganda.	90

History of Makerere University Lung Institute (MLI) 91

History of Makerere University Lung Institute	92
---	----

Foreword

Foreword from Vice Chancellor, Makerere University



Prof. Barnabas Nawangwe

Dear delegates and dignitaries of the Makerere University Lung Institute 1st International Lung Science Symposium and Lung Institute inauguration, I welcome you to Makerere University. A warm welcome to those who have crossed borders and oceans to attend this special occasion. Today, Makerere University has the honor of opening yet another center of excellence as part of its mandate of providing innovative teaching, learning, research and services that are responsive to national and global needs. This is indeed in line with the university's vision of being the leading institution for academic excellence and innovations in Africa.

Makerere University has a clear record of pioneering the establishment of leading research and clinical care centers in the country. These include the Infectious Diseases Institute (IDI) and the Makerere University Joint AIDS Program (MJAP) that helped to generate research and clinical care evidence that was critical to the HIV epidemic response not only in Uganda, but in the whole of Africa and beyond. Makerere University and its faculty were also pivotal to the founding of the Uganda Cancer Institute (UCI) and the Uganda Heart Institute (UHI).

In the recent past it has become clear that there is an under-recognized non-communicable lung diseases epidemic in Uganda. Despite this recognition, data on the true magnitude and the drivers of these diseases, and how they can be prevented and treated is very limited. As the premier University in Uganda and Africa, we recognized this and supported the founding of the Makerere University Lung Institute to help generate this much-needed evidence. Since its opening four years ago, the Lung Institute has made significant strides in meeting the objectives of its creation. To a great extent, the magnitude of the lung diseases in Uganda has been defined. Work is ongoing to generate innovative ways for disease prevention and patient care.

I thank all national and international level collaborators who have partnered with us in the different work that is going on in the Lung Institute. The management of Makerere University will continue to provide strategic direction to the Lung institute. We call upon all partners in health especially the line health and science ministries to continue working with us to foster growth of these service-oriented institutes in Makerere University, and tap into the large wealth of knowledge and expertise within the university.

Prof Barnabas Nawangwe
VC Makerere University

Foreword from the Principal, Makerere University College of Health Sciences



Prof. Charles Ibingira

I warmly welcome you to the (MakCHS), the leading medical school and research college in Africa. On behalf of MakCHS, I warmly welcome you to this 1st International Lung Science Symposium and inauguration of Makerere University Lung Institute (MLI). MLI is f the newest units within MakCHS. The MLI is the second institute to open in the college after the Infectious Diseases Institute (IDI). Our strategy is to respond to the most pressing societal needs and solving pressing health problems in the country through research and training. Through our world class experts in all fields of health, we generate the evidence needed to plan for health programs as well as coming up

with innovative ways of preventing and treating diseases.

Today Uganda and the whole world is threatened by the raising NCD epidemic. Studies conducted at the MLI indicate that the prevalence of asthma in the country is 11.3% while that of chronic obstructive pulmonary disease (COPD) ranges from 6-16% depending on the urbanization level of the location where the study is done. Our country has one of the most polluted air in the world but this remains unrecognized and unattended to and therefore remains a big risk factor of air way diseases. For this reason, we started MLI to act as a center of excellence in generating evidence on the magnitude of lung diseases and their risk factors in the country and beyond. In addition, MLI is involved in designing and testing innovative low-cost ways of preventing, diagnosing and treating lung diseases that are relevant to low income settings and can be adopted by other settings with similar economic situations.

During these two days of the symposium, a rich scientific program has been prepared. I hope you find it interesting and educative. In addition to the scientific program, I welcome you to attend the official inauguration of the institute. This event will act as a symbol that the institute is now open to everyone who wishes to conduct any lung health research and to all who need care for any complicated lung related illness. Going forward, the Lung Institute shall provide all the components of lung care, prevention, diagnosis, all forms of treatment and rehabilitation. The MLI is also open for all trainees who wish to learn different skills in lung health.

I want to take this opportunity to thank all our national and international partners for their continued support which has contributed to the many achievements that have so far been realized by the institute. I thank the University Management for supporting this initiative from inception; I thank and applaud the management of the MLI for the work well done.

Prof Charles Ibingira
Principal, MakCHS

Foreword from the Director, Makerere University Lung Institute



Dr. Bruce Kirenga

Dear all delegates and Guests

I thank you so much for finding the time to join us during these two days of the Makerere University Lung Institute (MLI) 1st International Lung Science Symposium

and the institute's opening ceremony. We appreciate you for making the time to join us. We will dedicate the first one and half days to share knowledge on lung science and on the evening of the second day, we will perform ceremonies to officially open the MLI. This ceremony will feature a key note address and remarks from a wide range of dignitaries from academics to top health and science leaders in the country. We hope you find this program exciting.

In 2013, I started approaching fellow lung health professionals on the Mulago Hill and abroad to discuss how we could address the problem of the lung diseases epidemic in Uganda and other low-income settings. This was after realizing that very little attention was being paid to the problem of chronic lung diseases. Over 2 years that followed up until September 2015, we developed a proposal to start the lung institute at Makerere University. This center would act as a center of excellence for lung health research, training and care in Uganda and beyond.

Today marks about four years since MLI started and we have had tremendous progress in terms of stimulating lung health research. We have been part of pioneer studies on air pollution (including indoor air pollution). MLI has been part of national lung disease surveys such as the National asthma survey, National tuberculosis survey, chronic obstructive pulmonary disease surveys, among others. We have a number of clinical studies that are aimed at finding new and better treatments for tuberculosis and other chronic lung diseases. We have developed and implemented respiratory medicine training programs for primary health

care providers and initiated super specialized skills training programs. In line with our mission, we opened a translational chest clinic which offers clinical services found in very few centers in Africa such as a sleep disorders clinic and lab, pulmonary function testing, allergy testing and pulmonary rehabilitation among others.

Despite these achievements, several challenges remain including under utilization of the services that have been set up mainly because of lack of awareness by fellow health care providers and the population. While the cost of providing specialist care is high, it is the most economically disadvantaged who need such care which has limited our reach to them. Availability of specialists remains a challenge creating heavy workloads for the few who are available. In terms of research, key research capacities to support top notch research exist like lack of first-class statistical support, translational scientists, grant and project management skills to mention but a few. Furthermore, lack of local research funding which creates frustration, especially among junior scientists, who need seed grants to start their research careers exists.

To move forward MLI will have to harness opportunities that exist while creating others. These include advocating for the integration of lung health messages in all available health education and promotion products, advocating for inclusion of lung diseases medicines in the essential medicines kits and expanding collaboration base. For sustainability MLI will need to have researchers and specialists funded through the main government channels such as the ministry of health and the ministry science and the ministry of education. Advocating for faculty positions funding at the MLI by the private sector could also be a key strategy.

I wish you an enjoyable symposium and celebrations

Bruce J Kirenga
Director

Welcome Remarks - Chair 1st Makerere University Lung Science Symposium & Inauguration organising Committee



Dr. Ivan Kimuli

Dear Participants,

On behalf of the Organizing Committee, it is with great pleasure and honor that I extend you a warm welcome to the First Makerere University Lung Institute International Lung Science Symposium, and Institute inauguration.

As the inaugural international symposium in the field of lung health held in Uganda, this historic event underlines the fact that it is time for research and knowledge in this field to be placed high on the agenda. The symposium will feature a highly interactive, stimulating and multidisciplinary program including oral abstract and poster sessions, presentations, panel discussions and a press conference. It promises to bridge the latest scientific evidence with contemporary clinical practice. The symposium program represents the efforts of many people. I would want to express my gratitude to all the members of the Institute Organizing Committee, members of the wider College committee as well as partners of MLI that have supported us morally, financially and otherwise. I also thank all the invited speakers without whom the symposium would not have been possible, for sharing their insights with us.

Throughout this conference, I ask that you stay engaged and help us shape the future of Lung health in the region.

My personal thanks goes out to all of you!

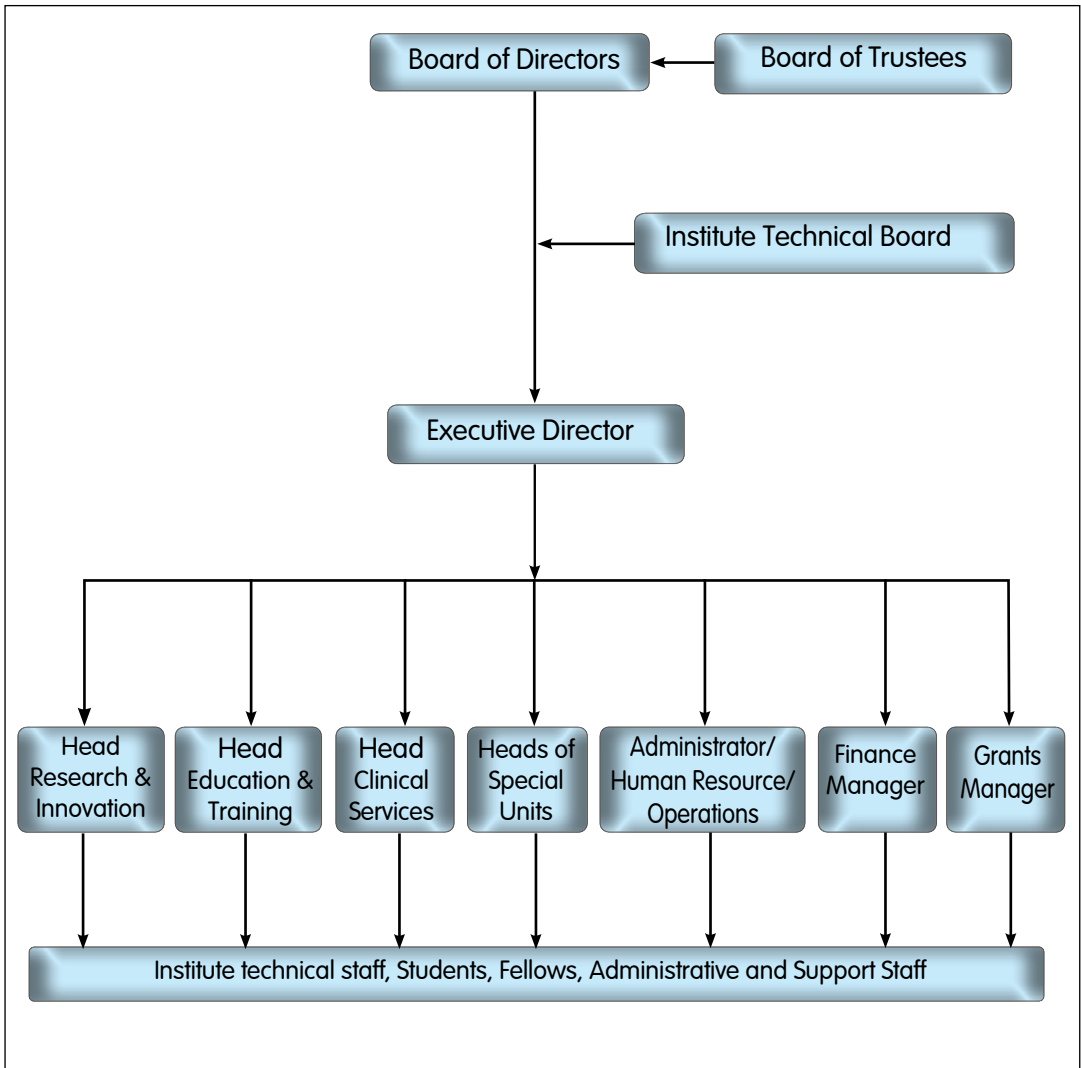
Best wishes,

Dr. Ivan Kimuli

Chairperson

Symposium and Inauguration Organising Committee

The MLI Governance and Management Structure



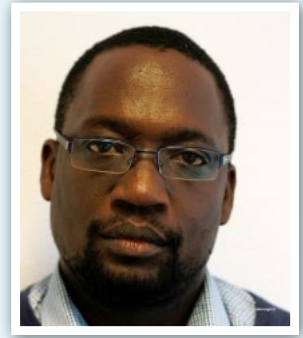
Board of Directors, Makerere University Lung Institute



Prof. Barnabas Nawangwe
Vice Chancellor, Makerere University



Prof. Charles Ibingira
Chair of the Board



Dr. Bruce J. Kirenga
MLI Managing Director



Prof. Thys van der Molen
Board Member



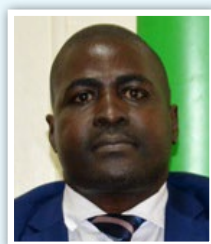
Prof. Nelson K. Sewankambo
Board Member



Prof. Josephine N. Kasolo
Board Member



Mr. Charles Barugahare
University Secretary



Mr. Henry Mwebe
Director, Directorate of
Legal Affairs - Makerere
University, Member



Dr. Henry Mwebesa
Ag. Director General of
Health Sciences, Ministry of
Health, Uganda, Member

MLI Technical Board



Achilles Katamba
Member



Dr. Frank Mugabe
Member



Dr. Abel Nkolo
Member



Dr. Hellen Aanyu -Tukamuhebwa
Member



Dr. Okot Nwang
Member



Dr. Frederik van Gemert
Member



Dr. Alphonse Okwera
Member



Dr. William Wordria
Member



Prof. Isaac Okullo
Member



Dr. Fred Nakwagala
Member



Dr. Rupert Jones
Member



Prof. Moses L. Joloba
Member



Dr. Simon Kasasa
Member

Management team

1. Dr. Bruce J Kirenga, Director
2. Dr. Rupert Jones, Co-Director
3. Dr. Wincelaus Katagira, Head, Department of Research and Innovation
4. Dr. Rebecca Nantanda, Head, Department of Education and Training
5. Dr. Ivan Kimuli, Head, Department of Clinical Services
6. Mr. James Ninsiima, Ag. Finance Manager
7. Mr. Jones Tumwebaze, Ag. Chief Accountant
8. Mr. Simon Mugambe, Chief Operations Officer
9. Ms. Jackline Nakabira- Administrator & Ag. Human Resources Manager
10. Ms. Susan Mugumya, Ag. Grants Manager

Current status of the MLI

Department of Research and Innovation

Supported by the Data and Quality Control units, the department of research and innovation supports researchers within MLI, ensuring that they successfully deliver their projects. In addition, the department also coordinates the journal and research conferences/ discussions that take place every Friday morning.

We also facilitate proposal development for fellows submitting grants through research meetings which critique research questions and methodology prior to submission to potential funders.

Successes

We have successfully made it a habit to bring together MLI research fellows every Friday morning starting 7:30 am to discuss a lung health related research article, learning about what's new and its relevance to the Ugandan community.

We also fostered a learning and operational environment where young researchers can dedicate time to develop, as well as work on their respective research projects.

Grants Unit

The Institute has over 20 contracted and active projects and 4 won in contracting process projects as indicated in the table below.

Table showing awarded and contracted grants from 2015 to 2019

PROJECT NAME	FUNDER	PROJECT PERIOD	PROJECT DURATION (YEARS)	GRANT AMOUNT
H2020 FA	EU	1/11/2015-30/11/2018	3	240,000.00
STREAM TRIAL	USAID/UNION/VIS	1/1/2018-30/6/2023	5	2,724,000.00
MERK	MERK		3	314,279.09
TB PCS	WHO/USAID/CIAM	15/8/2017-31/1/2018	1	4,830.00
Mapronano ACE	WB		5	27,772.00
ASAP	GSK	1/4/2016-30/4/2019	3	998,113.02
iBREATHE- BU	BU	1/1/2018-30/6/2018	0.5	7,124.00
iBREATHE-CIPLA	CIPLA	1/1/2018-30/6/2019	0.5	1,620.00
LULI	LSTM/MRC	1/1/2018-31/12/2021	3	18,850.00
IMPALA	LSTM/MRC	1/1/2018-31/12/2022	3	160,000.00
LSTM STREAM	USAID/LSTM	1/6/2018-30/6/2020	2	72,000.00
EXIT T. B	EDCTP	1/4/2018-30/4/2021	3	314,705.59
LUNG MICROBIOME	GSK	1/9/2018-30/9/2020	2	123,000.00
CLINIC(ANNUAL)	CLINIC	15/6/2018-ON	ON GOING	19,450.00
SLUM AIR QUALITY	UoB/NIHR	1/2/2019-28/2/2020	1	15,000.00
RECHARGE	UoB/NIHR	1/4/2018-31/3/2021	3	204,600.00
ACACIA	UoB/NIHR	1/4/2018-31/3/2021	3	276,060.00
KUPUMUA	UoP		1	37,000.00
PEDIATRIC MDR TB TMC207-C211	Janssen	9/2018-10/2023		14,709.1
Awarded grants				
MEASURE	USAID/JSI		1	159,000.00
COPA	GSK		2	123,000.00

Department of Training and Education

The mandate of department of Training and Education is to design and implement training and education programmes aimed at improving the care of people with lung diseases, prevention of lung diseases and health promotion to prevent lung diseases.

Since its creation, the development has been involved in a number of programmes;

- a) **Integrated Primary Respiratory Care Training Programme (iBREATH):** This is an in-service training programme aimed at improving knowledge, skills and competencies of primary care workers in management of respiratory illnesses such as asthma, Chronic Pulmonary Obstructive Disease (COPD), Tuberculosis, among others. The long-term goal is capacity building in respiratory care and strengthening health systems in Uganda. The programme was informed by a national-level training needs assessment that was conducted among primary care health workers, health care planners, and academicians, which revealed low competencies for management of common respiratory diseases. The curriculum is unique because, in addition to clinical competencies, it also focuses on chronic disease models, family and patient centered approaches, and team-based care. To date, courses on asthma, spirometry and respiratory physiology have been conducted.
- b) **Day of Lung Science:** This is a monthly event during which academicians, researchers, clinicians and healthcare planners come together to learn and gain an in-depth understanding of the science behind lung diseases and how these impacts on patient outcomes. The discussions also provide a platform for identification of practice and research gaps. The presenters include MLI fellows, local and international partners and collaborators.
- c) **Development of the Pulmonary Critical Care and Sleep Medicine fellowship curriculum (PCCM curriculum):** In collaboration with the Department of Medicine, Makerere College of Health Sciences, MLI has developed a training curriculum for Pulmonary Critical Care and Sleep Medicine fellowship curriculum (PCCM curriculum), which is in advanced stages (received local international review, and cleared by Department of Medicine).
- d) **Guidelines for interns, Research fellows and Associates, and Principal Investigators:** The department spearheaded the development of guidelines academicians who wish to work with the institute as interns, fellows, associates or principal investigators. These guidelines were approved by the Institute Technical Board and Board of Governors, and are fully operational.

Clinic department

The Lung Institute Clinic (LIC) was opened on 19th June 2018 with the goal of supporting lung health research and providing highly specialized clinical pulmonary services. The clinic runs from Monday to Friday, 8 am – 5pm, except on public holidays. The clinic offers strictly outpatient care and patient follow up, primarily on physician referral basis. We do, however, also see patients on self-referral. We have cared for over 300 patients to date.

Staff

The clinic is run by 7 physicians, 2 paediatricians, 1 pharmacist, 2 radiologist, 1 respiratory technician, 1 nurse and 1 clinic administrator.

Clinical services

The Clinic provides consultations on booking and walk in basis for all pulmonary conditions including Asthma, Chronic Obstructive Pulmonary Disease, Obstructive Sleep Apnea, Interstitial Lung disease, Smoking cessation services, pulmonary rehabilitation among others.

Diagnostic services

We are providing pulmonary function testing (Spirometry), Fraction of Expired Nitric Oxide (FeNO). We recently received equipment to enable us do Diffusing capacity of the Lung for Carbon Monoxide which we anticipate will be running soon. We are offering sleep testing and allergy skin testing. We anticipate offering bronchoscopy services soon since we have acquired our bronchoscopy equipment.

Pharmacy

The clinic provides some medication to our clients at affordable prices and we aim to provide the cheapest medication for pulmonary disease nationwide.

Human Resource

The Institute currently employs 76 persons. Most of these are attached to projects run by the Institute.

HR policy development

The Institute has embarked on development of an HR manual however previously the Mak HR manual was used as a guide in recruitment and personnel management.

Full time staff (Central and project staff)	44
Part time (Inclusive of locum staff and fellows)	32
Total personnel number	76

SYMPOSIUM KEYNOTE



Ladies and gentlemen;

Last week an estimated number of 1200 people in Uganda died from asthma and 2500 from COPD. In comparison in the same week 500 people died from HIV. I am sure that the place where they are now will be better than the place they had during their last days of their life. I say this not because Uganda is such a bad place to live. With its super climate, certainly as compared to the Northern European climate where I am used to- its fertile land and fine people Uganda is one of the nicest places in the world to live. I say this because being a clinician I think I know how their life was in the past years and certainly in the last days of their lives. The victims of asthma and COPD most likely suffocated and in their last hours they fought for air. Most of them died at home or in their village leaving behind their devastated family.

Asthma is a disease that is caused by a non-infectious inflammation of the airways and starts mostly in the early years of life. The disease cannot be cured but with luck and proper medication only very few people would die from it. In Uganda an estimated 11 % of the population suffers from any form of asthma making the total number of asthma patients around 4 million.

COPD is in essence a disease that is caused by lung damage due to air pollution such as smoke and smoking woodfire. From the studies done by the MLI research group we know that around 17 % of people older than 30 suffer from COPD. From this we can calculate that around 2 million people in Uganda suffer from COPD. In Uganda Asthma and COPD together currently claim more lives than HIV, Malaria and Tuberculosis together.

The point of my presentation is how do we know this and where is this information from? In essence the answer on this question is twofold clinical curiosity, followed by robust research. I might illustrate this with some personal story. In the early nineties of the last century I was a humble rural primary care physician in The Netherlands. I had nothing to do with any science and spent all my time taking care for my patients. I had many asthma patients in my practice and in one family with 5 children all had asthma. In those times I still made home visits and I remember that I was there almost weekly because one of these children was very short of breath. From the literature I knew that proper management encompassed the use of preventive medication and proper housing. I managed to arrange this for this family and the health of the children improved enormously. Triggered by this I became interested in doing research in primary care respiratory medicine and after 4 years of hard work I got my PhD when I was 46. I started up a research group around the subject how to manage asthma and COPD in primary care and discovered that in many countries GP's had the same interest. In the UK The General Practitioners in Asthma groups was formed and appointed me to their professor. In the years after we founded 36 of these groups in as many countries over the world bound them together as the International Primary care Respiratory group (IPCRG). From this position I also became professor of primary care respiratory medicine in Groningen and the Netherlands.

So why do I bring this forward. Because here the story begins why we are all here today.

One day a local GP in The Netherlands Frederik van Gemert who is in the audience as well, came to me and asked me if I would allow him to do research under my supervision. Now many people ask me this but I cannot and certainly do not want to supervise too many PhD students. My trick is that I invite them to join me in a long walk of 15 kms around the lake nearby in order to discuss their plans. Mostly I never hear from them again. But Frederik came and during our hike we decided that he would do research regarding COPD in sub-Saharan Africa. We managed to get funding from an American Pharma company -Mundifarma_ and we started from scratch. The main question we wanted to be answered was what is the prevalence of COPD in rural Sub-Saharan Africa. In the journey that such a project is we got the warm and welcoming co-operation of Prof. Kanya and Dr. Bruce Kirenga. They secured the cooperation of the health authorities in Masindi district and after hard and precise work we obtained the results. From this we learned that COPD is a frequent and invalidating disease in rural Masindi and therefore most likely also in Sub-Saharan Africa. The study was endorsed by the WHO and partly based on the results WHO, charities, governments, and private companies have initiated a number of initiatives to seek solutions for replacing indoor cooking. The IPCRG and a number of academic institutions initiated a study proposal that was endorsed by the European community and rewarded by a grant of 4 Million Euros seeking to understand the implementation of better cooking devices and the danger of indoor health circumstances.

Inspired by this success Dr. Bruce Kirenga started to do asthma research and initiated the African Severe Asthma Project study including three countries Uganda, Kenya and Ethiopia in order to understand the problems and background of severe asthma in Africa. My current employer GSK pharma rewarded this project with a grant of nearly one million Pounds.

So what did we achieve? That is not only that we know that asthma is as prevalent in Sub-Saharan Africa as in many other countries; not only that currently asthma is still a disease that unfortunately takes many lives as published by Dr. Kirenga in Thorax. The one most important issue is here that based on the studies that were performed until now the cooperation between the Groningen University and Makerere university and the supporters of the study Makerere university succeeded to form the Makerere University Lung Institute. Because the real leap forward should come from training young doctors and scientists over here the studies that still have to be performed.

The MLI is a true very positive example of the fast developing medical care in low and middle income countries like Uganda where health care in the LMIC only a decade ago was merely directed on communicable infectious diseases. We are now in a stage where these infectious diseases fortunately take less lives. Although we still have to be cautious HIV, Malaria, and tuberculosis seem to be under control due to the enormous advantages in treatment and the dedicated care of the medical community supported by the government. Now the focus of medical care will in the coming decades slowly go to the prevention and treatment of chronic diseases such as chronic heart disease, asthma and chronic Obstructive Pulmonary disease. In the past two days during the conference we heard presentations about both the prevention and treatment of tuberculosis as a classic example of a communicable disease but also presentations about Asthma, COPD. These diseases are typically non communicable diseases. Moreover Dr. Rupert Jones reported results from his studies regarding pulmonary rehabilitation for patients suffering from the chronic pulmonary disablement caused by a range of pulmonary diseases. In my view African medical care in general is with MLI on the

brink of a new era in medicine in Africa but also in the world. As I described the first step is the battle against the overwhelming need of direct medical help for infectious diseases and urgent medical care. The second step is preventive medicine prevention against both communicable and non-communicable diseases such as asthma and COPD. The third step in medicine is always the reflection and the development. The reflection is, are we on the right way? With the development of the economy are we still providing a health care that is covering the demand and the needs of our population? Are the instruments that we use and the health care policy supporting the goals we all want to achieve? The development is what can we do to support local progress and what can we do to support international progress in medicine? The latter might be more important than you currently may think! International cutting edge pulmonary research is traditionally focussed in some centres in high income countries in western Europe, America and Asia. Research institutes typically include top facilities, top researchers and creative leaders. Something that we may not be able to achieve in the MLI right now. But instead we can do research and provide up to date medical care and education in one institution right there where it is needed most. Namely in an area where there is an overwhelming demand for proper basic care. There is where the challenge is how do we provide sophisticated diagnosis and affordable but up to date care for the millions of patients that currently lack any care. This needs clinical research in LMIC on top level. Exactly that can be delivered by the MLI in conjunction with research institutes elsewhere such as the Groningen Research Institute for Asthma and COPD, international organisations Like ERS and IPCRG and finally of course the other sub-Saharan research institutes we already work with. I hope and wish that MLI will bring pulmonary medicine forward and will be an example of a well organised hands on research institute not only for Uganda but also for the Global community.

Thank you for your attention.

PANEL DISCUSSION



MAKERERE UNIVERSITY LUNG INSTITUTE (MLI) THE 1ST INTERNATIONAL LUNG SCIENCE SYMPOSIUM AND INSTITUTE INAUGURATION



PANEL DISCUSSION: UGANDA'S HEALTH SYSTEM'S READINESS TO PROVIDE UNIVERSAL LUNG HEALTH COVERAGE

Globally, respiratory diseases are among the leading causes of morbidity and mortality. Low and middle-income countries such as Uganda, are disproportionately affected due to the double burden of communicable (such as Tuberculosis and pneumonia), and non-communicable respiratory diseases (such as asthma, Chronic Obstructive Pulmonary diseases (COPD), lung cancer and other environmentally related interstitial lung diseases). Recent studies by the Makerere University Lung Institute (MLI) and collaborators indicate high prevalence of communicable and none communicable lung diseases: COPD 16.2%, asthma 11.2%, TB 253/100,000.

Despite this high disease burden, there has been little attention and limited human resource capacity, diagnostics, medicines and supplies to manage these diseases. A survey of 105 health workers revealed that up to 60% of primary care clinicians were not comfortable to manage patients with lung diseases largely due to lack of competencies. Another survey in 22 public hospitals, 23 private and 85 private pharmacies has revealed that 26.1% of public hospital had salbutamol stocked, 4% had inhaled corticosteroids monotherapies and 34.8% had spirometry.

As part of the MLI lung science symposium a panel discussion titled ***“Uganda’s Health System’s readiness to provide Universal Lung Health Coverage”*** has been organized. The aim of this panel is to discuss Uganda’s health system’s readiness to address the double burden of communicable and non-communicable lung diseases in Uganda. The specific objectives are;

1. To discuss health system (human resource, infrastructure, financing, medicines and supplies, diagnostics) gaps in the early detection, management and prevention of lung diseases at all ages in Uganda.
2. To identify country-specific research priorities to address the high burden of lung diseases
3. To identify innovative solutions to the growing burden of non-communicable lung diseases that are relevant to the local setting, scalable, low cost and high impact.

We anticipate that by the end of the discussions, there will be a new beginning for strengthening health systems to address the lung disease burden in Uganda.

THE PANEL DISCUSSANTS WILL INCLUDE



Dr. Patrick Kadama
Director for Policy and Strategy at African Centre for Global Health & Social Transformation



Dr. Diana Atwine
Permanent Secretary, Ministry of Health



Prof. Harriet Mayanja
School of Medicine, Makerere University



Dr. Freddie Bwanga
School of Biomedical Sciences, Makerere University



Dr. Simon Luzige
Pulmonologist, Nakasero Hospital

MODERATOR



Dr. Peter Eriki

Date **APRIL 29TH**
Time **03:00-05:00PM** 2019

Venue Davis Lecture Theatre, Makerere University
College of Health Sciences, Mulago Hospital

SYMPOSIUM SCIENTIFIC PROGRAM



MAKERERE UNIVERSITY LUNG INSTITUTE (MLI) THE 1ST INTERNATIONAL LUNG SCIENCE SYMPOSIUM AND INSTITUTE INAUGURATION

Makerere University College of Health Sciences, Kampala Uganda 29th -30th April 2019



SCIENTIFIC PROGRAMME

DAY ONE: 29 TH APRIL 2019		
8:30-9:00	Arrival and Registration	MLI Secretariat
9:00 -9:05	Welcome Remarks by Chair - Organizing Committee	Ivan Kimuli
9:05 -9:10	Remarks by Chair – Scientific Committee	Rebecca Nantanda
SESSION 1: TUBERCULOSIS		
<i>Chairs: Dr. Stavia Turyahabwe/Dr Andrew Ozero</i>		
9:10-9:25	Economic burden of TB in Uganda; findings from a nationwide survey	Winters Muttamba
9:25-9:40	The other face of TB: the social impact of TB in Africa	Irene Ayakaka
9:40-10:05	The paradigm shift to end TB: USAID DEFEAT TB experience	DEFEAT TB
10:05 -10:20	Improving TB diagnosis among HIV positive patients in western Kenya	Steve Wandiga
10:20 -10:35	TB case finding, historic perspectives and future prospects: Is it time to move from passive to active TB case findings in high prevalence HIV/TB areas?	Esther Ngadaya
10:35 -10:50	GeneXpert Ultra: Analytical Performance and Clinical Diagnostic Accuracy	Lydia Nakiyingi
10:50 -11:05	From Directly Observed Therapy (DOT) to Digital Adherence Technology (DAT) for TB Treatment	Achilles Katamba
11:05 -11:30	<i>Tea/Coffee Break and Poster viewing</i>	ALL
SESSION 2: Sub-Theme: Asthma/COPD/Post TB		
<i>Chairs: Prof Thys van der Molen and Dr. Opio Rejani</i>		
11:30 -11:45	COPD: The Global Perspective	Shumonta Quaderi
11:45-12:00	Burden of COPD in Africa	Frederik van Gemert
12:00-12:15	The Epidemiology of asthma in Africa	Bruce Kirenga
12:15-12:30	The burden of COPD and management challenges in Uganda and Nepal: Field experiences and preliminary results	Natalie Rykiel
12:30 -12:45	Economic burden of Chronic Lung Disease in 3 LMICs Fresh Air Project	Simon Walusimbi
12:45 -13:00	Exacerbations and mortality rates of asthma and COPD in Uganda: Findings from a prospective cohort study- The Uganda Registry for Asthma and COPD	Patricia Alupo
13:00-13:15	Characterization of asthma in 3 African countries	Wincelaus Katagira
13:15-13:30	Access and affordability of asthma and COPD medicines and diagnostics	Davis Kibirige
13:30 -14:00	Lunch Break	ALL
SESSION 3: Sub-Theme: Post TB Lung Disease		
<i>Chairs: Dr. William Worodria and Dr. Jamie Rylance</i>		
14:00-14:15	Pulmonary rehabilitation in low resource settings	Rupert Jones
14:15 -14:30	Pre and post intervention study of pulmonary rehabilitation for adults with post-TB lung disease in Uganda	Wincelaus Katagira
14:30 -14:45	Chronic Respiratory Symptoms and Lung Abnormalities Among People with a History of Tuberculosis in Uganda: A National Survey	Harriet Kisembo
14:45 -15:00	<i>Tea/Coffee Break and Poster viewing</i>	ALL
PANEL DISCUSSION		
15:00-17:00	Uganda's Health System's readiness to provide Universal Lung Health Coverage MODERATOR: Dr. Peter Eriki PANELLISTS: Prof Harriet Mayanja, Dr. Patrick Kadama, Dr. Freddie Bwanga, Dr Diana Atwine, Dr. Simon Luzige , Dr. Abel Nkolo	
DAY TWO: 30 TH APRIL 2019		
SESSION 4: CHILDHOOD LUNG HEALTH IN INFANCY AND CHILDHOOD		
<i>Chairs: Prof Grace Ndeezi and Dr Hellen Aanyu</i>		
8:30-9:00	Arrival and Registration	Secretariat
9:00-9:15	Early life determinants of lung health: IMPALA Project	Rebecca Nantanda
9:15- 9:30	Raising awareness of the dangers of biomass smoke in pregnant mothers in rural Uganda-Fresh air midwife project	Rupert Jones
9:30-9:45	Pneumonia in children: Burden and advances in therapeutics	Victor Musiime
9:45-10:00	Paediatric asthma	Hellen Aanyu
10:00 -10:15	Paediatric TB: What it takes to find the missing children with TB.	DEFEAT TB
10:15-10:30	Discussion	
10:30 -11:00	<i>Tea/Coffee Break and Poster viewing</i>	ALL
SESSION 5: LUNG HEALTH AND THE ENVIRONMENT		
<i>Chairs: Prof. Lynn Atuyambe and Ivan Kimuli</i>		
11:00-11:15	Household Air Pollution and Lung Health	Jamie Rylance
11:15-11:30	Interventions for reducing household air pollution	William Checkley
11:30 -11:45	Design and deployment of low-cost technology for air quality monitors in Kampala	E. Bainomugisha
11:45 -12:00	Role of technology in reducing Household Air Pollution (HAP)	Derrick Kiwana
PRESS CONFERENCE		
PANELLISTS: Eng.Andrew Kitaka, Dr. Okello Daniel, Dr. Tom Okurut, Dr. Bruce Kirenga, Dr. Lynn Atuyambe, H.E. Attilio PACIFICI, H.E. Deborah R. Malac		
13:00 -14:00	Lunch Break	ALL
MLI INAUGURATION CEREMONY: 14:00-17:00		

SYMPOSIUM INAUGURATION PROGRAM

Time	Activity	Responsible
1.00:2.00pm	Arrival of invited guests	Master of Ceremonies/Ushers
2.00: 2.05 pm	Welcome remarks by Chair inauguration organizing committee	Dr. Ivan Kimuli
2.05: 2.15 pm	Welcome remarks by Principal College of Health Sciences, Makerere University	Prof. Charles Ibingira
2.15: 2.40 pm	Key Note Address- Fostering clinical and policy relevant lung health research	Prof. Thys van der Molen (Professor of respiratory medicine University Medical Centre Groningen)
2.40-2.45	MLI Translational Clinic - a consumer perspective	Ms. Joyce Luwedde
2.45: 3.05 pm	Makerere University Lung Institute (MLI) - History, Current Status and future perspective	Dr. Bruce J Kirenga
3.05-3.15	Cultural performance	Dept. of Performing Arts and Film – Makerere University
3.15: 3.25 pm	Speech by Vice Chancellor, Makerere University	Prof Barnabas Nawangwe
3.25: 3.35 pm	Speech by Chairperson of Council, Makerere University	Mrs. Lorna Magara
3.35: 3.45 pm	Speech by Chancellor, Makerere University	Prof Ezra Suruma
3.45-3.55	Cultural performance	Dept. of Performing Arts and Film –Makerere University
3.55: 4.05 pm	Speech by Permanent Secretary, Ministry of Health	Dr. Diana Atwine
4.05: 4.15 pm	Speech by Minister of Health	Dr. Jane Ruth Aceng
4.15: 4.35 pm	Speech by Chief Guest- Minister of Science, Technology and Innovation	Dr. Elioda Tumwesigye
4.35-5.00pm	Opening ceremony- Cutting of the tape by Chief Guest and guided tour of Institute premises	Jackie Nakabira/ Simon Mugambe
5.00-7.00pm	Cocktail - Deans Quadrangle	Master of Ceremonies/Ushers

Venue: Deans Quadrangle, Makerere University College of Health Sciences, Mulago Hospital

Master of Ceremony: Dr. Sabrina Kitaka/Dr. Aggrey Semeere

Symposium abstracts

GEC_o – Global Excellence in COPD Outcomes project

Dr. S Quaderi – University College London

Background

Chronic Obstructive Pulmonary Disease remains a major public health problem and an unmet global burden, with over 328 million people suffering with it worldwide. Non-communicable diseases like COPD are the leading causes of death globally, killing more people each year than all other causes combined, with more than 90% of COPD related deaths occurring in LMICs. According to the Global Burden of Disease, COPD is already the third leading cause of death worldwide, something that WHO had not predicted to occur until 2030, and in 15 years, COPD is expected to become the leading cause of death. LMICs face unique challenges in managing COPD, including sub-optimal diverse primary care systems which present challenges with diagnosis and management, especially during exacerbations of COPD.

“Given the high and rising global burden of COPD, a revolution in diagnosis and management of COPD and exacerbations in LMICs is an urgent priority.”

Aims and Objectives

GEC_o 1 is aimed at testing the validity of simple case-finding instruments with and without PEF for identifying individuals with COPD and for GEC_o 2 we will be conducting a feasibility trial to evaluate COPD self-management plans facilitated by community health workers, both in LMICs. Our primary outcome is comparing change in a disease-specific quality of life measure (SGRQ) between the two groups.

Results

This is an ongoing study with GEC_o1 and GEC_o2 still recruiting. GEC_o1 has recruited 6,549/10,500 to date whilst GEC_o has enrolled 232/240 .

A sustainable framework for COPD Case Finding and Self-Management Action Plans which can be utilised in both rural and urban settings has the potential to make a real difference in countries of need.

Exploring local beliefs and behaviours regarding chronic lung diseases in rural Uganda – a mixed-method FRESH AIR study

Simon Walusimbi², Bruce Kirenga^{2,3}, A.C. Walsweer¹, E.A. Brakema¹, Rianne van der Kleij¹, Niels Chavannes¹

1 Department of Public Health and Primary Care, Leiden University Medical Center, Leiden, The Netherlands.

2 Makerere University Lung Institute, Mulago Hospital, Kampala, Uganda.

3 Department of Medicine, Makerere University, Kampala, Uganda

Corresponding author: E.A. Brakema, E.A.Brakema@lumc.nl +31(0)715268485

BACKGROUND: Chronic lung diseases (CLDs) have become a major burden in Africa, their mortality surpassing the combined mortality of HIV/AIDS, malaria and tuberculosis. A recent study in rural Uganda observed a prevalence of chronic obstructive pulmonary disease (COPD) of 16.2%. To reduce this growing burden, the implementation of evidence-based interventions targeting CLDs should be tailored to the rural Uganda setting.

OBJECTIVE(S): To explore local beliefs and behaviours regarding CLDs in rural Uganda.

METHODS: This mixed-method FRESH AIR sub-study was conducted in rural areas of the Jinja district. Qualitative interviews, focus groups, and observations were conducted among purposively selected community members (CMs) and healthcare professionals (HPs). Themes were identified via thematic analysis. Results were triangulated using a quantitative survey among 207 randomly selected CMs and 41 HPs.

KEY RESULTS: Symptoms of CLDs were almost exclusively attributed to tuberculosis. Although all HPs had heard of asthma, and many of COPD (56.1%), the majority (92.7%) was unable to recognise COPD in a written clinical scenario. CLDs were perceived as highly severe by both HPs and CMs. Their perception of risk factors was only partly adequate. The risk behaviour reported by CMs varied: most (97%) burned solid fuels, but smoking prevalence was low (1.5%). Many HPs (56.8%) did not adhere to COPD/asthma guidelines; 63.2% of them stated that guidelines are impossible to follow (amongst others because of lack of equipment/medication) and 36.8% was unaware of their existence.

CONCLUSION: In rural Jinja, awareness of CLDs and their risk factors is inadequate for both HPs and CMs. CLDs are often mislabelled as tuberculosis. Smoking prevalence is low among CMs, while solid fuel use is high. HPs lack awareness and equipment/medication for treating CLDs effectively.

RECOMMENDATIONS: Results of this study can inform the tailored implementation of interventions targeting CLDs in rural Uganda.

Conflicts of interest: The authors have no conflicts of interest do declare

Funding: FRESH AIR was funded by a research grant from European Union's Horizon 2020 research and innovation programme under grant agreement No 680997, TRIAL ID NTR5759 <http://www.trialregister.nl/trialreg/admin/rctsearch.asp?Term=23332>

Feasibility of conducting an internet-based Spirometry training for health care workers in Uganda: The Fresh Air H2020 experience

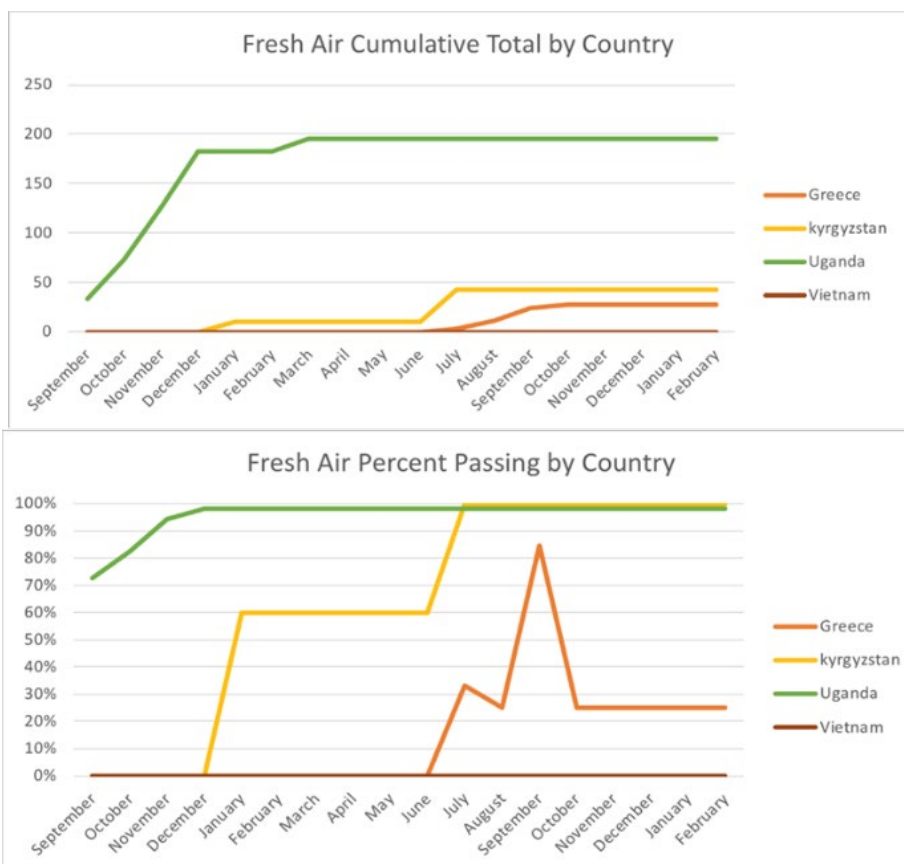
Wincelaus Katagira¹, Bruce Kirenga¹, Sharon W. Kiche², Louise C. Warren², James W. Stout²

1. Makerere University Lung Institute, Uganda
2. University of Washington, United States of America

Background: Spirometry is the “gold standard” measure of lung function, central to the diagnosis and management of chronic lung diseases such as Asthma and Chronic Obstructive Pulmonary Disease (COPD). However, patient access to this test is unavailable in most Low-Income Countries (LICs). Limiting factors include the lack of spirometers and the lack of training and feedback in performance and interpretation.

Aim: To explore the feasibility of providing an internet-based spirometry training to health care workers in Uganda

Methods: The University of Washington provided access to Spirometry 360, a comprehensive, interactive, and evidence-based training and feedback programme, which is delivered online enabling wide distribution. To overcome foreseeable challenges of internet connectivity and coordination and to ensure comprehension as well as skill acquisition, we planned a group training.



Invitations were sent to health care workers (HCWs) across the country. A wide range of HCWs participated in the training, from biomedical scientists, to medical assistants. Attendees gathered in one room with a steady internet connection. To allow adequate comprehension of training materials, the 6-hour training was spread out across 5 days. Participating practices then emailed all de-identified spirometry tests to over 7 months and received monthly feedback, summarizing the quantity and quality of spirometry tests received, and specific corrective action.

Results: In August 2017, 24 health care workers enrolled in the training, 22 (92%) completed its six modules, and of those, 20 (91%) completed the post-course survey. The training was well received; for example, 80% reported the training as very good or excellent, and 100% would recommend the program to a colleague. A total of 195 spirometry tests from 7 Ugandan practice teams were then received over 7 months, averaging a total 28 tests per month. The percent of acceptable tests was 73% in the first month of the feedback program, and increased to 98% by its conclusion. The participants appreciated the interactive nature of the training.

Conclusion: It is feasible to offer an internet-based training and feedback in settings with limited internet connectivity, and have the training be well received. Training health care workers to perform high quality administration and interpretation of spirometry testing is a critical step in building capacity to diagnose chronic lung diseases in LICs.

FRESH AIR was funded by the EU Research and Innovation program Horizon2020 under grant agreement no. 680997. This study is registered under trial registration number: NTR5759. <http://www.trialregister.nl/trialreg/admin/rctsearch.asp?Term=23332>

References: www.spirometry360

Mortality and associated factors among patients with Chronic Obstructive Pulmonary Disease (COPD) in Uganda

Patricia Alupo¹, Aadaeze C. Wosu^{1,2}, Levi Mugenyi¹, Katagira Winceslaus¹, Bruce Kirenga¹

1 Makerere University Lung Institute, Mulago Hill, Kampala, Uganda.

2 Department of Epidemiology, Bloomberg School of Public Health, Johns Hopkins University, Baltimore, MD, USA

Background

Chronic Obstructive Pulmonary Disease (COPD) is the third leading cause of death globally, with 90% of its attributable deaths occurring in low and middle-income countries like Uganda. Longitudinal data on mortality and its predictors among COPD patients is lacking in Uganda. We set up the Uganda Registry for Asthma and COPD (URAC) to fill this data gap.

Methodology

Individuals with a clinician diagnosis of COPD at six chest clinics in six referrals hospitals in Uganda were enrolled into the URAC registry and followed up to determine the incidence and predictors of mortality. At baseline, spirometry was performed, and a standardized clinical record form was used to collect information on socio-demographic factors and clinical profile. Mortality was ascertained through postmortem reports and verbal autopsies. Incidence rates and incidence rate ratios were computed to assess the association of socio-demographic and clinical factors with mortality.

Results

We recruited and evaluated a total of 296 COPD patients, (51.4% male). A total of 33 (11.2%) died. Higher mortality rates per 1000 person-years was observed in males IR=116, compared to females IR=76, IRR=1.51 (95% CI = 0.72–3.26). Incidence rates per 1000 person-years were 59.9, 27.4, 137.7, 89.9 and 113.6 for age groups <35, 35–44, 45–54, 55–64 and 65+, respectively. COPD stage by FEV₁ was significantly associated with mortality, GOLD 4 compared to 1 IRR 12.7 (95% CI = 2.71–119.2, P<0.001), GOLD 3 compared to 1 IRR: 5.8 (95% CI = 1.3–54.1, P=0.005) and GOLD 2 compared to 1 IRR 2.8 (95% CI = 0.6–25.9, P=0.090). Smoking history was borderline significant IRR 1.7 (95% CI = 0.8–3.7, P=0.061). Other factors that were not significantly associated with mortality include: HIV positive status: IRR 1.9 (95% CI = 0.6–4.7, P=0.090), and biomass smoke exposure: IRR 0.6 (95% CI = 0.2–2.8, P=0.172). Hypertension and obesity were not significantly associated with mortality.

Conclusion

Among COPD patients in this Ugandan population, mortality over a two-year period is high compared to higher income countries. GOLD stage by FEV₁ was prognostic for mortality. Co-morbidities did not significantly affect mortality outcomes in this patient population.

Prevalence of tuberculosis risk factors among bacteriologically negative and bacteriologically confirmed tuberculosis patients from five regional referral hospitals in Uganda

Winters Muttamba^{1*}, Bruce Kirenga¹, Willy Ssengooba², Rogers Sekibira¹, Achilles Katamba³, Moses L Joloba²

1 Makerere University Lung Institute, College of Health Sciences, Makerere University, Kampala Uganda

2 Department of Medical Microbiology, College of Health Sciences, Makerere University, Kampala Uganda

3 School of Medicine, College of Health Sciences, Makerere University, Kampala Uganda

Background

Understanding risk factors for TB and their prevalence helps guide early diagnosis. We determined their prevalence among bacteriologically negative and bacteriologically confirmed TB patients in five regional referral hospitals (RRHs) in Uganda.

Methods

This cross-sectional study considered 1862 adult presumptive TB participants. We performed fluorescent microscopy (FM), Xpert MTB/RIF (Xpert), Lowenstein Jensen (LJ) culture, HIV- and random blood sugar (RBS) testing on recruited patients. Prevalence and prevalence ratios of risk factors were compared among bacteriologically negative and confirmed cases. Odds ratios (ORs) and 95% confidence intervals (CI) were determined for significant risk factors in bacteriologically confirmed patients.

Results

Of the 1862 participants, 978 (55%) were male and median age 36 years (IQR: 27 - 48). Up to 273 (15%) had positive result on all three TB tests. Most prevalent risk factors (PR >1.0) among bacteriologically negative and positive TB patients were; Cigarette Smoking (9.3 % vs 2.1%; PR=2.1), Biosmoke (24% vs 39.7%; PR=1.7), Contact (4.2% vs 6.5 %; PR=1.6), Male gender (51.4% vs 72.5%; PR=1.4), alcohol use (17.2% vs 24.4 %; PR=1.4), Diabetes (0.7% vs 0.9%; PR=1.3), family history of TB (12.1% vs 13.7%; PR=1.1). Risk factors; adjPRR (95% CI) of being bacteriologically positive were; Male 1.8 (1.4-2.4), biosmoke exposure 1.5 (1.2-2.0), history of cigarette smoking 1.6 (1.1-2.4).

Conclusion

Among bacteriologically confirmed patients in Uganda, cigarette smoking, biosmoke exposure, contact, male gender, alcohol use, diabetes and family history of TB are important risk factors for TB. Interventions for TB control in people with these risk factors would help in TB control efforts.

Key words: *Prevalence, tuberculosis, risk factors, presumptive*

Health seeking behavior among individuals presenting with chronic cough symptoms at regional referral hospitals in Uganda; missed opportunity for early tuberculosis diagnosis

Winters Muttamba^{1,2¶}, Willy Ssengooba^{1,2¶}, Bruce Kirenga¹, Rogers Sekibira¹, Simon Walusimbi¹, Achilles Katamba³, Moses L Joloba²

¹ Makerere University Lung Institute, College of Health Sciences, Makerere University, Kampala Uganda

² Department of Medical Microbiology, College of Health Sciences, Makerere University, Kampala Uganda

³ School of Medicine, College of Health Sciences, Makerere University, Kampala Uganda

Background

Tuberculosis (TB) remains a global disease burden and is the 9th leading cause of death from a single infectious agent. Patients are in a complex health care system with both formal and informal providers and it's very important that a TB diagnosis is not missed at the first interaction with the health care system. In this study, we highlight the health system inefficiencies that lead to TB diagnostic delays for which interventions could be instituted to ensure early TB diagnosis and prompt TB treatment initiation.

Methods

This study was nested in a cross-sectional study that assessed the accuracy of different Xpert MTB/Rif implementation strategies in programmatic settings at the regional referral hospitals in Uganda. We assessed the health seeking behavior of the patients with chronic cough by calculating proportions of patients that visited each type of health facility and further calculated the odds of being TB positive given the type of health facility initially visited for consultation. We assessed the proportion of patients suspected to have TB at each of the facilities visited despite presenting with chronic cough.

Results

A total of 1,863 presumptive TB patients were enrolled of which 979 (54.5%) were male, and 1795 (99.9%) had chronic cough as a symptom. A total of 1352 (75.4%) had previously sought care for the chronic cough, with majority 805 (59.6%) seeking care from a public health facility followed by private health facility at 289 (21.4%). Up to 182 (13.5%) patients visited a drug store for their chronic cough. Patients who visited a private health facility before diagnosis were more likely to have a positive GeneXpert test (adj OR 1.5, $p = 0.011$, 95% CI 1.1-1.9).

Conclusions

Chronic cough is a main symptom for presumptive TB patients presenting at regional referral hospitals. The study highlights the health seeking behaviors of patients with chronic cough as a symptom, and highlights the missed opportunities for early TB diagnosis due to failure to investigate for TB when patients first interface with the health system. This ultimately leads to delayed TB diagnosis and continued transmission. Improved TB diagnosis possibly with the GeneXpert test, at first contact with the health care system has potential to increase TB case finding and break the transmission cycle in the community.

Feasibility and acceptability of a midwife-led health education strategy to reduce exposure to biomass smoke among pregnant women in Uganda

***Rebecca Nantanda^{1,2}, Shamim Buteme¹, Sanne van Kampen⁴, Lucy Cartwright⁴, Jill Pooler⁴, Andy Barton⁴, Lynne Callaghan⁴, Jean Mirembe⁵, Grace Ndeezi², James K Tumwine², Bruce Kirenga^{1,3}, Rupert Jones⁴**

1. *Makerere University Lung Institute, Makerere University College of Health Sciences*
2. *Department of Paediatrics and Child Health, Makerere University College of Health Sciences*
3. *Department of Internal Medicine, Makerere University College of Health Sciences*
4. *Clinical Trials and Population Studies Department, University of Plymouth*
5. *Directorate of Health Services, Jinja district, Uganda*

Background: Biomass smoke exposure is a threat to child and maternal health in many low and middle-income countries due to its association with diseases such as respiratory infections, chronic lung diseases and poor pregnancy outcomes. We aimed to assess the feasibility, acceptability and impact of a midwife-led education programme on biomass risks and prevention measures for pregnant and post-natal women attending health facilities in rural Uganda.

Methods: Education materials (flip charts, posters and leaflets) were developed through an iterative process that involved all levels of stakeholders from Ministry of Health to villagers in Jinja District. The materials were tested and improved in a series of cycles and finally approved by Ministry of Health. Education sessions on biomass smoke were delivered by midwives to the women and village health teams (VHTs) using the materials developed. Feasibility, acceptability and impact were assessed through qualitative interviews with women three months after the sessions.

Results: The district health team, twelve midwives and 40 VHTs were sensitized on biomass smoke. Overall, 244 women were educated about biomass smoke by midwives; pre- and post-session questionnaires highlighted significant improvements in knowledge regarding the dangers of biomass smoke by as high as 47.8% in some aspects. The qualitative data showed that participants had contemplated or made behavioural changes towards reducing exposure to smoke, such as staying away from the kitchen while cooking, using dry wood for cooking, burying not burning refuse, using solar power for lighting and improved ventilation in their kitchens. Intent to make futures change such as saving money to buy clean cookstoves and solar batteries was also reported. The major barrier to behavioural changes was poverty. The major facilitators were the 'discovery' of the range and duration of harms from biomass smoke, and that some improvements cost no money.

Conclusions: This project highlights that a programme delivered by midwives constitutes a feasible and acceptable approach to educate mothers and VHTs about the dangers of biomass smoke exposure. Implementing this programme has the potential to reduce exposure to smoke with benefits to mother, foetus, and young children throughout their lives.

Keywords: *biomass smoke exposure; respiratory health; antenatal education programme*

Household air pollution effects on cardio-respiratory health of urban slum dwellers in Kampala (HAPCRUSH)

Shelton T. Mariga¹, Wincellaus Katagira¹, Bruce Kirenga¹

1 Makerere University Lung Institute, College of Health Sciences, Makerere University

Background

Risk factors for cardio-respiratory diseases like household air pollution, burning biofuels and use of other traditional practices associated to increased air pollution rates are predominant in urban slum dwellings. Kampala, the capital city of Uganda has 60.5% of its population living in slums. We aim to identify cardio-respiratory risk factors and their related adverse health effects within slum residents in Kampala.

Objectives

To explore knowledge, attitudes and perceptions of slum communities towards household air pollution, as well as its impact on cardio-respiratory health.

Methods

The proposed study is a cross sectional; mixed-methods study combining both qualitative and quantitative methodology. The study areas are urban slums within Kampala, will include Bwaise, Namuwongo and Katwe. Using quantitative methodology, we will select 135 households and collect socio-demographic data as well as measurement of blood pressure and Spirometric measurements. Using qualitative methodology, we will conduct in-depth interviews with participants aged ≥ 12 years using interview guides to obtain perceptions, knowledge, beliefs and attitudes of urban slum dwellers.

Benefits from the findings

Findings obtained from this preliminary study will generate novel information regarding indoor exposure concentrations of PM and CO, a surrogate health burden of biomass cooking, as well as cardio-respiratory indicators (spirometry and hypertension) in this setting. Furthermore, information will also be obtained from the in-depth interview and survey questionnaire to facilitate intervention measures aimed at reducing household air pollution to be explored within the main urban community-based, mixed-methods epidemiological study in Phase II, in Kampala slum dwellings.

Policy and Regulatory Relevance

These results should provide useful basis and background of air pollution related Cardio-Respiratory health effects for further investigations including the prevalence and eventual mitigation studies/programmes planned for the Intervention Phase in subsequent studies to follow up these preliminary findings.

Geographic patterns of referral for TB evaluation with introduction of Xpert MTB/RIF at regional referral hospitals in Uganda: Evidence for country wide roll out.

Winters Muttamba ^{1,3}, Eric S Coker², Willy Ssengooba³, Rogers Sekibira¹, Bruce Kirenga¹, Achilles Katamba⁴, Moses L Joloba³

¹ Makerere University Lung Institute, College of Health Sciences, Makerere University, Kampala Uganda

² School of Public Health, University of California, Berkeley, CA, USA

³ Department of Medical Microbiology, College of Health Sciences, Makerere University, Kampala Uganda

⁴ School of Public Health, College of Health Sciences, Makerere University, Kampala Uganda

Background

Xpert MTB/RIF is an automated cartridge-based nucleic acid amplification test that has demonstrated its potential to detect tuberculosis and rifampicin resistance with high accuracy. To support roll out and deployment, a records review with emphasis on patient address data before and after Xpert MTB/RIF installation was conducted at 5 regional referral hospitals (Arua, Mbale, Mbarara, Lacor and Mulago).

Methods

Parish address data of the TB patients was obtained from hospital records and thereafter spatial data on the hospitals and the parishes in which TB patients lived in was obtained. In ArcGIS, we determined the geographic centroid of each parish polygon. In order to determine distance in kilometers from the geographic centroid of a parish to the hospital for each patient, we used the point distance function in ArcGIS. We calculated the average distance overall (stratified by hospital), and pre- and post-Xpert MTB/RIF installation at the hospitals.

Results

Overall, the mean distance was 75.5 km (95% CI: 73.2-77.8). There was a significant difference in distance based on study hospital, with the shortest distance observed for Arua (48.2 km) and the largest distances observed for Mbarara (94.8 km) and Mbale (93.9 km). Prior to Xpert TB/RIF installation at the hospitals, average and median distances were 60 km and 14.7 km, respectively. After Xpert MTB/RIF installation, average and median distances were 83.2 km and 44 km respectively. Univariate tests indicated this difference in distance was statistically significant, and multivariate adjusted models supported the univariate analyses. Specifically, Xpert MTB/RIF installation at the hospitals was associated with a 19.5% increase in distance between parish centroid and hospital for the TB patients.

Conclusion

Results on geographical referral patterns highlight the need to further decentralize Xpert MTB/RIF testing due to increased demand for the tests from the community and health facilities.

“Johns Hopkins and Makerere University collaboration: Four years of research and training. Qualitative insights into COPD management in Uganda and Nepal: field experiences and preliminary results.”

Natalie Rykiel, MSc, GECO Research Program Coordinator, Nepal

Background

Four years of a collaborative partnership between JHU and MLI have resulted in the development and implementation of high-impact research programs, cohorts and trainee programs. For the most recent research collaboration, GECO, we will delve into the preliminary findings and experiences from field work in Nepal and Uganda.

Objectives

We aim to build the local capacity and scientific rigor of collaborative field sites. Through preliminary field results, we will gain insights into the challenges and possibilities for COPD management in Uganda and Nepal.

Methods

As part of the process evaluation of the ongoing GECO trial, we utilized qualitative methods of in-depth interviews, informal discussions and field observations to evaluate trial adherence and explore barriers and facilitators to COPD management in Nepal and Uganda.

Results

Using the RE-AIM Framework to guide our understanding of trial implementation, we found various factors, often site-specific, which impact adherence and other outcomes. Perceived disease severity, social support networks, socioeconomic status and perceptions of community health worker reach and efficacy are a few of the elements that shape trial outcomes.

Conclusion

Site-specific factors and experiences of trial participants and community health workers should be considered in order to contextualize the larger quantitative results of the GECO trial.

Burden of fungal asthma in Africa

Richard Kwizera^{1,2}, Joseph Musaazi¹, David B. Meya^{1,3}, William Worodria^{3,4}, Freddie Bwanga⁵, Henry Kajumbula⁵, Stephen J. Fowler⁶, Bruce J. Kirenga^{2,3,4}, Robin Gore⁷, David W. Denning⁸.

¹Infectious Diseases Institute, College of Health Sciences, Makerere University, Kampala, Uganda. ²Makerere University Lung Institute, College of Health Sciences, Makerere University, Kampala, Uganda. ³Department of Medicine, School of Medicine, College of Health Sciences, Makerere University, Kampala, Uganda. ⁴Mulago National Referral Hospital, Kampala, Uganda. ⁵Department of Medical Microbiology, School of Biomedical Sciences, College of Health Sciences, Makerere University Kampala, Uganda. ⁶Division of Infection, Immunity and Respiratory Medicine, School of Biological Sciences, Faculty of Biology, Medicine and Health, The University of Manchester; NIHR Biomedical Research Centre, Manchester University Hospitals NHS Foundation Trust, United Kingdom. ⁷Cambridge University Hospitals NHS Foundation Trust, Cambridge, United Kingdom ⁸The National Aspergillus Centre, Wythenshawe Hospital, The University of Manchester, Manchester Academic Health Science Centre, Manchester, United Kingdom.

Background: Asthma is one of the neglected diseases in Africa with a high prevalence. Allergic fungal diseases have been reported to complicate asthma progression and treatment outcomes. However, data about fungal asthma and its associated complications are limited in Africa. We aimed to estimate the burden of fungal asthma among adults and children in Africa using a systematic review and meta-analysis.

Methods: We first engaged the Institute for Health Metrics and Evaluation (IHME) to highlight the trend in morbidity and mortality attributed to asthma in Africa. We then searched PubMed, HINARI and Google Scholar for all studies of any design focusing on fungal asthma in any African country. Languages were restricted to English and French, but not year of publication. We estimated the weighted prevalence of allergic fungal infections among asthmatics with a 95% CI and pooled the results using a random effects model. This study is registered with PROSPERO, number CRD42019117319.

Results: The IHME data showed that there has been a gradual increase in morbidity and mortality due to asthma in African adults with a prevalence of 4%. Our search retrieved 5233 citations. We retained 20 studies that met our selection criteria. These were from 13 African countries published between 1967 and 2018. There were eight cross-sectional studies and twelve review articles. The average asthma prevalence in Africa was 6% from these studies. The prevalence of fungal sensitisation was relatively high (3-52%) in the asthmatic population with an average of 28% and a pooled estimate of 23.3%, mostly due to *Aspergillus* species. Prevalence of ABPA was estimated at 1.6-21.2% and SAFS at 3.3%. Diagnosis of fungal allergy was mostly (7/8) made by skin prick tests. Only two studies reported factors associated with fungal allergy in asthma. There was no data on the use of medication to manage fungal asthma. None of the studies evaluated the association between fungal allergy and asthma severity. There were no data about mortality related to fungal asthma in Africa. Data were lacking in children.

Conclusion: There is a high prevalence of fungal sensitization among Africans with asthma. Fungal asthma is a significant problem in Africa but there remains a paucity of data on the epidemiology and associated complications. There is urgent need for national epidemiological studies to estimate the actual burden of fungal asthma in Africa.

MeSH Keywords: *Fungal sensitisation; fungal asthma; SAFS; ABPA; severe asthma; Africa.*

Maternal and socioeconomic determinants of lung function among infants in Uganda: a birth cohort study

Rebecca Nantanda^{1,2}, Zelalem Terfa¹, , Graham Devereux¹, Sean Semple³, Louis Niessen¹, Jahangir Khan¹, Maia Lesosky⁴, William Worodria⁵, Bruce Kirenga², Kevin Mortimer¹ Jamie Rylance¹

1 *Liverpool School of Tropical Medicine, Liverpool United Kingdom*

2 *Makerere University Lung Institute, Makerere University College of Health Sciences, Kampala Uganda*

3 *University of Stirling, United Kingdom*

4 *University of Cape Town, Cape Town, South Africa*

5 *Mulago National Referral hospital, Kampala Uganda*

Background

Lung diseases contribute up to 15% of overall deaths worldwide. Most of these deaths occur in low and middle-income countries. Intrauterine factors such as maternal diet and air pollution exposure during pregnancy and poverty have been associated with suboptimal neonatal lung function, which increases the risk of lung diseases in childhood and beyond. The relative contributions of these insults amongst African babies is unknown, but would directly inform preventative interventions.

Aim

The overall aim of this study is to describe the maternal and household factors associated with lung function in infants.

Methods

A birth cohort study within the rural Kyamulibwa Health Demographic Surveillance Site, Kalungu district, Uganda. Pregnant women will be recruited during routine antenatal care clinic attendance. Maternal diet will be assessed using the food frequency questionnaire, Minimum Dietary Diversity for Women (MDD-W), and serum Vitamin D. For infants, the minimum dietary diversity (IYCMDD) score will be adopted to collect infants and children's dietary diversity data. Exposure to air pollutants will be measured at community and household level by articulate monitoring (PM_{2.5}), and by personal carbon monoxide monitoring. Maternal use of tobacco, alcohol and other substances will also be assessed. Household socioeconomic status, food insecurity and energy use and expenditure will be assessed using standardised World Bank questionnaires.

Lung function of the mothers and their infants will be measured at six weeks after birth using Spirometry and Tidal Breath Analysis respectively. Linear and logistic regression analysis will determine the association between maternal nutrition, air pollution, and household socioeconomic status and lung function the infants.

It is anticipated that the information generated from this study will inform relevant strategies for primary prevention of lung diseases in Africa.

This study is funded by the NIHR Global Health Research Unit on Lung Health and TB in Africa at Liverpool School of Tropical Medicine (LSTM - "IMPALA"), Grant number 16/136/35.

Chest X-ray performs better than the WHO symptoms in screening for tuberculosis in Uganda

Joanitah Nalunjogi^{1, 2}, Achilles Katamba¹, Frank Mugabe³, Irene Najjingo¹, Pastan Lusiba¹, Bruce Kirenga^{2, 4}

1 *Clinical Epidemiology Unit, College of Health Sciences, Makerere University, Uganda.*

2 *Makerere University Lung Institute, College of Health Sciences, Makerere University, Uganda.*

3 *National Tuberculosis and Leprosy Program, Ministry of Health Uganda.*

4 *Division of Pulmonary Medicine, College of Health Sciences, Makerere University, Uganda.*

Text: Background

Tuberculosis (TB) is a major cause of morbidity and mortality worldwide. The WHO END TB strategy indicates a need for $\geq 90\%$ TB case detection among others to combat TB. In order to achieve increased TB case detection there is need for a more sensitive and specific screening tool. Currently, the WHO symptoms are recommended for screening tuberculosis (TB) in resource-limited settings. The objective of this study was to determine the performance of the Chest X-ray (CXR) in screening for tuberculosis in Uganda.

Methods

4512 complete records of participants above 15 years who consented to participate in the Uganda Tuberculosis Prevalence Survey (UTPS) were analysed. Sputum Löwenstein–Jensen (LJ) culture results were used as the gold standard. The WHO symptoms included presence of any of cough, fever, weight loss and night sweats. This was considered as a positive result. The CXR results that were suggestive of active TB disease were considered positive. The performance of the WHO symptoms or CXR was determined using 2 by 2 tables and reported as sensitivity, specificity, positive predictive value, negative predictive value, positive likelihood ratio and negative likelihood ratio.

Results

160(3.5%) TB cases were prevalent.

The WHO symptoms had sensitivity 76% (95%CI 70–83), specificity 31% (95%CI 29-32), positive predictive value 3.9% (95%CI 3.2-4.6), negative predictive value 97.2% (95%CI 96.2-98.0), positive likelihood ratio 1.1 (95%CI 1.0-1.2) and negative likelihood ratio 0.8 (95%CI 0.6-1.0).

The CXR had sensitivity 93% (95%CI 87–96), specificity 97% (95%CI 96-98), positive predictive value 53.8% (95%CI 47.7-59.8), negative predictive value 99.7% (95%CI 99.5-99.9), positive likelihood ratio 31.2 (95%CI 26.1-37.2) and negative likelihood ratio 0.1 (95CI 0.0-0.1).

Conclusion

The CXR is a good screening tool for tuberculosis and performs better than the WHO symptoms in Uganda. Therefore, the CXR should be adopted in the TB screening algorithm for Uganda.

Proportion of Tuberculosis affected households experiencing catastrophic costs due to TB in Uganda: main cost drivers

Winters Muttamba¹, Racheal Tumwebaze¹, Levicatus Mugenyi¹, Charles Batte¹, Abel Nkolo², Achilles Katamba³, Simon Kasasa⁴, Stavia Turyahabwe⁵, Frank Mugabe⁵, Peter Lochoro⁶, Seyoum Dejene⁷, Estella Birabwa⁷, Claudio Mara⁵, Ines Garcia Baena⁸, Bruce Kirenga¹

1 *Makerere University Lung Institute, College of Health Sciences, Makerere University, Kampala Uganda*

2 *University Research Co., LLC (URC) & Center for Human Services (CHS)*

3 *School of Medicine, College of Health Sciences, Makerere University, Kampala Uganda*

4 *School of Public Health, College of Health Sciences, Makerere University, Kampala Uganda*

5 *Ministry of Health, National Tuberculosis and Leprosy Program, Kampala Uganda*

6 *Doctors with Africa, CUAMM*

7 *USAID Mission, Kampala – Uganda*

8 *World Health Organization, Geneva-Switzerland*

Introduction

Tuberculosis (TB) patients incur large costs related to illness. Other costs are incurred while seeking and receiving health care. Such costs create access and adherence barriers which affect health outcomes and increase transmission of disease. Until the survey, the proportion of households incurring catastrophic costs and the main drivers of these costs were unknown.

Methods

A Cross sectional survey with retrospective data collection and projections was conducted in 2017. A total of 1,178 Drug resistant (DR) TB (44) and Drug sensitive (DS) TB patients (1134), 2 weeks into intensive or continuation phase of treatment were consecutively enrolled across 67 randomly selected TB treatment facilities

Results

Of the respondents, 62.7% were male, 44.7 % were aged 15-34 years and 55.5% were HIV positive. For each TB episode, patients on average incurred in costs of USD 396 for a DS-TB episode and USD 3722 for an MDR TB episode. Up to 48.5 % of households borrowed, used savings or sold assets to face these costs. More than half (53.1%) of TB affected households experienced TB-related costs above 20% of their annual household expenditure, with the main cost cost drivers being non-medical expenditure such as travel, nutritional supplements and food.

Conclusion/Recommendations

Despite free health care in public health facilities, over half of Ugandan TB affected households experience catastrophic costs. Roll out of social protection interventions like TB assistance programs, insurance schemes, and enforcement of legislation related to social protection through multisectoral action plans with central NTP involvement would palliate these costs.

The silent economic impact of chronic lung diseases in low-resource settings in Africa, Asia and Europe – a FRESH AIR study

Brakema EA¹ & Tabyshova A^{2,3}, van der Kleij MJJ¹, Sooronbaev T², Lionis C⁵ Anastasaki M⁵, Pham Le An⁶, Nguyen Than L⁶, Kirenga B⁷, Walusimbi S⁷, Postma MJ³, Chavannes NH¹, van Boven JFM⁴

¹ Department of Public Health and Primary Care, Leiden University Medical Center, Leiden, the Netherlands

² Pulmonary Department, National Center of Cardiology and Internal Medicine, Bishkek, Kyrgyzstan

³ Unit of Global Health, Department of Health Sciences, University of Groningen, University Medical Center Groningen, Groningen, The Netherlands

⁴ Department of General Practice & Elderly Care, Groningen Research Institute for Asthma and COPD (GRIAC), University of Groningen, University Medical Center Groningen, Groningen, The Netherlands

⁵ Clinic of Social and Family Medicine, School of Medicine, University of Crete, Heraklion, Crete, Greece

⁶ University of Medicine and Pharmacy, Ho Chi Minh City, Vietnam

⁷ Department of Medicine and Lung Institute, Makerere University, Kampala, Uganda

Corresponding author: Evelyn Brakema: e.a.brakema@lumc.nl

Category: research results

Abstract

Aim: Data on the socioeconomic impact of COPD/asthma are key to raising awareness and informing national action plans. These data are largely lacking for low-resource settings such as Uganda, Vietnam, Kyrgyzstan and rural Greece. Indirect costs, such as the impact of COPD/asthma on work productivity, are particularly unknown. We aimed to estimate the work productivity and activity impairment due to COPD/asthma in diverse lower-resource settings, and to identify predictors for a higher impairment.

Method: This cross-sectional, observational study is part of the FRESH AIR study. In Uganda (N=102), Vietnam (N=491), Kyrgyzstan (N=308), and rural Greece (N=100), we administered questionnaires to representative samples of patients with spirometry-confirmed COPD and/or asthma. Impairment was assessed using the validated work productivity and activity impairment (WPAI) questionnaire. We performed descriptive statistics and employed a multivariable logistic regression to identify predictors for the impairment. Predictors included demographics, disease severity (MRC breathlessness scale) and comorbidities.

Results: A total of 1001 patients were included, 47.8% was male, with a mean age of 59.4 (SD 24.5), and 36.9% was classified as working. 42.3% had COPD, 48.5% asthma, and the rest had both. Workers reported a median [IQR] of 0.0% [0.0-27.7] work time missed, 20.0% [0.0-40.0] productivity impairment while working, and an overall work impairment of 30% [0.0-60.0] due to asthma/COPD in the past seven days. The total group reported 40.0% [20.0-60.0] impairment on other activities. Disease severity (MRC) was a strong predictor for a higher activity impairment (OR 2.2; 95%CI 1.9-2.6), whereas age, gender, and the presence comorbidities were insignificant in the multivariable model.

Conclusion: Although in these low-resource settings generally not much work time is missed due to COPD/asthma, the disease-related productivity and activity impairment is substantial. Awareness of the extent of the problem and (un)associated factors could inform public health policies and ultimately serve national COPD/asthma strategies.

Declaration of interest: This study was funded by the EU Research and Innovation program Horizon2020 under grant agreement no. 680997.

Trial registration: This study is registered under trial registration number: NTR5759. <http://www.trialregister.nl/trialreg/admin/rctsearch.asp?Term=23332>

A COMPEDIUM OF
RESEARCH CONDUCTED
AT MAKERERE UNIVERSITY
LUNG INSTITUTE (MLI) SINCE
2015

Quality in Practice

Improving inpatient medication adherence using attendant education in a tertiary care hospital in Uganda

PATRICIA ALUPO¹, RICHARD SSEKITOLEKO¹, TRACY RABIN²,
ROBERT KALYESUBULA¹, IVAN KIMULI¹, and BENJAMIN E. BODNAR³

¹School of Medicine, College of Health Sciences, Makerere University, P.O. Box 7072, Mulago Hill, Kampala, Uganda, ²School of Medicine, Yale University, 333 Cedar Street, New Haven, CT 06510, USA, and ³School of Medicine, Johns Hopkins University, 733 N Broadway, Baltimore, 21205 MD, USA

Address reprint requests to: Patricia Alupo, School of Medicine, College of Health Sciences, Makerere University, P.O. Box 7072, Mulago Hill, Kampala, Uganda. Tel: +256-70-112-4540; E-mail:alupopat@gmail.com

Editorial Decision 25 May 2017; Accepted 5 June 2017

Abstract

Quality problem: Although widely utilized in resource-rich health care systems, the use of quality improvement (QI) techniques is less common in resource-limited environments. Uganda is a resource-limited country in Sub-Saharan Africa that faces many challenges with health care delivery. These challenges include understaffing, inconsistent drug availability and inefficient systems that limit the provision of clinical care.

Initial assessment: Poor adherence to prescribed inpatient medications was identified as a key shortcoming of clinical care on the internal medicine wards of Mulago National Referral Hospital, Kampala, Uganda. Baseline data collection revealed a pre-intervention median inpatient medication adherence rate of 46.5% on the study ward. Deficiencies were also identified in attendant (lay caretaker) education, and prescriber and pharmacy metrics.

Choice of solution: A QI team led by a resident doctor and consisting of a QI nurse, a pharmacist and a ward nurse supervisor used standard QI techniques to address this issue.

Implementation: Plan-Do-Study-Act cycle interventions focused on attendant involvement and education, physician prescription practices and improving pharmacy communication with clinicians and attendants.

Evaluation: Significant improvements were seen with an increase in overall medication adherence from a pre-intervention baseline median of 46.5% to a post-intervention median of 92%. Attendant education proved to be the most effective intervention, though resource and staffing limitations made institutionalization of these changes difficult.

Lessons learned: QI methods may be the way forward for optimizing health care delivery in resource-limited settings like Uganda. Institutionalization of these methods remains a challenge due to shortage of staff and other resource limitations.


Key words: quality improvement, quality management, training/education, human resources, leadership

STUDY PROTOCOL

Open Access



Effectiveness-implementation of COPD case finding and self-management action plans in low- and middle-income countries: global excellence in COPD outcomes (GECO) study protocol

Trishul Siddharthan^{1,2} , Suzanne L Pollard^{1,2}, Shumonta A Quaderi³, Andrew J Mirelman⁴, Maria Kathia Cárdenas⁵, Bruce Kirenga⁶, Natalie A Rykiel^{1,2}, J Jaime Miranda^{5,7}, Laxman Shrestha⁸, Ram K Chandyo⁹, Adithya Cattamanchi¹⁰, Susan Michie¹¹, Julie Barber¹², William Checkley^{1,2†}, John R Hurst^{3*†} and GECO Study Investigators

Abstract

Background: Chronic obstructive pulmonary disease (COPD) is the end result of a susceptible individual being exposed to sufficiently deleterious environmental stimuli. More than 90% of COPD-related deaths occur in low- and middle-income countries (LMICs). LMICs face unique challenges in managing COPD; for example, deficient primary care systems present challenges for proper diagnosis and management. Formal diagnosis of COPD requires quality-assured spirometry, which is often limited to urban health centres. Similarly, standard treatment options for COPD remain limited where few providers are trained to manage COPD. The Global Excellence in COPD Outcomes (GECO) studies aim to assess the performance of a COPD case-finding questionnaire with and without peak expiratory flow (PEF) to diagnose COPD, and inform the effectiveness and implementation of COPD self-management Action Plans in LMIC settings. The ultimate goal is to develop simple, low-cost models of care that can be implemented in LMICs. This study will be carried out in Nepal, Peru and Uganda, three distinct LMIC settings.

(Continued on next page)

* Correspondence: jhurst@ucl.ac.uk

[†]William Checkley and John R Hurst contributed equally to this work.

³UCL Respiratory, University College London, London, UK

Full list of author information is available at the end of the article



© The Author(s). 2018 **Open Access** This article is distributed under the terms of the Creative Commons Attribution 4.0 International License (<http://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license, and indicate if changes were made. The Creative Commons Public Domain Dedication waiver (<http://creativecommons.org/publicdomain/zero/1.0/>) applies to the data made available in this article, unless otherwise stated.

(Continued from previous page)

Methods/design: We aim to assess the diagnostic accuracy of a simple questionnaire with and without PEF to case-find COPD (GEC01), and examine the effectiveness, cost-effectiveness and implementation of a community-health-worker-supported self-management Action Plan strategy for managing exacerbations of COPD (GEC02). To achieve the first aim, we will enrol a randomly selected sample of up to 10,500 adults aged ≥ 40 years across our three sites, with the goal to enrol 240 participants with moderate-to-severe COPD in to GEC02. We will apply two case-finding questionnaires (Lung Function Questionnaire and CAPTURE) with and without PEF and compare performance against spirometry. We will report ROC areas, sensitivity and specificity. Individuals who are identified as having COPD grades B–D will be invited to enrol in an effectiveness-implementation hybrid randomised trial of a multi-faceted COPD self-management Action Plan intervention delivered by CHWs. The intervention group will receive (1) COPD education, (2) facilitated-self management Action Plans for COPD exacerbations and (3) monthly visits by community health workers. The control group will receive COPD education and standard of care treatment provided by local health providers. Beginning at baseline, we will measure quality of life with the EuroQol-5D (EQ-5D) and St. George's Respiratory Questionnaire (SGRQ) every 3 months over a period of 1 year. The primary endpoint is SGRQ at 12 months. Quality-adjusted life years (QALYs) using the Short-Form 36 version 2 will also be calculated. We will additionally assess the acceptability and feasibility of implementing COPD Action Plans in each setting among providers and individuals with COPD.

Discussion: This study should provide evidence to inform the use of pragmatic models of COPD diagnosis and management in LMIC settings.

Trial registration: [NCT03359915](#) (GEC01). Registered on 2 December 2017 and [NCT03365713](#) (GEC02). Registered on 7 December 2017. Trial acronym: Global Excellence in COPD Outcomes (GEC01; GEC02).

Keywords: COPD, COPD exacerbations, COPD case finding, COPD action plan, Non-communicable disease, Self-management

ORIGINAL ARTICLE

Prednisolone and *Mycobacterium indicus pranii* in Tuberculous Pericarditis

B.M. Mayosi, M. Ntsekhe, J. Bosch, S. Pandie, H. Jung, F. Gumedze, J. Pogue, L. Thabane, M. Smieja, V. Francis, L. Joldersma, K.M. Thomas, B. Thomas, A.A. Awotedu, N.P. Magula, D.P. Naidoo, A. Damasceno, A.C. Banda, B. Brown, P. Manga, B. Kirenga, C. Mondo, P. Mntla, J.M. Tsitsi, F. Peters, M.R. Essop, J.B.W. Russell, J. Hakim, J. Matenga, A.F. Barasa, M.U. Sani, T. Olunuga, O. Ogah, V. Ansa, A. Aje, S. Danbauchi, D. Ojji, and S. Yusuf, for the IMPI Trial Investigators*

ABSTRACT

BACKGROUND

Tuberculous pericarditis is associated with high morbidity and mortality even if antituberculosis therapy is administered. We evaluated the effects of adjunctive glucocorticoid therapy and *Mycobacterium indicus pranii* immunotherapy in patients with tuberculous pericarditis.

METHODS

Using a 2-by-2 factorial design, we randomly assigned 1400 adults with definite or probable tuberculous pericarditis to either prednisolone or placebo for 6 weeks and to either *M. indicus pranii* or placebo, administered in five injections over the course of 3 months. Two thirds of the participants had concomitant human immunodeficiency virus (HIV) infection. The primary efficacy outcome was a composite of death, cardiac tamponade requiring pericardiocentesis, or constrictive pericarditis.

RESULTS

There was no significant difference in the primary outcome between patients who received prednisolone and those who received placebo (23.8% and 24.5%, respectively; hazard ratio, 0.95; 95% confidence interval [CI], 0.77 to 1.18; $P=0.66$) or between those who received *M. indicus pranii* immunotherapy and those who received placebo (25.0% and 24.3%, respectively; hazard ratio, 1.03; 95% CI, 0.82 to 1.29; $P=0.81$). Prednisolone therapy, as compared with placebo, was associated with significant reductions in the incidence of constrictive pericarditis (4.4% vs. 7.8%; hazard ratio, 0.56; 95% CI, 0.36 to 0.87; $P=0.009$) and hospitalization (20.7% vs. 25.2%; hazard ratio, 0.79; 95% CI, 0.63 to 0.99; $P=0.04$). Both prednisolone and *M. indicus pranii*, each as compared with placebo, were associated with a significant increase in the incidence of cancer (1.8% vs. 0.6%; hazard ratio, 3.27; 95% CI, 1.07 to 10.03; $P=0.03$, and 1.8% vs. 0.5%; hazard ratio, 3.69; 95% CI, 1.03 to 13.24; $P=0.03$, respectively), owing mainly to an increase in HIV-associated cancer.

CONCLUSIONS

In patients with tuberculous pericarditis, neither prednisolone nor *M. indicus pranii* had a significant effect on the composite of death, cardiac tamponade requiring pericardiocentesis, or constrictive pericarditis. (Funded by the Canadian Institutes of Health Research and others; IMPI ClinicalTrials.gov number, NCT00810849.)

The authors' full names, academic degrees, and affiliations are listed in the Appendix. Address reprint requests to Dr. Mayosi at the Department of Medicine, Old Groote Schuur Hospital, J Fl., Rm. J46-53, Groote Schuur Dr., Observatory, Cape Town, 7925, South Africa, or at bongani.mayosi@uct.ac.za.

*A complete list of the investigators in the Investigation of the Management of Pericarditis (IMPI) trial is provided in the Supplementary Appendix, available at NEJM.org.

This article was published on September 2, 2014, at NEJM.org.

N Engl J Med 2014;371:1121-30.

DOI: 10.1056/NEJMoa1407380

Copyright © 2014 Massachusetts Medical Society.

ARTICLE OPEN

Socio-economic factors, gender and smoking as determinants of COPD in a low-income country of sub-Saharan Africa: FRESH AIR Uganda

Frederik van Gemert¹, Niels Chavannes², Bruce Kirenga³, Rupert Jones⁴, Sian Williams⁵, Ioanna Tsiligianni¹, Judith Vonk⁶, Janwillem Kocks¹, Corina de Jong¹ and Thys van der Molen¹

In Uganda, biomass smoke seems to be the largest risk factor for the development of COPD, but socio-economic factors and gender may have a role. Therefore, more in-depth research is needed to understand the risk factors. The aim of this study was to investigate the impact of socio-economic factors and gender differences on the COPD prevalence in Uganda. The population comprised 588 randomly selected participants (> 30 years) who previously completed the FRESH AIR Uganda study. In this *post hoc* analysis, the impact of several socio-economic characteristics, gender and smoking on the prevalence of COPD was assessed using a logistic regression model. The main risk factors associated with COPD were non-Bantu ethnicity (odds ratio (OR) 1.73, 95% confidence interval (CI) 1.06–2.82, $P=0.030$), biomass fuel use for heating (OR 1.76, 95% CI 1.03–3.00, $P=0.038$), former smoker (OR 1.87, 95% CI 0.97–3.60, $P=0.063$) and being unmarried (OR 0.087, 95% CI 0.93–2.95, $P=0.087$). A substantial difference in the prevalence of COPD was seen between the two ethnic groups: non-Bantu 20% and Bantu 12.9%. Additional analysis between these two groups showed significant differences in socio-economic circumstances: non-Bantu people smoked more (57.7% vs 10.7%), lived in tobacco-growing areas (72% vs 14.8%) and were less educated (28.5% vs 12.9% had no education). With regard to gender, men with COPD were unmarried (OR 3.09, 95% CI 1.25–7.61, $P=0.015$) and used more biomass fuel for heating (OR 2.15, 95% CI 1.02–4.54, $P=0.045$), and women with COPD were former smokers (OR 3.35, 95% CI 1.22–9.22, $P=0.019$). Only a few socio-economic factors (i.e., smoking, biomass fuel use for heating, marital status and non-Bantu ethnicity) have been found to be associated with COPD. This applied for gender differences as well (i.e., for men, marital status and biomass fuel for heating, and for women being a former smoker). More research is needed to clarify the complexity of the different risk factors.

npj Primary Care Respiratory Medicine (2016) 26, 16050; doi:10.1038/npjpcrm.2016.50; published online 1 September 2016

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a major health problem in low- and middle-income countries (LMICs).¹ In 2010, COPD was the fourth leading cause of death globally, and it was expected to be the third by 2030.^{2,3} Unfortunately, the prediction has been overtaken by reality: at this moment, COPD is the third leading cause of mortality worldwide.^{4,5} Approximately 90% of COPD deaths occur in LMICs.⁶ Despite these high numbers, COPD is an unknown disease in most of the rural areas of sub-Saharan Africa, both in terms of public awareness and in public health planning. The people are unaware of the potential damage to respiratory and non-respiratory health caused by tobacco and biomass smoke.^{7–9} Biomass fuel use is the third largest contributor to the global burden of disease.¹⁰

Although the development of COPD is multifactorial, biomass smoke is probably the largest risk factor for COPD in LMICs.^{11–13} Worldwide, around 3 billion people, most of them living in LMICs, rely on the use of open fires and burning of biomass fuels (wood, animal dung, crop residues, straw and charcoal) for

cooking and heating in poorly ventilated conditions.¹⁴ Solid fuel burning is incomplete and produces high levels of household air pollution with a range of more than 250 health-damaging pollutants, including carbon monoxide, nitrogen and sulphur oxides, as well as a variety of pollutants, irritants, carcinogens, co-carcinogens and free radicals.^{12,13,15}

Until recently, data on the prevalence of COPD, the risk factors and socio-economic determinants in LMICs were scarce.^{9,16,17} In 2012, a prospective cross-sectional observational study (FRESH AIR Uganda) was conducted to assess the prevalence of COPD and its risk factors in a rural district of Uganda. Among adults above the age of 30 years, the prevalence of spirometry-based COPD was 16.2% (52.6% women), as defined according to the methods used in FRESH AIR Uganda.¹⁸ The prevalence of COPD was remarkably high (39%) among adults aged 30–39 years, both for men (37%) and for women (40%). In addition to tobacco smoking, particularly by young men, > 90% of the participants were exposed to smoke caused by biomass fuel use.¹⁸

The FRESH AIR Uganda study was conducted in rural Masindi district (population 350,000) of Uganda, a low-income country

¹Department of General Practice, Groningen Institute for Asthma and COPD (GRIAC), University of Groningen, University Medical Center Groningen, Groningen, The Netherlands;

²Department of Public Health and Primary Care, Leiden University Medical Center, Leiden, The Netherlands; ³Division of Pulmonary Medicine, Makerere University Lung Institute, Mulago Hospital, Makerere University, Kampala, Uganda; ⁴Centre for Clinical Trials and Population Studies, Plymouth University Peninsula School of Medicine and Dentistry, Plymouth, UK; ⁵Executive Office, International Primary Care Respiratory Group, London, UK and ⁶Department of Epidemiology, Groningen Research Institute for Asthma and COPD (GRIAC), University of Groningen, University Medical Center Groningen, Groningen, The Netherlands.

Correspondence: F van Gemert (f.gemert@xs4all.nl)

Received 10 September 2015; revised 6 June 2016; accepted 17 June 2016

Electric scooters: batteries in the battle against ambient air pollution?



Ambient air pollution is a major global health threat, responsible for an estimated loss of 103 million disability-adjusted life-years in 2015,^{1,2} and a main contributor to numerous health problems, such as cardiovascular and respiratory diseases.^{3,4} Within the traffic domain of air pollution, cars, lorries, busses, mopeds, and scooters are all partly responsible, with the latter being of particular importance regarding, amongst others, black carbon, carcinogenic benzene, and (ultrafine) particulate matter exhaust.⁵

In the last decade, most traffic-related anti-air pollution policy focused on reduction of emissions from cars, busses, and lorries, especially because diesel fuel was thought to be the main source of pollution. Regulations on scooter emission lagged behind for a long time, yet promising policy developments seem to be imminent. Strict European Union regulations effective from 2018 onwards will restrict the sale of the most polluting scooters—ie, those with a two-stroke engine type. At the same time, new electric scooters (e-scooters) could help reduce the burden of air pollution.

From summer, 2017, the citizens of Amsterdam, Netherlands, will be able to benefit from a shared e-scooter initiative, following San Francisco, Paris, and Barcelona. At first sight, the absolute impact of introduction of e-scooters in the so-called bicycle capital of the world might be considered moderate given the relative low number of scooters compared with regular bicycle users. However, these regular cyclists have relatively high air pollution exposure due to their elevated respiratory minute volume combined with the short distance between scooters and cyclists on Dutch bicycle lanes.

On a more global scale, and taking into account the popularity of two-stroke scooters and less stringent regulations in regions such as Asia and Africa, the expected health effects of e-scooter introduction are substantial.⁶ In Vietnam's capital city Hanoi, steep economic development and fast urbanisation have been associated with a rapid increase in the vehicle fleet, with an annual growth of about 15% in the number of motorcycles. Traffic contributes largely to the air

pollution in the city, and accounts for about 70% of the total pollution, with profound peaks during the morning and afternoon rush hours. Calculation of the health risks caused by traffic shows that daily commuting in Hanoi causes a substantial health burden. In 2009, traffic exhaust caused more than 3000 deaths.⁷ In addition, the prevalence of chronic obstructive pulmonary disease in non-smoking inhabitants of urban Vietnam is more than 10% which seems, next to indoor air pollution, to be partly as a result of heavy traffic air pollution.⁸ Therefore, Vietnam has launched the Vietnam-Integrated Action Plan to Reduce Vehicle Emission,⁹ with its main goal to reduce mobile sources of air pollution in Vietnam's largest cities. Specific subgoals include the facilitation of use of alternative fuels, environmentally friendly vehicles, and implementation of energy efficiency measures in the transport sector. E-scooters are considered one of the promising solutions for this Action plan and offer an acceptable alternative for urban citizens having to travel daily distances of 20–25 km with frequent traffic jams during which they are exposed to pollution for several hours.

Strict scooter emission regulations and the stimulation of e-scooters could also have striking effects elsewhere in the Asian region. In Guangzhou (China), benzene, toluene, ethylbenzene, and xylene concentration levels



Figure: Boda boda

dropped from 228 $\mu\text{g}/\text{m}^3$ to 37 $\mu\text{g}/\text{m}^3$ after a total ban of scooters from the inner city in 2005.⁵ The same may hold true for Africa. For example, in Kampala (Uganda), a city where 300 000 scooters called boda bodas operate (figure), dangerously high concentrations of air pollutants have been reported.¹⁰ Replacement of two-stroke scooters with e-scooters would greatly reduce air pollution here too.

The technology is available and it may seem time for large scale adoption. Yet several challenges have to be overcome. The comparatively high price of e-scooters might necessitate government subsidies, safety will remain an issue (in Shanghai and Beijing, scooters were banned from public roads in summer, 2016, for safety reasons), and battery life may be problematic so sufficient charging points will be needed, as well as parking places.

In conclusion, e-scooters seem to offer a promising solution in the battle against air pollution, sustainable energy use and healthy living environments. Implementation generally takes several years however, and traditional polluting scooters do still largely outnumber their e-variants. Will the battery eventually win the battle?

*Job F M van Boven, Pham Le An, Bruce J Kirenga, Niels H Chavannes

Department of General Practice, Groningen Research Institute for Asthma and COPD (GRIAC), University Medical Center Groningen, University of Groningen, Groningen, Netherlands (JFMVB);

Department of Family Medicine, University of Medicine and Pharmacy, Ho Chi Minh City, Vietnam (PLA); Department of Pulmonology, Makerere University, Makerere University Lung Institute, Kampala, Uganda (BJK); and Department of Public Health and Primary Care, Leiden University Medical Center, Leiden, Netherlands (NHC)

j.f.m.van.boven@rug.nl

We declare no competing interests.

Copyright © The Author(s). Published by Elsevier Ltd. This is an Open Access article under the CC BY 4.0 license.

- 1 GBD 2015 Risk Factor Collaborators. Global, regional, and national comparative risk assessment of 79 behavioural, environmental and occupational, and metabolic risks or clusters of risks, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. *Lancet* 2016; **388**: 1659–724.
- 2 Cohen AJ, Brauer M, Burnett R, et al. Estimates and 25-year trends of the global burden of disease attributable to ambient air pollution: an analysis of data from the Global Burden of Diseases Study 2015. *Lancet* 2017; **389**: 1907–18.
- 3 Vu VH, Le XQ, Pham NH, et al. Application of GIS and modelling in health risk assessment for urban road mobility. *Environ Sci Pollut Res* 2013; **20**: 5138.
- 4 Luong LM, Phung D, Sly PD, Morawska L, Thai PK. The association between particulate air pollution and respiratory admissions among young children in Hanoi, Vietnam. *Sci Total Environ* 2017; **578**: 249–55.
- 5 Platt SM, Haddad IE, Pieber SM, et al. Two-stroke scooters are a dominant source of air pollution in many cities. *Nature Commun* 2014; **5**: 3749.
- 6 The Lancet. UK air pollution and public health. *Lancet* 2017; **389**: 1860.
- 7 Hieu VV, Quynh LX, Ho PH, Hens L. Health risk assessment of mobility-related air pollution in Ha Noi, Vietnam. *J Environ Protect* 2013; **4**: 1165–72.
- 8 Nguyen Viet N, Yunus F, Nguyen Thi Phuong A, et al. The prevalence and patient characteristics of chronic obstructive pulmonary disease in non-smokers in Vietnam and Indonesia: an observational survey. *Respirology* 2015; **20**: 602–11.
- 9 Asian Development Bank. Vietnam-Integrated Action Plan to Reduce Vehicle Emissions. http://en.openei.org/wiki/Vietnam-Integrated_Action_Plan_to_Reduce_Vehicle_Emissions (accessed June 28, 2017).
- 10 Kirenga BJ, Meng Q, van Gemert F, et al. The state of ambient air quality in two Ugandan cities: a pilot cross-sectional spatial assessment. *Int J Environ Res Public Health* 2015; **12**: 8075–91.

RESEARCH ARTICLE

Predictors for MTB Culture-Positivity among HIV-Infected Smear-Negative Presumptive Tuberculosis Patients in Uganda: Application of New Tuberculosis Diagnostic Technology

Lydia Nakiyingi^{1,2*}, Bareng A. S. Nonyane³, Willy Ssengooba⁴, Bruce J. Kirenga², Damalie Nakanjako^{1,2}, Gloria Lubega¹, Pauline Byakika-Kibwika^{1,2}, Moses L. Joloba⁴, Jerry J. Ellner⁶, Susan E. Dorman⁵, Harriet Mayanja-Kizza², Yukari C. Manabe^{1,5}

1 Infectious Diseases Institute, Makerere University College of Health Sciences, Kampala, Uganda, **2** Department of Medicine, School of Medicine, Makerere University College of Health Sciences, Kampala, Uganda, **3** Department of International Health, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland, United States of America, **4** Department of Medical Microbiology, Makerere University College of Health Sciences, Kampala, Uganda, **5** Division of Infectious Diseases, Department of Medicine, Johns Hopkins University School of Medicine, Baltimore, Maryland, United States of America, **6** Boston Medical Center, Boston University School of Medicine, Boston, MA, United States of America

* lydikiyingi@yahoo.com



 OPEN ACCESS

Citation: Nakiyingi L, Nonyane BAS, Ssengooba W, Kirenga BJ, Nakanjako D, Lubega G, et al. (2015) Predictors for MTB Culture-Positivity among HIV-Infected Smear-Negative Presumptive Tuberculosis Patients in Uganda: Application of New Tuberculosis Diagnostic Technology. PLoS ONE 10(7): e0133756. doi:10.1371/journal.pone.0133756

Editor: Yoshihiko Hoshino, National Institute of Infectious Diseases, JAPAN

Received: February 11, 2015

Accepted: June 30, 2015

Published: July 29, 2015

Copyright: © 2015 Nakiyingi et al. This is an open access article distributed under the terms of the [Creative Commons Attribution License](https://creativecommons.org/licenses/by/4.0/), which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Data Availability Statement: Third party data underlying the findings in this study is part of the Tuberculosis Clinical Diagnostic Research Consortium (TB CDRC) study data that is available for public access through <https://www.tbcdrc.org>. Request forms that include a TB CDRC Data Proposal Application Form and the TB CDRC Data Sharing Agreement form can be freely obtained on the link: <https://www.tbcdrc.org>. In order to obtain TB CDRC study data, the interested researcher sends filled data request forms to the following address:

Abstract

Background

The existing World Health Organization diagnostic algorithms for smear-negative TB perform poorly in HIV-infected individuals. New TB diagnostics such as urine TB lipoarabinomannan (LAM) could improve the accuracy and reduce delays in TB diagnosis in HIV-infected smear-negative presumptive TB. We sought to determine predictors for MTB culture-positivity among these patients.

Methods

This study was nested into a prospective evaluation of HIV-infected outpatients and inpatients clinically suspected to have TB who were screened by smear-microscopy on two spot sputum samples. Data on socio-demographics, clinical symptoms, antiretroviral therapy, CXR, CD4 count, mycobacterial sputum and blood cultures and TB-LAM were collected. Logistic regression and conditional inference tree analysis were used to determine the most predictive indicators for MTB culture-positivity.

Results

Of the 418 smear-negative participants [female, 64%; median age (IQR) 32 (28-39) years, median CD4 106 (IQR 22 - 298) cells/mm³], 96/418 (23%) were sputum and/ or blood culture-positive for *Mycobacterium tuberculosis* (MTB) complex. Abnormal CXR (aOR 3.68, 95% CI 1.76- 7.71, p=0.001) and positive urine TB-LAM (aOR 6.21, 95% CI 3.14-12.27, p< 0.001) were significantly associated with MTB culture-positivity. Previous TB treatment

David Hom, Administrative, Data & Operations Center, TB Clinical Diagnostics Research Consortium, Boston University Medical Center, 771 Albany Street, Boston, Tel: 617-414-45277, Fax: 617-414-2875, Email: David.Hom@bmc.org.

Funding: LN is a PhD candidate funded by Medical Education for Equitable Services to All Ugandans (MESAU), a Medical Education Partnership Initiative (MEPI) grant number 5R24TW008886 from the Office of Global AIDS Coordinator and the U. S. Department of Health and Human Services, Health Resources and Services Administration and National Institutes of Health. The study project was funded with federal funds from the Division of Microbiology and Infectious Diseases, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Department of Health and Human Services, under contract #HHSN2722000900050C, "TB Clinical Diagnostics Research Consortium." Additional support to YCM was by the Johns Hopkins University Center for AIDS Research (Grant Number 1P30AI094189 from the National Institute of Allergy and Infectious Diseases). The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Competing Interests: The authors have declared that no competing interests exist.

(aOR 0.41, 95% CI 0.17-0.99, $p=0.049$) reduced the likelihood of a positive MTB culture. A conditional inference tree analysis showed that positive urine TB-LAM and abnormal CXR were the most predictive indicators of MTB culture-positivity. A combination of urine TB-LAM test and CXR had sensitivity and specificity of 50% and 86.1% respectively overall, and 70.8% and 84.1% respectively among those with $CD4 < 100$ cells/mm³.

Conclusions

A positive urine TB-LAM test and an abnormal CXR significantly predict MTB culture-positivity among smear-negative HIV-infected presumptive TB patients while previous TB treatment reduces the likelihood of a positive MTB culture. Validation studies to assess the performance of diagnostic algorithms that include urine TB-LAM in the diagnosis of smear-negative TB in HIV-infected individuals are warranted.

Association between Household Air Pollution Exposure and Chronic Obstructive Pulmonary Disease Outcomes in 13 Low- and Middle-Income Country Settings

Trishul Siddharthan^{1,2*}, Matthew R. Grigsby^{1,2*}, Dina Goodman^{1,2}, Muhammad Chowdhury³, Adolfo Rubinstein⁴, Vilma Irazola⁴, Laura Gutierrez⁴, J. Jaime Miranda^{5,6}, Antonio Bernabe-Ortiz^{5,6}, Dewan Alam⁷, Bruce Kirenga⁸, Rupert Jones⁹, Frederick van Gemert¹⁰, Robert A. Wise¹, and William Checkley^{1,2}

¹Division of Pulmonary and Critical Care and ²Center for Global Non-Communicable Diseases, School of Medicine, Johns Hopkins University, Baltimore, Maryland; ³Centre for Control of Chronic Diseases, icddr,b, Dhaka, Bangladesh; ⁴Institute for Clinical Effectiveness and Health Policy, Buenos Aires, Argentina; ⁵CRONICAS Centre of Excellence in Chronic Diseases and ⁶Departamento de Medicina, Facultad de Medicina, Universidad Peruana Cayetano Heredia, Lima, Peru; ⁷School of Kinesiology and Health Science, Faculty of Health, York University, Toronto, Ontario, Canada; ⁸Makerere Lung Institute, Makerere University, Kampala, Uganda; ⁹Plymouth University, Plymouth, United Kingdom; and ¹⁰University of Groningen, University Medical Centre Groningen, Harlingen, the Netherlands

ORCID IDs: 0000-0001-9914-1839 (T.S.); 0000-0001-7311-8673 (M.R.G.); 0000-0003-1106-8812 (W.C.).

Abstract

Rationale: Forty percent of households worldwide burn biomass fuels for energy, which may be the most important contributor to household air pollution.

Objectives: To examine the association between household air pollution exposure and chronic obstructive pulmonary disease (COPD) outcomes in 13 resource-poor settings.

Methods: We analyzed data from 12,396 adult participants living in 13 resource-poor, population-based settings. Household air pollution exposure was defined as using biomass materials as the primary fuel source in the home. We used multivariable regressions to assess the relationship between household air pollution exposure and COPD outcomes, evaluated for interactions, and conducted sensitivity analyses to test the robustness of our findings.

Measurements and Main Results: Average age was 54.9 years (44.2–59.6 yr across settings), 48.5% were women (38.3–54.5%), prevalence of household air pollution exposure was 38% (0.5–99.6%), and 8.8% (1.7–15.5%) had COPD. Participants with household air pollution exposure were 41% more likely to have COPD (adjusted odds ratio, 1.41; 95% confidence interval, 1.18–1.68) than those without the exposure, and 13.5% (6.4–20.6%) of COPD prevalence may be caused by household air pollution exposure, compared with 12.4% caused by cigarette smoking. The association between household air pollution exposure and COPD was stronger in women (1.70; 1.24–2.32) than in men (1.21; 0.92–1.58).

Conclusions: Household air pollution exposure was associated with a higher prevalence of COPD, particularly among women, and it is likely a leading population-attributable risk factor for COPD in resource-poor settings.

Keywords: COPD; air pollution, indoor/adverse effects; biomass

(Received in original form September 13, 2017; accepted in final form January 11, 2018)

*Joint first authorship.

This study was sponsored and funded by the NHLBI, a division of the NIH in the United States, under contract numbers HHSN268200900033C and HHSN26820900032C. In addition, W.C. is supported under UM1HL134590. T.S. is supported by a National Research Service Award through the National Institute of Environmental Health Sciences of the NIH (1F32ES028577). A.R. was supported by the NIH Office of the Director, Fogarty International Centre, and NHLBI through the International Clinical Research Fellows Program at Vanderbilt University (R24 TW007988) and the American Relief and Recovery Act.

Author Contributions: Conception and design, T.S., M.R.G., and W.C. Analysis and interpretation, T.S., M.R.G., D.G., and W.C. Drafting the manuscript for important intellectual content, T.S., M.R.G., D.G., L.G., J.J.M., A.B.-O., D.A., B.K., R.J., M.C., V.I., A.R., F.v.G., R.A.W., and W.C.

Correspondence and requests for reprints should be addressed to William Checkley, M.D., Ph.D., Division of Pulmonary and Critical Care, School of Medicine, Johns Hopkins University, 1830 Monument Street, Room 555, Baltimore, MD 21205. E-mail: wcheck1@jhmi.edu.

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

Am J Respir Crit Care Med Vol 197, Iss 5, pp 611–620, Mar 1, 2018

Copyright © 2018 by the American Thoracic Society

Originally Published in Press as DOI: 10.1164/rccm.201709-1861OC on January 11, 2018

Internet address: www.atsjournals.org

Evaluation of Automated Molecular Testing Rollout for Tuberculosis Diagnosis Using Routinely Collected Surveillance Data — Uganda, 2012–2015

Colleen Scott, DrPH^{1,2}; Simon Walusimbi, PhD³; Bruce Kirenga, MD³; Moses Joloba, PhD⁴; Muttamba Winters, MPH³; Nyombi Abdunoor, MSc⁴; Rommel Bain, PhD²; Heather Alexander, PhD²; Tom Shinnick, PhD²; Sean Toney²; Rosemary Odeke, MPH³; Christine Mwangi, MD³; Estella Birabwa, MPH⁶; Seyoum Dejene, MPH⁶; Frank Mugabe, MSc⁴; Mukadi YaDiul, PhD⁷; J. Sean Cavanaugh, MD²

In 2012, Uganda introduced the use of GeneXpert MTB/RIF (Cepheid, Sunnyvale CA), a sensitive, automated, real-time polymerase chain reaction–based platform for tuberculosis (TB) diagnosis, for programmatic use among children, adults with presumptive human immunodeficiency virus (HIV)-associated TB, and symptomatic persons at risk for rifampicin (RIF)-resistant TB. The effect of using the platform's Xpert MTB/RIF assay on TB care and control was assessed using routinely collected programmatic data; in addition, a retrospective review of district quarterly summaries using abstracted TB register data from purposively selected facilities in the capital city of Kampala was conducted. Case notification rates were calculated and nonparametric statistical methods were used for analysis. No statistically significant differences were observed in case notification rates before and after the Xpert MTB/RIF assay became available, although four of 10 districts demonstrated a statistically significant difference in bacteriologically confirmed TB. Once the GeneXpert MTB/RIF platform is established and refined, a more comprehensive evaluation should be conducted.

The Xpert MTB/RIF assay detects genetic sequences of *Mycobacterium tuberculosis* complex as well as mutations associated with resistance to RIF and provides results in 2 hours. The test is much more sensitive than the conventional diagnostic test (sputum smear microscopy), with a pooled sensitivity among persons living with HIV infection of 80% (1). The World Health Organization recommends use of the Xpert MTB/RIF assay as the initial diagnostic test in adults and children with presumptive HIV-associated TB or multidrug resistant TB (2). It is hoped that the use of a more sensitive diagnostic test will increase case detection and notification; however, an evaluation of the Xpert MTB/RIF assay in Nepal found that use of Xpert MTB/RIF testing was associated with an increase in the proportion of TB diagnoses that were bacteriologically confirmed, but had little impact on overall rate of diagnoses or patient care, which might be the case in locations where clinical diagnosis and empiric TB treatment are common (3).

In Uganda, the HIV prevalence in adults is >7% (4), and the Xpert MTB/RIF assay is used as the initial diagnostic test for all persons living with HIV, children, and persons at risk for RIF-resistant TB who have any of the principal signs or

symptoms of TB (cough, weight loss, night sweats, or fever). As of February 2016, there were 111 GeneXpert instruments installed in 76 (68%) of 111 districts throughout Uganda.

Two retrospective data reviews were conducted. The first was a review of district quarterly reports from 2012 to 2015 submitted to the National Tuberculosis and Leprosy Program; regional case notification rates before and after availability of GeneXpert MTB/RIF testing were compared. Ten districts that had data reported and available for multiple quarters before and after the installation of a GeneXpert instrument were selected, and deidentified data from multiple calendar-year quarters before and after GeneXpert instruments were installed were abstracted. Case notification rates were calculated using the Uganda National Population and Housing Census 2014 (5). For the second review, line-listed data (including longitudinal data such as treatment outcomes) were abstracted on all patients registering for TB therapy during 2012–2015 at a convenience sample of six facilities in Kampala, which were selected based on size, ease of access, and completeness of records. At five facilities, data were collected from patients registered during one quarter before and two quarters after the availability of Xpert MTB/RIF assays; at four of those facilities, data were collected over a 24-month period, and at the fifth, data were collected over an 18-month period. Because of high patient volume at the sixth facility (Mulago National Referral Hospital), data were collected from patients registered during the first month of the quarter immediately before introduction of Xpert MTB/RIF testing, and the first month of each of the two quarters immediately after introduction of Xpert MTB/RIF testing.

The Wilcoxon rank sum test was used to test for differences in case notification rates between districts before and after Xpert MTB/RIF testing initiation, and differences were considered statistically significant if $p < 0.05$. Because of small sample sizes and uncertainty about the population from which the samples were drawn, nonparametric bootstrap sampling was used to construct confidence intervals for the difference in facility diagnoses before and after installation of GeneXpert instruments. Bootstrap sampling was also used to evaluate treatment outcomes reported by health facilities, specifically evaluating the differences between facilities in the proportion of patients with TB in three mutually exclusive categories:

1) completed TB treatment, 2) stopped TB treatment without completing, and 3) continuing TB treatment at the time of data collection. A total of 100,000 bootstrap samples were used to approximate the true sampling distribution for each model.

Forty quarterly report summaries from the 10 selected districts were abstracted. Although no statistically significant differences in case notification rates before and after Xpert MTB/RIF testing initiation were identified, statistically significant increases in the percentage of bacteriologically confirmed TB cases were found in four districts (Table 1).

A total of 1,650 patient records were abstracted from the six Kampala facility treatment registers. Records from one (Kisenyi Health Center IV) indicated a statistically significant increase in the proportion of TB cases that were bacteriologically confirmed after availability of Xpert MTB/RIF testing (Table 2). This health facility also had a statistically significant increase in the proportion of patients who completed TB treatment after Xpert MTB/RIF testing initiation and a decrease in the proportion who stopped treatment before completion. In a second facility (Nsambya Hospital), records indicated a statistically significant decrease in the proportion of patients completing treatment and an increase in the proportion of TB cases continuing in TB treatment (Table 2).

Discussion

This early impact evaluation of the rollout of Xpert MTB/RIF testing did not demonstrate an apparent increase in overall TB case notification rates after testing became available in Uganda, although the proportion of bacteriologically confirmed TB cases increased in a few selected districts. Both findings validate previous reports (3,6,7).

Overall, there were no observable differences in treatment outcomes before and after Xpert MTB/RIF testing availability in reviewed health facilities in Kampala, although there was an apparent increase in TB treatment completion in one facility (Kisenyi). Time from specimen collection to treatment initiation (time to treatment), which elsewhere has been reduced by Xpert MTB/RIF test availability and use (8,9), was not evaluated in this analysis. Reducing time to treatment would be expected to reduce transmission, and could have an epidemiologic impact; moreover, reducing time to treatment might improve outcomes for the sickest patients and patients with multidrug resistant TB.

The lack of effect on TB case notification rates likely reflects the overall low usage rates, given that Xpert MTB/RIF testing was available only to a minority of patients with presumptive TB disease and might have been underused even in the target populations, and also corroborates findings from a previously reported facility-level review (10). It is also possible that Xpert MTB/RIF testing might be replacing clinically diagnosed

Summary

What is already known about this topic?

The World Health Organization recommends use of the Xpert MTB/RIF assay as the initial diagnostic test in adults and children with presumptive HIV-associated TB or multidrug-resistant TB. Currently, data on the effect of the Xpert MTB/RIF assay on case notification or TB treatment outcomes are limited. Published studies indicate the Xpert MTB/RIF assay might improve the proportion of TB diagnoses that are bacteriologically confirmed, but appears to have little effect on overall rate of diagnoses or patient care, especially in locations where clinical diagnosis and empiric TB treatment are high.

What is added by this report?

This early impact evaluation of the Xpert MTB/RIF rollout demonstrated no apparent increase in overall TB case notification rates after testing became available in Uganda. However, within a few selected districts the proportion of bacteriologically confirmed TB cases did increase after testing became available. These two findings validate previous reports.

What are the implications for public health practice?

The impact of Xpert MTB/RIF testing on TB case notification has not yet been fully realized in Uganda. Findings from this evaluation will help direct operations research, such as a review of the diagnostic algorithm for TB, as well as programmatic interventions, such as training health care workers on Xpert MTB/RIF usage and results interpretation.

cases, which represented a large proportion of TB cases before Xpert MTB/RIF testing became available, with biologically confirmed cases, as has been suggested in other similar evaluations (6). In addition, this might be partially explained by overestimation of the test's sensitivity by clinical staff members. If staff members assume a negative test is definitive, leaving them reluctant to make a clinical diagnosis, then Xpert MTB/RIF testing might have the paradoxical effect of decreasing the likelihood of diagnosing those with bacillary burdens below the level of detection. This possibility merits investigation with focused research; if found to be true, additional training on the sensitivity of the Xpert MTB/RIF assay and the importance of complete clinical appraisal of persons with suspected TB might lead to improved case detection.

The findings in this report are subject to at least five limitations. First, the sampling and the geographic focus of the facility data limit definitive and generalizable conclusions. Second, bootstrapping methods assume the original sample represents the population from which the sample was drawn; as such, the facility-level findings are generalizable only to those facilities. Third, because the study was conducted shortly after Xpert MTB/RIF testing became programmatically available (i.e., during the first 6 months of introduction), limited experience might have resulted in suboptimal usage of the

TABLE 1. Median case notification rates and percentage of cases bacteriologically confirmed before and after Xpert MTB/RIF availability, by selected district (N = 10) — Uganda, 2012–2015*

Region	District	No. quarters [†] before Xpert MTB/RIF	No. quarters [†] after Xpert MTB/RIF	Median case notifications per 100,000 population			Median percentage bacteriologically confirmed		
				Before Xpert MTB/RIF	After Xpert MTB/RIF	p value	Before Xpert MTB/RIF	After Xpert MTB/RIF	p value
Northern	Arua	7	2	23	23	0.58	52	62	0.09
Northern	Kitgum	5	3	47	39	0.80	48	67	0.02 [§]
Western	Kabale	5	4	19	21	0.50	64	71	0.06
Western	Kabarole	5	4	34	31	0.87	54	68	0.14
Western	Kisoro	8	3	26	16	0.97	46	55	0.09
Western	Ntungamo	7	3	20	19	0.96	74	89	0.13
Eastern	Mbale	6	4	38	38	0.67	58	73	0.02 [§]
Eastern	Tororo	6	6	31	27	0.99	50	55	0.03 [§]
Central	Mpigi	6	6	26	33	0.17	77	68	0.99
Central	Rakai	7	5	24	29	0.17	67	77	0.01 [§]

* Based on Wilcoxon rank sum test.

[†] 3-month calendar period.[§] Statistically significant (p<0.05).**TABLE 2. Difference in proportion of bacteriologically confirmed* TB cases before and after Xpert MTB/RIF installation, and Bootstrap mean difference estimates and 95% CIs for treatment outcomes, by health facility (N = 6) — Kampala, Uganda, 2012 – 2015**

Characteristics	Health facility					
	Alive Medical Services	Kisenyi Health Center IV	Kisugu	Mengo	Mulago Ward 5 and 6	Nsambya Hospital
Difference in proportion of bacteriologically confirmed* TB cases %, (95% CI)	8.3 (–3.1 to 29.8)	30.8 (21.3 to 40.2) [†]	14.9 (–3.8 to 33.3)	–10.1 (–26.3 to 6.3)	–1.7 (–12.6 to 9.3)	5.1 (–14.0 to 24.2)
Bootstrap mean difference estimates (95% CI)[§] for TB treatment outcomes						
TB treatment completed	–0.119 (–0.357 to 0.119)	0.184 (0.059 to 0.307) [†]	–0.153 (–0.364 to 0.056)	–0.012 (–0.130 to 0.097)	–0.064 (–0.169 to 0.040)	–0.728 (–0.839 to –0.598)
Stopped TB treatment before completion	0.000 (–0.214 to 0.214)	–0.179 (–0.292 to 0.063) [†]	0.071 (–0.105 to 0.249)	0.040 (–0.056 to 0.149)	0.030 (–0.063 to 0.125)	–0.018 (–0.134 to 0.098)
Continuing TB treatment	0.119 (–0.048 to 0.298)	–0.006 (–0.081 to 0.074)	0.082 (–0.051 to 0.233)	–0.028 (–0.079 to 0.031)	0.034 (–0.031 to 0.102)	0.746 (0.608 to 0.866) [†]

Abbreviations: CI = confidence intervals; TB = tuberculosis.

* Bacteriologically confirmed TB includes cases diagnosed using either GenXpert or culture.

[†] Statistically significant (p<0.05).[§] Bootstrap percentile CIs using 100,000 samples per model.

test, misinterpretation of test results, and unreliable data recording. Fourth, because routine programmatic data were used for district-level analyses, it is possible some data were incomplete or erroneous. Finally, data on severity of patient illness, such as clinical stage of HIV infection or CD4 cell count, were not collected, and the number of RIF-resistant TB cases in the sample was very few, precluding assessment of the impact of the Xpert MTB/RIF assay on treatment outcomes in specific subpopulations.

The effect of Xpert MTB/RIF testing on TB case notification has not yet been fully realized in Uganda. Findings from this evaluation will help direct operations research, such as a review of the algorithm for TB diagnosis, as well as programmatic interventions, such as training health care workers on using Xpert MTB/RIF tests and interpreting results. Once the GeneXpert platform is fully established and made more widely available, the national program could consider conducting a reevaluation of the impact of the Xpert MTB/RIF assay and a

review of the diagnostic algorithm for TB in Uganda to validate and expand these findings. Additional studies might include a longitudinal study to conduct a more targeted evaluation of the overall introduction of Xpert MTB/RIF testing and the effects on clinical diagnoses, the impact of Xpert MTB/RIF testing on the sickest patients and those with RIF-resistant disease, and an assessment of feasibility and effect of expanding the Xpert MTB/RIF testing algorithm.

Acknowledgments

Grace Nyakoojo, Kenneth Musisi, Samuel Eyanu, Patrick Ademun, Mary Naluguzza, staff members, Uganda National TB and Reference Laboratory.

¹Epidemic Intelligence Service, CDC; ²Division of Global HIV and TB, CDC; ³Lung Institute Makerere University, College of Health Sciences, Kampala, Uganda; ⁴TB/Leprosy Control Program, Ministry of Health, Republic of Uganda, Kampala Uganda; ⁵Division of Global HIV and TB, CDC, Uganda; ⁶U.S. Agency for International Development, Uganda; ⁷U.S. Agency for International Development, Washington DC.

Corresponding author: Colleen Scott, CScott2@cdc.gov, 404-718-8692.

References

1. Steingart KR, Schiller I, Horne DJ, Pai M, Boehme CC, Dendukuri N. Xpert® MTB/RIF assay for pulmonary tuberculosis and rifampicin resistance in adults. *Cochrane Database Syst Rev* 2014;1:CD009593.
2. World Health Organization. Automated real-time nucleic acid amplification technology for rapid and simultaneous detection of tuberculosis and rifampicin resistance: Xpert MTB/RIF assay for the diagnosis of pulmonary and extrapulmonary TB in adults and children. Policy update. Geneva, Switzerland: World Health Organization; 2013. http://who.int/tb/laboratory/xpert_policyupdate/en/
3. Creswell J, Rai B, Wali R, et al. Introducing new tuberculosis diagnostics: the impact of Xpert(®) MTB/RIF testing on case notifications in Nepal. *Int J Tuberc Lung Dis* 2015;19:545–51. <https://doi.org/10.5588/ijtld.14.0775>
4. Joint United Nations Programme on HIV/AIDS. HIV and AIDS estimates. Geneva, Switzerland: Joint United Nations Programme on HIV/AIDS; 2015. <http://www.unaids.org/en/regionscountries/countries/uganda>
5. Uganda Bureau of Statistics. Uganda National Population and Housing Census 2014 provisional results: November 2014. Kampala, Uganda: Uganda Bureau of Statistics; 2014. <https://unstats.un.org/unsd/demographic/sources/census/wphc/Uganda/UGA-2014-11.pdf>
6. Theron G, Zijenah L, Chanda D, et al.; TB-NEAT team. Feasibility, accuracy, and clinical effect of point-of-care Xpert MTB/RIF testing for tuberculosis in primary-care settings in Africa: a multicentre, randomised, controlled trial. *Lancet* 2014;383:424–35. [https://doi.org/10.1016/S0140-6736\(13\)62073-5](https://doi.org/10.1016/S0140-6736(13)62073-5)
7. Van Den Handel T, Hampton KH, Sanne I, Stevens W, Crous R, Van Rie A. The impact of Xpert(®) MTB/RIF in sparsely populated rural settings. *Int J Tuberc Lung Dis* 2015;19:392–8. <https://doi.org/10.5588/ijtld.14.0653>
8. Cox H, Dickson-Hall L, Ndjeka N, Nicol M. The drug-resistant TB treatment gap and treatment initiation delays in South Africa: impact of Xpert implementation. 46th Union World Conference on Lung Health; December 2–6, 2015; Cape Town, South Africa.
9. van Kampen SC, Susanto NH, Simon S, et al. Effects of introducing Xpert MTB/RIF on diagnosis and treatment of drug-resistant tuberculosis patients in Indonesia: a pre-post intervention study. *PLoS One* 2015;10:e0123536. <https://doi.org/10.1371/journal.pone.0123536>
10. Hanrahan CF, Haguma P, Ochom E, et al. Implementation of Xpert MTB/RIF in Uganda: missed opportunities to improve diagnosis of tuberculosis. *Open Forum Infect Dis* 2016;3:ofw068. <https://doi.org/10.1093/ofid/ofw068>

RESEARCH ARTICLE

Open Access

Tuberculosis risk factors among tuberculosis patients in Kampala, Uganda: implications for tuberculosis control

Bruce J Kirenga^{1*}, Willy Ssengooba^{2,6}, Catherine Muwonge³, Lydia Nakiyingi¹, Stephen Kyaligonza³, Samuel Kasozi³, Frank Mugabe³, Martin Boeree⁴, Moses Joloba² and Alphonse Okwera⁵

Abstract

Background: Slow decline in the incidence of tuberculosis (TB) has been observed in most high TB burden countries. Knowledge of the prevalence of different TB risk factors can help expand TB control strategies. However with the exception of Human Immunodeficiency Virus (HIV) the prevalence of the other TB risk factors are poorly studied in Uganda. We aimed to determine the prevalence of different TB risk factors and TB disease presentation among TB patients in Kampala Uganda.

Methods: We assessed 365 adult TB patients and used descriptive statistics to summarize their socio-demographic, clinical, radiological, sputum mycobacteriology and TB risk factors (HIV, diabetes, TB contact, alcohol use, tobacco smoking, poverty and overcrowding) data.

Results: A total of 158 (43.3%) patients were male and the median age was 29 (IQR 28–30). Majority of the patients (89.2%) had pulmonary TB, 86.9% were new and 13.2% were retreatment. Wasting (i.e. body mass index of $<18.5 \text{ kg/m}^2$) was found in 38.5% of the patients and 63% presented with cough. Constitutional symptoms (fever, anorexia, night sweats and weight loss) were reported by 32.1%. Most patients (78.6%) presented with non-cavity lung parenchyma disease (infiltrates, nodules, masses) but 35.2% had cavity disease. Pleural disease was detected in 19.3% of patients. Positive smear microscopy and culture (irrespective of month of treatment) was found in 52.7% and 36.5% of patients respectively. Any drug resistance was detected in 21.1% of patients while multidrug resistance (MDR) TB defined as resistance to rifampicin and isoniazid was detected in 6.3% of patients. All MDR patients were new patients. The prevalence of TB risk factors were as follows: HIV 41.4%, diabetes 5.4%, close contact 11.5%, family history 17.5%, smoking 26.37%, poverty 39.5%, overcrowding 57.3% and alcohol use 50.7%. Overcrowding increased smear positive rate, prevalence ratio 1.22, $p = 0.09$ but all the other studied risk factors did not affect clinical, radiological and mycobacteriological study patient characteristics.

Conclusions: Among TB patients in Kampala, Uganda, there is high prevalence of the known TB risk factors. Targeting reducing their prevalence may lead to better TB control in the country. Tuberculosis, risk factors, Uganda.

Background

Uganda is one of the 22 high tuberculosis (TB) burden countries (HBC) in the world [1]. From an estimated population of 35 million people with national HIV prevalence of 7.3%, 45,546 TB patients were diagnosed in the in the year 2010 of which 54% were

HIV-infected [1-4]. Of these 56% were smear positive, 28% were smear negative and 11% had extra pulmonary TB [1].

Despite implementation of the WHO recommended directly observed therapy short course (DOTS) TB control strategy, the reductions in the incidence of TB have been minimal in HBC [5]. Because of this slow decline of TB incidence there is currently renewed interest in finding new TB control strategies. Focus has been on such strategies as adding to the current arsenal of TB drugs, finding a TB vaccine and designing shorter TB

* Correspondence: brucekirenga@yahoo.co.uk

¹Department of Medicine, Makerere University College of Health Sciences, P.O. Box 7072, Kampala, Uganda

Full list of author information is available at the end of the article

Patient satisfaction with TB care clinical consultations in Kampala: a cross sectional study.

Willy Ssengooba¹, Bruce Kirenga², Catherine Muwonge³, Steven Kyaligonza³, Samuel Kasozi³, Frank Mugabe³, Martin Boeree⁴, Moses Joloba⁵, Alphonse Okwera⁶ and PanACEA Consortium

1. Department of Medical Microbiology Makerere University Kampala and Academic Medical Centre University of Amsterdam
2. Department of Medicine, Makerere University College of Health Sciences
3. National TB and Leprosy Program, Ministry of Health, Uganda
4. Department of Pulmonary Diseases, Radboud University Nijmegen Medical
5. Department of Microbiology, Makerere University College of Health Sciences
6. National Tuberculosis treatment unit, Mulago Hospital

Abstract

Background: Patient satisfaction towards care during encounter with clinicians is key for better treatment outcomes. We assessed patient satisfaction with TB clinical care consultations in Kampala, Uganda.

Methods: This was a facility-based cross sectional study done between September 2012 and February 2013 using qualitative method of data collection. Participants consecutively completed a pre-tested structured satisfaction questionnaire. A criteria of the rating as good; >75% was considered acceptable, (50-75%) as more effort is needed and <50 as unacceptable and require immediate action was used to categorize data for analysis using Epi-info 7.1.4.0.

Results: Of the 260 registered TB patients, 178(68.5%) completed the questionnaire. Overall, 162 (91.0%) were satisfied with the clinical consultation. Factors that contributed to high patient satisfaction, were: time spent with clinician (85.4%), explanation of what was done (87.6%), technical skills (91.6%), personal manner of the clinician seen (91.6%). Factors for low satisfaction were; waiting time before getting an appointment (61.8%), convenience of location of consultation office (53.4%), getting through to the office by phone (21.3%) and length of time waiting at the office (61.2%).

Conclusion: Tuberculosis patients in Kampala are satisfied with TB clinical care consultations. Addressing factors with low patient satisfaction may significantly impact on treatment outcome.

Keywords: Patient satisfaction, TB care clinical consultations, cross sectional study.

DOI: <http://dx.doi.org/10.4314/abs.v16i4.28>

Cite as: Ssengooba W, Kirenga B, Muwonge C, Kyaligonza S, Kasozi S, Mugabe F, Boeree M, Joloba M, Okwera A, PanACEA. Patient satisfaction with TB care clinical consultations in Kampala: a cross sectional study. Afri Health Sci. 2016;16(4): 1101-1108. <http://dx.doi.org/10.4314/abs.v16i4.28>

Background: Tuberculosis (TB) remains a major global health problem¹. In 2013, there were estimated 9.0 million globally with (8.6–9.4 million) new tuberculosis (TB) cases annually. Those who died due to TB disease were 1.5 million of which 82% were from the 22 high burden Countries². In the same year, Uganda was estimated to have a TB incidence rate of 166/100,000 and TB mor-

tality rate of 11/100,000². The burden of Multidrug Resistant TB (MDR-TB) in Uganda is estimated at 1.4% and 12% among new and re-treatment TB cases respectively³.

There is a high level of treatment failure and growing threat of MDR-TB cases despite the fact that TB is curable⁴. Collective efforts between the treating clinician and TB patient are urgently needed in the fight against tuberculosis. Understanding whether patients are satisfied with the clinical care they receive during clinical consultation may be one of the key avenues to improve early patient presentation to the clinic for early diagnosis as well as adherence to treatment for better treatment outcome.

Patients who are satisfied with clinical consultations are more likely to return to clinics, in case of treatment fol-

Corresponding author:

Willy Ssengooba BBS,
Department of Medical Microbiology
Makerere University Kampala
and Academic Medical Centre
University of Amsterdam
Email: willyssengooba@gmail.com

Publisher: African Networks on Ethnomedicines

Website: <http://journals.sfu.ca/africanem/index.php/AJID>

<http://dx.doi.org/10.4314/ajid.v6i2.2>

ADVANCES IN THE DIAGNOSIS, TREATMENT AND CONTROL OF HIV ASSOCIATED TUBERCULOSIS

Bruce J^{1*} Kirenga, Duncan M² Chanda, Catherine M³ Muwonge, Getnet⁴ Yimer, Francis E⁵ Adatu and Philip C⁶ Onyebujoh

¹Division of Pulmonary Medicine, Mulago National Referral and teaching Hospital /Makerere College of Health Sciences, P.O. Box 7072 Kampala, ²University Teaching Hospital, Lusaka Zambia, Institute

of Medical Research and Training, ³National Tuberculosis and Leprosy Program, Uganda,

⁴Department of Pharmacology, College of Health Sciences, Addis Ababa University, ⁵National Tuberculosis and Leprosy Program, Uganda, ⁶WHO/TDR- Geneva.

*E-mail: brucekirenga@yahoo.co.uk

Summary

There has been an increase in the number of published tuberculosis/HIV (TB/HIV) research findings in recent times. The potential impact of these findings on routine care has informed this review which aims at discussing current concepts and practices underpinning TB/HIV care and control. Any HIV infected person with a cough of any duration is currently considered a TB suspect. Preliminary results also show that the diagnostic yield of same day sputum samples (front loading) is comparable to two-day samples. Laboratory diagnosis is shifting from Ziehl–Neelsen (ZN) smear microscopy and solid culture to fluorescent microscopy, molecular tests and liquid culture. Concomitant TB/HIV therapy improves survival and WHO has recommended ART for all TB/HIV patients. Unless CD4 cell counts are less than 50 cells/ μ l, ART can be deferred until end of intensive phase. Evidence of survival benefit at high CD4 cell counts is still lacking. New TB drugs and treatment shortening studies are underway but so far no new TB drugs has been added to the current arsenal and treatment duration still remains six months or more. WHO has recommended the 3Is (intensified TB case finding, isoniazid prophylaxis and infection control) for TB/HIV control in addition to effective therapy, Antiretroviral therapy and TB vaccines. There has been immense progress in TB/HIV research, however optimal management of HIV-Infected TB patients, will require further research and appropriate translation of emerging evidence to policy and practice.

Key words: Tuberculosis, HIV, Diagnosis , Treatment, Control

Article

The State of Ambient Air Quality in Two Ugandan Cities: A Pilot Cross-Sectional Spatial Assessment

Bruce J. Kirenga^{1,†,*}, **Qingyu Meng**^{2,†}, **Frederik van Gemert**³, **Hellen Aanyu-Tukamuhebwa**⁴,
Niels Chavannes⁵, **Achilles Katamba**⁶, **Gerald Obai**⁷, **Thys van der Molen**³,
Stephan Schwander^{2,†} and **Vahid Mohsenin**^{8,†}

¹ Division of Pulmonary Medicine, Department of Medicine, Makerere University College of Health Sciences, Kampala, Uganda; E-Mail: brucekirenga@yahoo.co.uk

² Department of Environmental and Occupational Health and Center for Global Public Health, School of Public Health, Rutgers University, NJ 07107, USA; E-Mails: mengqi@sph.rutgers.edu (Q.M.); schwansk@sph.rutgers.edu (S.S.)

³ Department of General Practice, University Medical Center Groningen, University of Groningen, Groningen 9700 RB, The Netherlands; E-Mails: frgemert@xs4all.nl (F.G.); t.van.der.molen@umcg.nl (T.M.)

⁴ Department of Paediatrics and Child Health, Makerere University College of Health Sciences, Kampala, Uganda; E-Mail: hellen.aanyut@gmail.com

⁵ Department of Public Health and Primary Care, Leiden University Medical Center, Leiden 2333 ZA, The Netherlands; E-Mail: n.h.chavannes@lumc.nl

⁶ Clinical Epidemiology and Biostatistics Unit, Department of Medicine, Makerere University College of Health Sciences, Kampala, Uganda; E-Mail: akatamba@yahoo.com

⁷ Department of Physiology, Faculty of Medicine, Gulu University, Gulu, Uganda; E-Mail: lekobai@gmail.com

⁸ Department of Medicine, Yale University School of Medicine, New Haven, CT 06510, USA; E-Mail: vahid.mohsenin@yale.edu

† These authors contributed equally to this work.

* Author to whom correspondence should be addressed; E-Mail: brucekirenga@yahoo.co.uk; Tel.: +25-678-240-4431.

Academic Editor: Paul B. Tchounwou

Received: 11 May 2015/ Accepted: 7 July 2015/ Published: 15 July 2015

Abstract: Air pollution is one of the leading global public health risks but its magnitude in many developing countries' cities is not known. We aimed to measure the concentration of particulate matter with aerodynamic diameter $<2.5 \mu\text{m}$ ($\text{PM}_{2.5}$), nitrogen dioxide (NO_2), sulfur dioxide (SO_2), and ozone (O_3) pollutants in two Ugandan cities (Kampala and Jinja). $\text{PM}_{2.5}$, O_3 , temperature and humidity were measured with real-time monitors, while NO_2 and SO_2 were measured with diffusion tubes. We found that the mean concentrations of the air pollutants $\text{PM}_{2.5}$, NO_2 , SO_2 and O_3 were $132.1 \mu\text{g}/\text{m}^3$, $24.9 \mu\text{g}/\text{m}^3$, $3.7 \mu\text{g}/\text{m}^3$ and $11.4 \mu\text{g}/\text{m}^3$, respectively. The mean $\text{PM}_{2.5}$ concentration is 5.3 times the World Health Organization (WHO) cut-off limits while the NO_2 , SO_2 and O_3 concentrations are below WHO cut-off limits. $\text{PM}_{2.5}$ levels were higher in Kampala than in Jinja ($138.6 \mu\text{g}/\text{m}^3$ vs. $99.3 \mu\text{g}/\text{m}^3$) and at industrial than residential sites ($152.6 \mu\text{g}/\text{m}^3$ vs. $120.5 \mu\text{g}/\text{m}^3$) but residential sites with unpaved roads also had high $\text{PM}_{2.5}$ concentrations ($152.6 \mu\text{g}/\text{m}^3$). In conclusion, air pollutant concentrations in Kampala and Jinja in Uganda are dangerously high. Long-term studies are needed to characterize air pollution levels during all seasons, to assess related public health impacts, and explore mitigation approaches.

Keywords: ambient air pollution; particulate matter; nitrogen dioxide; sulfur dioxide; ozone; Uganda; Kampala; Jinja

1. Introduction

On the 25 March 2014, the World Health Organization (WHO) released new estimates of the contribution of air pollution to global mortality showing that seven million deaths were attributable to air pollution worldwide in the year 2012 (3.7 million due to ambient air pollution (AAP) and 4.3 million due to indoor air pollution (IAP)) [1]. This number represents a doubling from the air pollution mortality rates estimated by WHO in the year 2004 [1,2].

Air pollution is thus one of the leading global public health risks. Health problems commonly associated with air pollution exposure include: respiratory diseases (e.g., chronic obstructive pulmonary disease, asthma, lung cancer and acute respiratory infections in children) and cardiovascular diseases (such as ischemic heart disease and stroke) [2]. Adverse health effects associated with air pollution exposure are particularly severe among vulnerable populations (e.g., people with respiratory diseases like asthma), older people, and children. Available data also show that air pollution has the potential to impair lung growth as a result of perinatal exposures thus threatening the health of entire generations [3–6]. Although over 3000 substances are known to potentially contaminate air [7], the WHO has identified particulate matter (PM), nitrogen dioxide (NO_2), carbon monoxide (CO), sulfur dioxide (SO_2) and ozone (O_3) as the pollutants with greatest public health importance [2]. The United States (US) National Ambient Air Quality Standard (NAAQS) [8] designates all of the above plus airborne lead (Pb) as criteria pollutants.

WHO and the US Environmental Protection Agency (USEPA) have defined guideline limits for these pollutants that should not be exceeded in order to maintain and protect public health [9,10]. The WHO limits for $\text{PM}_{2.5}$, PM_{10} , NO_2 , SO_2 , and O_3 are $25 \mu\text{g}/\text{m}^3$ (24-hour mean), $50 \mu\text{g}/\text{m}^3$ (24-hour mean), 200

RESEARCH ARTICLE

Open Access



Access to affordable medicines and diagnostic tests for asthma and COPD in sub Saharan Africa: the Ugandan perspective

Davis Kibirige^{1,2*}, Leaticia Kampiire³, David Atuhe⁴, Raymond Mwebaze⁵, Wincelous Katagira⁶, Winters Muttamba⁶, Rebecca Nantanda^{6,7}, William Worodria⁸ and Bruce Kirenga^{6,8}

Abstract

Background: Equitable access to affordable medicines and diagnostic tests is an integral component of optimal clinical care of patients with asthma and chronic obstructive pulmonary disease (COPD). In Uganda, we lack contemporary data about the availability, cost and affordability of medicines and diagnostic tests essential in asthma and COPD management.

Methods: Data on the availability, cost and affordability of 17 medicines and 2 diagnostic tests essential in asthma and COPD management were collected from 22 public hospitals, 23 private and 85 private pharmacies. The percentage of the available medicines and diagnostic tests, the median retail price of the lowest priced generic brand and affordability in terms of the number of days' wages it would cost the least paid public servant were analysed.

Results: The availability of inhaled short acting beta agonists (SABA), oral leukotriene receptor antagonists (LTRA), inhaled LABA-ICS combinations and inhaled corticosteroids (ICS) in all the study sites was 75%, 60.8%, 46.9% and 45.4% respectively. None of the study sites had inhaled long acting anti muscarinic agents (LAMA) and inhaled long acting beta agonist (LABA)-LAMA combinations. Spirometry and peak flow-metry as diagnostic tests were available in 24.4% and 6.7% of the study sites respectively. Affordability ranged from 2.2 days' wages for inhaled salbutamol to 17.1 days' wages for formoterol/budesonide inhalers and 27.8 days' wages for spirometry.

Conclusion: Medicines and diagnostic tests essential in asthma and COPD care are not widely available in Uganda and remain largely unaffordable. Strategies to improve access to affordable asthma and COPD medicines and diagnostic tests should be implemented in Uganda.

Keywords: Access, Medicines, Diagnostic tests, Asthma, COPD, Sub Saharan Africa, Uganda

Background

Globally, chronic respiratory diseases pose a major public health threat. Notably, the burden of asthma and chronic obstructive pulmonary disease (COPD) is steadily increasing in both developed and developing countries. According to recent World Health Organisation (WHO) estimates, about 235 million people have asthma

and 65 million people have moderate to severe COPD. High rates of mortality due to both conditions have been documented in low-and middle income countries (LMIC). In 2012, > three million people died of COPD, which accounted for about 6% of the all the deaths globally. An estimated 90% of these deaths occurred in LMIC [1].

In Uganda, a similar growing trend of mortality related to asthma and COPD has been described. A descriptive retrospective study conducted at an urban national referral hospital reported the burden of asthma and COPD of 70.6% and 21.6% respectively in 558 patients admitted to

* Correspondence: kibirigedavis@gmail.com

¹Department of Medicine, Uganda Martyrs Hospital Lubaga, P.O. BOX 7146, Kampala, Uganda

²Medical unit, GlaxoSmithKline Pharmaceutical Kenya Limited, Kampala, Uganda

Full list of author information is available at the end of the article



© The Author(s). 2017 **Open Access** This article is distributed under the terms of the Creative Commons Attribution 4.0 International License (<http://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license, and indicate if changes were made. The Creative Commons Public Domain Dedication waiver (<http://creativecommons.org/publicdomain/zero/1.0/>) applies to the data made available in this article, unless otherwise stated.

(Continued from previous page)

Methods/design: We aim to assess the diagnostic accuracy of a simple questionnaire with and without PEF to case-find COPD (GEC01), and examine the effectiveness, cost-effectiveness and implementation of a community-health-worker-supported self-management Action Plan strategy for managing exacerbations of COPD (GEC02). To achieve the first aim, we will enrol a randomly selected sample of up to 10,500 adults aged ≥ 40 years across our three sites, with the goal to enrol 240 participants with moderate-to-severe COPD in to GEC02. We will apply two case-finding questionnaires (Lung Function Questionnaire and CAPTURE) with and without PEF and compare performance against spirometry. We will report ROC areas, sensitivity and specificity. Individuals who are identified as having COPD grades B–D will be invited to enrol in an effectiveness-implementation hybrid randomised trial of a multi-faceted COPD self-management Action Plan intervention delivered by CHWs. The intervention group will receive (1) COPD education, (2) facilitated-self management Action Plans for COPD exacerbations and (3) monthly visits by community health workers. The control group will receive COPD education and standard of care treatment provided by local health providers. Beginning at baseline, we will measure quality of life with the EuroQol-5D (EQ-5D) and St. George's Respiratory Questionnaire (SGRQ) every 3 months over a period of 1 year. The primary endpoint is SGRQ at 12 months. Quality-adjusted life years (QALYs) using the Short-Form 36 version 2 will also be calculated. We will additionally assess the acceptability and feasibility of implementing COPD Action Plans in each setting among providers and individuals with COPD.

Discussion: This study should provide evidence to inform the use of pragmatic models of COPD diagnosis and management in LMIC settings.

Trial registration: [NCT03359915](#) (GEC01). Registered on 2 December 2017 and [NCT03365713](#) (GEC02). Registered on 7 December 2017. Trial acronym: Global Excellence in COPD Outcomes (GEC01; GEC02).

Keywords: COPD, COPD exacerbations, COPD case finding, COPD action plan, Non-communicable disease, Self-management

A pre–post intervention study of pulmonary rehabilitation for adults with post-tuberculosis lung disease in Uganda

This article was published in the following Dove Press journal:
International Journal of COPD

Rupert Jones¹
Bruce J Kirenga²
Wincelsa Katagira²
Sally J Singh³
Jill Pooler⁴
Alphonse Okwera²
Richard Kasiita⁵
Doyo G Enki⁶
Siobhan Creanor⁶
Andy Barton⁴

¹Population Studies and Clinical Trials, Peninsula Schools of Medicine and Dentistry, Plymouth University, Plymouth, UK; ²Population Studies and Clinical Trials, Makerere Lung Institute, Makerere University College of Health Sciences, Mulago Hospital, Kampala, Uganda; ³Cardio-Respiratory Directorate, University Hospitals of Leicester NHS Trust, Leicester; ⁴Population Studies and Clinical Trials, Peninsula Schools of Medicine and Dentistry, Plymouth University, Plymouth, UK; ⁵Department of Physiotherapy, Mulago Hospital, Kampala, Uganda; ⁶Medical Statistics, Peninsula Schools of Medicine and Dentistry, Plymouth University, Plymouth, UK

Correspondence: Rupert Jones
Peninsula Schools of Medicine and Dentistry, Plymouth University, N14, ITTC Building, Plymouth PL6 8BX, UK
Tel +44 1752 76 4258
Email rupert.jones@plymouth.ac.uk

Setting: The study was conducted at Mulago Hospital, Kampala, Uganda.

Objective: As chronic respiratory disease (CRD) is a huge, growing burden in Africa, with few available treatments, we aimed to design and evaluate a culturally appropriate pulmonary rehabilitation (PR) program in Uganda for people with post-tuberculosis lung disorder (p-TBLD).

Design: In a pre–post intervention study, a 6-week, twice-weekly PR program was designed for people with p-TBLD. Outcome measures included recruitment, retention, the Clinical COPD Questionnaire (CCQ), tests of exercise capacity, and biometrics. Given this was a developmental study, no formal statistical significance testing was undertaken.

Results: In all, 34 participants started PR and 29 (85%) completed all data collection. The mean age of the 29 participants was 45 years, and 52% were female. The mean (95% confidence interval) CCQ score at baseline was 1.8 (1.5, 2.0), at the end of PR was 1.0 (0.8, 1.2), and at 6 weeks after the end of PR was 0.8 (0.7, 1.0). The Incremental Shuttle Walking Test (ISWT) was 299 m (268.5, 329.4) at baseline, 377 (339.6, 413.8) at the end of PR, and 374 (334.2, 413.5) at 6 weeks after the end of PR. Improvements were seen in measures of chest pain; 13/29 (45%) participants reported chest pain at baseline but only 7/29 (24%) at the end of PR, and in those with persistent pain, the mean pain scores decreased. Mild hemoptysis was reported in 4/29 (17%) participants at baseline and in 2/29 (7%) at the end of PR.

Conclusion: PR for people with p-TBLD in Uganda was feasible and associated with clinically important improvements in quality of life, exercise capacity, and respiratory outcomes. PR uses local resources, requires little investment, and offers a new, sustainable therapy for p-TBLD in resource-limited settings. With the rising global burden of CRD, further studies are needed to assess the value of PR in p-TBLD and other prevalent forms of CRD.

Keywords: tuberculosis, exercise training, self-management, nonpharmacological intervention

Introduction

The World Health Organization considers the control and management of noncommunicable diseases (NCDs) a top priority – NCDs cause more deaths than all other causes combined and are projected to increase from 38 million worldwide in 2012 to 52 million by 2030.¹ Lung diseases are preeminent, and COPD is now the third leading cause of death globally and the ninth highest cause of disability.¹ The burgeoning prevalence of chronic respiratory disease (CRD) is fueled by an aging population, the combination of respiratory infections such as tuberculosis (TB) with human immunodeficiency virus (HIV), tobacco smoking, household air pollution, and nutritional impairment.^{2–4}



Article

Household Air Pollution Is Associated with Chronic Cough but Not Hemoptysis after Completion of Pulmonary Tuberculosis Treatment in Adults, Rural Eastern Democratic Republic of Congo

Patrick D.M.C. Katoto ^{1,2,*}, Aime Murhula ², Tony Kayembe-Kitenge ^{1,3}, Herve Lawin ⁴, Bertin C. Bisimwa ^{2,5}, Jean Paul Cirhambiza ⁶, Eric Musafiri ⁶, Freddy Birembano ⁶, Zacharie Kashongwe ⁶, Bruce Kirenga ⁷, Sayoki Mfinanga ⁸, Kevin Mortimer ⁹, Patrick De Boever ^{10,11}, Tim S. Nawrot ^{1,10}, Jean B. Nachega ^{12,13,14,†} and Benoit Nemery ^{1,†}

- ¹ Centre for Environment and Health, Department of Public Health and Primary Care, KU Leuven, 300 Leuven, Belgium; tonykayemb@gmail.com (T.K.-K.); tim.nawrot@uhasselt.be (T.S.N.); ben.nemery@kuleuven.be (B.N.)
 - ² Department of Internal Medicine and Prof Lurhuma Biomedical Research Laboratory, Mycobacterium Unit, Faculty of Medicine, Catholic University of Bukavu, 02BP, Bukavu, Congo; draime2006@yahoo.fr (A.M.); bcasinga@gmail.com (B.C.B.)
 - ³ Unit of Toxicology and Environment, University hospital of Lubumbashi, School of Public Health Faculty of Medicine, Lubumbashi 1825BP, Congo
 - ⁴ Unit of Teaching and Research in Occupational and Environmental Health, Faculty of Health Sciences, University of Abomey-Calavi (UAC), Cotonou 03BP0490, Benin; hervelawin@gmail.com
 - ⁵ Département de Biologie médicale, Institut Supérieur des Techniques Médicales (ISTM) Bukavu, BP 3036, Bukavu, Congo
 - ⁶ National TB Program, Provincial and national Anti-Leprosy and TB Coordination, BP. 1899, Bukavu, Congo; jeanpaulchira@gmail.com (J.P.C.); emulume@gmail.com (E.M.); freddybirembano@yahoo.fr (F.B.); zkashongwe@yahoo.fr (Z.K.)
 - ⁷ Department of Pulmonary Medicine and Lung Institute, Makerere University, PB 7072, Kampala, Uganda; brucekirenga@yahoo.co.uk
 - ⁸ National Institute for Medical Research Muhimbili Medical Research Centre, PB 65001, Dar es Salaam, Tanzania; gsmfinanga@yahoo.com
 - ⁹ Liverpool School of Tropical Medicine, Liverpool L3 5QA, UK; Kevin.Mortimer@lstm.ac.uk
 - ¹⁰ Centre for Environmental Sciences, Hasselt University, Agoralaan, building D, 3590, Diepenbeek, Belgium; patrick.deboever@vito.be
 - ¹¹ Health Unit, Flemish Institute for Technological Research (VITO), Vlasmeeuw, 2400 Mol, Belgium
 - ¹² Department of Medicine and Center for Infectious Diseases, Faculty of Medicine and Health Sciences, Stellenbosch University, 8000, Francie Van Zijl Drive, PB 241, Cape Town, South Africa; jnachega@sun.ac.za
 - ¹³ Departments of Epidemiology and International Health, Johns Hopkins Bloomberg School of Public Health, Baltimore, 21205, MD, USA
 - ¹⁴ Departments of Epidemiology, Infectious Diseases and Microbiology, University of Pittsburgh Graduate School of Public Health, Pittsburgh, 15210, PA, USA
- * Correspondence: patrick.katoto@kuleuven.be or katotopatrick@gmail.com
† Joint senior authors.

Received: 16 October 2018; Accepted: 12 November 2018; Published: 15 November 2018



Abstract: Little is known about the respiratory health damage related to household air pollution (HAP) in survivors of pulmonary tuberculosis (PTB). In a population-based cross-sectional study, we determined the prevalence and associated predictors of chronic cough and hemoptysis in 441 randomly selected PTB survivors living in 13 remote health zones with high TB burden in the South Kivu province of the Democratic Republic of Congo (DRC). Trained community and health-care workers administered a validated questionnaire. In a multivariate logistic regression, chronic cough was independently associated with HAP (adjusted odds ratios (aOR) 2.10, 95% CI:

1.10–4.00) and PTB treatment >6 months (aOR 3.80, 95% CI: 1.62–8.96). Among women, chronic cough was associated with cooking ≥ 3 h daily (aOR 2.74, 95% CI: 1.25–6.07) and with HAP (aOR 3.93, 95% CI: 1.15–13.43). Independent predictors of hemoptysis were PTB retreatment (aOR 3.04, 95% CI: 1.04–5.09) and ignorance of treatment outcome (aOR 2.24, 95% CI: 1.09–4.58) but not HAP (aOR 1.86, 95% CI: 0.61–5.62). Exposure to HAP proved a major risk factor for chronic cough in PTB survivors, especially in women. This factor is amenable to intervention.

Keywords: biomass fuel; kerosene; respiratory symptoms; post-pulmonary tuberculosis; South Kivu

1. Introduction

With an estimated 10.4 million new cases and over 1.7 million deaths globally in 2016, tuberculosis (TB) remains of great public health importance [1]. In the Democratic Republic of Congo (DRC), the 2015 targets for TB control have not been met, i.e., neither the incidence nor the prevalence or mortality of TB were reduced by 50% compared to the situation in 1990 [2]. Consequently, in this country with a high TB burden (World Health Organization, global tuberculosis report 2018) [3], the number of pulmonary TB (PTB) survivors continues to increase. After completion of TB treatment, complications such as obstructive airways diseases have been documented since the days of the sanatoria treatment [4]. It is unclear why such a residual morbidity has remained neglected in many countries. National TB programs, even from high-burden TB countries, do not integrate long-term follow-up data of PTB survivors, nor do they provide information about complications in post-PTB life [1,2,5,6].

Although effective cures exist for the treatment of active TB disease, PTB survivors may still face various long-term complications from the architectural compromise of lung parenchyma (residual cavitation, scarring, or fibrosis, with mainly restrictive functional impairment) or airways (bronchiectasis, tracheobronchial stenosis, broncholithiasis, with obstructive impairment) due to colonization and infection (mycetoma or fungal ball) [5]. It is conceivable that exposure to household air pollution (HAP) increases the morbidity caused by the structural and functional impairment resulting from the previous mycobacterial infection. Exposure to HAP caused by the use of unclean domestic energy (biomass fuel, kerosene) has been associated with several lung illnesses [6]. Among HAP, wood is the most commonly used in Africa and especially in the Democratic Republic of Congo (DRC), which harbors the second largest forest in the world. In the DRC, with a rural electrification rate of 0.4%, the population relies on biomass fuel [7] for cooking and even for heating during the night time (mountain regions) and rainy seasons. Inadequately burnt wood generates a complex mixture of carbon-based particles, inorganic particles, irritant gases, and carcinogens, as in tobacco smoke [6,8].

Tuberculosis is associated with about 1.2 quality-adjusted life years lost, with 80% related to disability after TB cure. Of the disability-adjusted life years (DALYs) lost due to TB, 77% are linked to pulmonary impairment after successful treatment [9]. On the other hand, the comparative risk assessment for the 2010 Global Burden of Disease lists HAP as the third highest risk factor for lost DALYs in the world. Deaths and DALYs due to HAP are very unequally distributed; the DRC is among the top-10 worst-affected countries, where HAP has been estimated to be responsible for more than 1.5 million yearly deaths [10]. The burden of TB and that of HAP are related and inextricably linked to poverty. Hence, one can anticipate that HAP adds substantial morbidity for PTB survivors and costs for health systems. In resource-limited countries such as the DRC, with high TB burden and widespread use of biomass for domestic energy, we hypothesized that among PTB survivors, exposure to HAP would be associated with chronic complications, as assessed by chronic cough and hemoptysis. Our study aimed at providing quantitative data on the impact of HAP in PTB survivors and bring the issue of exposure to this modifiable risk factor under the attention of the community at large.

Chronic Obstructive Pulmonary Diseases: Journal of the COPD Foundation



Original Research

Urban-Rural Disparities in Chronic Obstructive Pulmonary Disease Management and Access in Uganda

Nicole M. Robertson¹ Emily M. Nagourney, MSPH² Suzanne L. Pollard, PhD, MSPH^{1,2} Trishul Siddharthan, MD¹ Robert Kalyesubula, MBChB, MMed³ Pamela J. Surkan, PhD, ScD² John R. Hurst, PhD, FRCP⁴ William Checkley, MD, PhD^{1,2} Bruce J. Kirenga, MBChB, MMed⁵

Abstract

Introduction: Almost 90% of chronic obstructive pulmonary disease (COPD) deaths occur in low- and middle-income countries (LMICs), where there are large rural populations and access to health care for COPD is poor. The purpose of this study was to compare urban-rural provider experiences regarding systemic facilitators and barriers to COPD management and treatment access.

Methods: We conducted a qualitative study using direct observations and in-depth semi-structured interviews with 16 and 10 health care providers in urban Kampala and rural Nakaseke, Uganda, respectively. We analyzed interviews by performing inductive coding using generated topical codes.

Results: In both urban and rural districts, exposure to evidence-based practices for COPD diagnosis and treatment was limited. The biomedical definition of COPD is not well distinguished in rural communities and was commonly confused with asthma and other respiratory diseases. Urban and rural participants alike described low availability of medications, limited access to diagnostic tools, poor awareness of the disease, and lack of financial means for medical care as common barriers to seeking and receiving care for COPD. While there was greater access to COPD treatment in urban areas, rural populations faced more pronounced barriers in access to diagnostic equipment, following standard treatment guidelines, and training medical personnel in non-communicable disease (NCD) management and treatment.

Conclusion: Our results suggest that health system challenges for the treatment of COPD may disproportionately affect rural areas in Uganda. Implementation of diagnostic and treatment guidelines and training health professionals in COPD, with a special emphasis on rural communities, will assist in addressing these barriers.

Abbreviations: chronic obstructive pulmonary disease, **COPD**; low-and middle-income countries, **LMIC**; non-communicable disease, **NCD**; tuberculosis, **TB**; chronic respiratory disease, **CRD**; Global initiative for chronic Obstructive Lung Disease, **GOLD**

Funding Support: This research was funded by the Medical Research Council Grant MR/P008984/1 under the Global Excellence in COPD Outcomes study and the Irvin F. and Alice S. Etscorn International Summer Research Award.

Date of Acceptance: July 16, 2018

Citation: Robertson NM, Nagourney EM, Pollard SL, et al. Urban-rural disparities in chronic obstructive pulmonary disease management and access in Uganda. *Chronic Obstr Pulm Dis*. 2019;6(1):17-28. doi: <https://doi.org/10.15326/jcopdf.6.1.2018.0143>

1 Division of Pulmonary and Critical Care, School of Medicine, Johns Hopkins University, Baltimore, Maryland

2 Department of International Health, Bloomberg School of Public Health, Johns Hopkins University, Baltimore, Maryland

3 Department of Physiology, College of Health Sciences, Makerere University, Kampala, Uganda

4 UCL Respiratory, University College London, United Kingdom

5 Department of Medicine and Lung Institute, College of Health Sciences, Makerere University, Kampala, Uganda

For personal use only. Permission required for all other uses.

International research and guidelines on post-tuberculosis chronic lung disorders: a systematic scoping review

Sanne C van Kampen,¹ Amanda Wanner,¹ Miles Edwards,¹ Anthony D Harries,^{2,3} Bruce J Kirenga,⁴ Jeremiah Chakaya,^{2,5} Rupert Jones¹

To cite: van Kampen SC, Wanner A, Edwards M, *et al.* International research and guidelines on post-tuberculosis chronic lung disorders: a systematic scoping review. *BMJ Glob Health* 2018;3:e000745. doi:10.1136/bmjgh-2018-000745

Handling editor Alberto L Garcia-Basteiro

► Additional material is published online only. To view please visit the journal online (<http://dx.doi.org/10.1136/bmjgh-2018-000745>).

Received 30 January 2018
Revised 18 May 2018
Accepted 28 May 2018



© Author(s) (or their employer(s)) 2018. Re-use permitted under CC BY-NC. No commercial re-use. See rights and permissions. Published by BMJ.

For numbered affiliations see end of article.

Correspondence to
Dr Sanne C van Kampen;
sanne.vankampen@gmail.com

ABSTRACT

Introduction Pulmonary tuberculosis (TB) is an important risk factor for chronic respiratory disease due to residual lung damage. Yet, the WHO End TB strategy does not mention post-TB chronic lung disorders (PTBLDs) and programmatic interventions to address PTBLD are lacking. This study assessed the scope of current guidelines and evidence on PTBLD to inform policy and research action.

Methods A systematic literature search was conducted following Preferred Reporting Items for Systematic Review and Meta-Analysis guidelines. Eight databases (TRIP, International Guideline Library, MEDLINE/PubMed, EMBASE, Web of Science, Global Health, Cochrane Library) were searched for records on PTBLD published between 1 January 1990 and 1 December 2017. Non-English records, case series, conference abstracts and letters to editors were excluded. Data were extracted and charted on publication year, location, PTBLD condition(s) and main study outcome.

Results A total of 212 guidelines and 3661 articles were retrieved. After screening, only three international TB guidelines mentioned TB sequelae, but none described how to identify or manage the condition. A total of 156 articles addressed PTBLD: 54 (35%) mentioned unspecified TB sequelae; 47 (30%) specific post-TB conditions including aspergillosis, bronchial stenosis or bronchiectasis; 52 (33%) post-TB obstructive disorders or lung function impairment; and 20 (13%) post-TB respiratory symptoms or chest X-ray abnormalities. The first two groups mostly assessed surgery or ventilation techniques for patient management, while the last two groups typically assessed prevalence or predictors of disease.

Conclusion This is the first review to provide a comprehensive overview of the current literature on PTBLD. The scope of evidence around the burden of PTBLD warrants inclusion and recognition of the problem in international TB guidelines. Research is now needed on early detection of PTBLD and patient management options that are suitable for high-burden TB countries.

INTRODUCTION

The burden of chronic respiratory disease is growing worldwide with chronic obstructive pulmonary disease (COPD) now being the third leading cause of death.¹ An estimated

Key questions

What is already known?

- Pulmonary tuberculosis (TB) is an important risk factor for chronic respiratory disease due to residual lung damage.
- The scope of current guidelines and evidence on post-TB chronic lung disorders (PTBLDs) is unknown.

What are the new findings?

- Out of 212 international TB guidelines, only three mentioned TB sequelae and none described how to identify or manage the condition.
- Of 156 scientific articles on PTBLD, around two-thirds addressed treatment by surgery or ventilation techniques and one-third addressed prevalence or predictors of the condition.

What do the new findings imply?

- While the scope of evidence on the burden of PTBLD justifies inclusion in international guidelines, more research is needed on patient management options that are suitable for high-burden TB countries.

3.2 million people died of COPD globally in 2015; an increase of 12% compared with 1990.² The main known risk factors for chronic respiratory diseases are smoking and outdoor air pollution, followed by household smoke exposure, occupational dust exposure, ozone and second-hand smoke.³ In recent years, evidence has emerged that tuberculosis (TB) is also an important predictor of COPD. Systematic reviews and international surveys have shown that a history of TB can increase the odds of COPD by an average of threefold and even more in countries with a high burden of TB.^{4–8} Pulmonary TB can lead to irreversible lung damage visible as scarring, fibrosis, cavitation or other types of damage on radiological images. This in turn can lead to loss of lung function, long-term respiratory symptoms and eventually chronic respiratory disease, including COPD, bronchiectasis and aspergillosis.^{9–13} These conditions can

RESEARCH ARTICLE

Open Access



Access to affordable medicines and diagnostic tests for asthma and COPD in sub Saharan Africa: the Ugandan perspective

Davis Kibirige^{1,2*}, Leaticia Kampiire³, David Atuhe⁴, Raymond Mwebaze⁵, Wincelous Katagira⁶, Winters Muttamba⁶, Rebecca Nantanda^{6,7}, William Worodria⁸ and Bruce Kirenga^{6,8}

Abstract

Background: Equitable access to affordable medicines and diagnostic tests is an integral component of optimal clinical care of patients with asthma and chronic obstructive pulmonary disease (COPD). In Uganda, we lack contemporary data about the availability, cost and affordability of medicines and diagnostic tests essential in asthma and COPD management.

Methods: Data on the availability, cost and affordability of 17 medicines and 2 diagnostic tests essential in asthma and COPD management were collected from 22 public hospitals, 23 private and 85 private pharmacies. The percentage of the available medicines and diagnostic tests, the median retail price of the lowest priced generic brand and affordability in terms of the number of days' wages it would cost the least paid public servant were analysed.

Results: The availability of inhaled short acting beta agonists (SABA), oral leukotriene receptor antagonists (LTRA), inhaled LABA-ICS combinations and inhaled corticosteroids (ICS) in all the study sites was 75%, 60.8%, 46.9% and 45.4% respectively. None of the study sites had inhaled long acting anti muscarinic agents (LAMA) and inhaled long acting beta agonist (LABA)-LAMA combinations. Spirometry and peak flow-metry as diagnostic tests were available in 24.4% and 6.7% of the study sites respectively. Affordability ranged from 2.2 days' wages for inhaled salbutamol to 17.1 days' wages for formoterol/budesonide inhalers and 27.8 days' wages for spirometry.

Conclusion: Medicines and diagnostic tests essential in asthma and COPD care are not widely available in Uganda and remain largely unaffordable. Strategies to improve access to affordable asthma and COPD medicines and diagnostic tests should be implemented in Uganda.

Keywords: Access, Medicines, Diagnostic tests, Asthma, COPD, Sub Saharan Africa, Uganda

Background

Globally, chronic respiratory diseases pose a major public health threat. Notably, the burden of asthma and chronic obstructive pulmonary disease (COPD) is steadily increasing in both developed and developing countries. According to recent World Health Organisation (WHO) estimates, about 235 million people have asthma

and 65 million people have moderate to severe COPD. High rates of mortality due to both conditions have been documented in low-and middle income countries (LMIC). In 2012, > three million people died of COPD, which accounted for about 6% of the all the deaths globally. An estimated 90% of these deaths occurred in LMIC [1].

In Uganda, a similar growing trend of mortality related to asthma and COPD has been described. A descriptive retrospective study conducted at an urban national referral hospital reported the burden of asthma and COPD of 70.6% and 21.6% respectively in 558 patients admitted to

* Correspondence: kibirigedavis@gmail.com

¹Department of Medicine, Uganda Martyrs Hospital Lubaga, P.O. BOX 7146, Kampala, Uganda

²Medical unit, GlaxoSmithKline Pharmaceutical Kenya Limited, Kampala, Uganda

Full list of author information is available at the end of the article



© The Author(s). 2017 **Open Access** This article is distributed under the terms of the Creative Commons Attribution 4.0 International License (<http://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license, and indicate if changes were made. The Creative Commons Public Domain Dedication waiver (<http://creativecommons.org/publicdomain/zero/1.0/>) applies to the data made available in this article, unless otherwise stated.

CASE-BASED LEARNING OPEN

A young child with a history of wheeze

James Paton¹, Patrick Bindels², Ann McMurray³, Jodie Biggins⁴, Rebecca Nantanda⁵ and Marianne Stubbe Østergaard⁶

The parents of a 3-year old boy are anxious about their son who has recurring episodes of wheezing. They are frustrated that no one seems to be able to give them answers to their questions and would like a referral to a specialist. Does their son have asthma and what is the prognosis; how can the recurrent wheezing be managed and can the risk of asthma be reduced; are there lifestyle changes that could improve the environment and avoid triggers? Communication and support from the family practice team were essential. Listening to the parents' concerns, explaining the diagnostic uncertainty, being realistic about what drug treatments could achieve, and providing practical advice on inhaler use and trigger avoidance reassured the parents that there was a strategy for managing their son's wheeze. The specialist referral was postponed.

npj Primary Care Respiratory Medicine (2017)27:19; doi:10.1038/s41533-017-0020-3

Case study

- The parents of a 3 year old boy have come to see their family doctor about their son whose recurrent episodes of wheeze and respiratory symptoms are causing concern. They are frustrated that no-one seems able to give them a clear diagnosis, and worried because the treatment they have been given is not controlling his symptoms. They would like a referral to a specialist to see if they can get some answers.
- Looking back through the records, the first episode of wheeze was at the age of 6 months. This was diagnosed as bronchiolitis and resulted in a brief admission. He had one further admission the following winter that was labelled as 'viral associated wheeze', and two subsequent attendances at the emergency department, on the last occasion being told that he had 'asthma'. In addition there are six primary care consultations for 'wheeze' or 'chest infections'. These episodes have been variously treated with bronchodilators, steroids (inhaled and oral) and/or antibiotics—none of which have had any convincing effect.
- He was a normal full term delivery and thrived well from birth. Mother had hay fever as a teenager, and father smokes (though 'never in the house')

A clinical case, such as this 3-year old boy with recurrent wheeze, raises many questions that need to be explored in order to address parental concerns and manage the child's condition. The boy is thriving, height and weight just above the 50th centile.

WHY DO THE PARENTS REQUEST A REFERRAL?

A host of reasons may underpin the parent's request. Is their concern that the wheezy episodes are harmful? Are they unable to sleep because the child is disturbed at night? Is it the lack of a clear

diagnosis and uncertainty about the boy's long-term prognosis that is causing the worry? Do the parents want advice on avoiding triggers or information on what to do when the wheezing recurs, or is the main focus of this consultation the (perceived) additional value of a referral to a specialist? Or all of these?

DOES OUR SON HAVE ASTHMA, AND WHAT IS THE PROGNOSIS?

Wheezing is common in young children

Wheezing in children under 3 years of age is common. By 30 months, 26% of children in a UK birth cohort (ALSPAC, Avon longitudinal study of parents and children) had wheezed in the previous 12 months.¹ Wheezing, as in this case, is often not just a minor inconvenience. Data from the latest British Thoracic Society national paediatric audit of wheezing/asthma showed that 24% of all the children admitted to hospital were between 12 and 24 months, boys outnumbering girls in a ratio of nearly 2 to 1.²

Longitudinal birth cohort studies have transformed our understanding of wheezing in early childhood,³ demonstrating that the origins of most asthma lie in early childhood and that variations in the natural history of childhood wheezing are associated with different long-term outcomes. Between 4–6 of these 'phenotypes' have been identified.^{4, 5} One major group is transient early wheezers whose symptoms remit by the time the child is school age. The absence of atopy is, at present, the best marker for this group.⁵ Early onset of wheezing is associated with lower lung function at adolescence and the presence of atopy is associated with persisting asthma.⁴ However, at present, it is not possible to assign a particular phenotype to an individual child to determine either treatment or prognosis; indeed, it is common for the features to change during early childhood.⁵ A summary of the recent evolution of the terminology of 'asthma' in children is given in Table 1.

¹School of Medicine Dentistry & Nursing, Child Health, College of Medical, Veterinary, and Life Sciences, Queen Elizabeth University Hospital, University of Glasgow, Zone 1, Ground Floor, Office Block, Glasgow, UK; ²Department of General Practice, Erasmus Medical Centre, Rotterdam, Netherlands; ³Department of Respiratory and Sleep Medicine, Royal Hospital for Sick Children, Sciennes Road, Edinburgh EH9 1LF Scotland, UK; ⁴Patient and Public Involvement Group, Asthma UK Centre for Applied Research, Usher Institute of Population Health Sciences and Informatics, University of Edinburgh, Doorway 3, Medical School, Teviot Place, Edinburgh EH8 9AG, UK; ⁵Makerere University Lung Institute Makerere University College of Health Sciences, Kampala, Uganda and ⁶The Research Unit for General Practice and Section of General Practice, Department of Public Health, University of Copenhagen, Copenhagen, Denmark
Correspondence: James Paton (james.paton@glasgow.ac.uk)

Received: 17 December 2016 Revised: 3 February 2017 Accepted: 14 February 2017
Published online: 16 March 2017

Published in partnership with Primary Care Respiratory Society UK

Table 1. Asthma: What's in a name?

Historically, there has been a reluctance to diagnose asthma in children. In 1983, Speight et al, highlighted that children who were not given a diagnosis of asthma were not treated appropriately and suffered unnecessary morbidity.ⁱ Fears that the label of 'asthma' might cause distress were unfounded; parents were 'uniformly relieved' that the cause of their child's symptoms had been identified. There followed a drive to reduce under-diagnosis and under-treatment, though the status of wheezy infants (under 1 year of age) remained contentious.^{ii, iii} Studies of the natural history of asthma in children,^{iv} however, began to define phenotypes of 'transient early wheezers', 'late-onset wheezers' and 'persistent wheezing' which seemed to contradict the drive to 'encourage healthcare professionals to make a positive diagnosis of asthma whenever recurrent wheezing, breathlessness and cough occur',^{vii} by suggesting that only a minority of wheezy toddlers would prove to have persistent asthma. The concern now was over-diagnosis and over-treatment of young children with guidelines highlighting the 'difficulty of making a confident diagnosis of asthma in young children'.^v

In some healthcare contexts under-diagnosis of asthma remains a problem, as respiratory symptoms are routinely labelled (and treated) as pneumonia,^{vi} or described symptomatically to avoid the perceived stigma of the label 'asthma'.

This case study has adopted a pragmatic approach, sharing uncertainties of diagnosis and prognosis with the parents, objectively monitoring trials of treatment so that symptoms that can be treated are relieved, a strategy that resonates with the contemporary approach of 'treatable traits'.^{vii}

i. Speight, A. N. P., Lee, D. A., & Hey, E. N. Underdiagnosis and undertreatment of asthma in childhood. *BMJ* **286**, 1253–1256 (1983).

ii. British Thoracic Society. The British guidelines on asthma management. *Thorax* **52** (Suppl. 1), 1–21 (1997).

iii. Global Initiative for Asthma. Global strategy for asthma management and prevention. GINA (1995) Diagnosis: pp 47–61

iv. Martinez, F.D., Wright, A.L., Taussig, L.M., Holberg, C.J., Halonen, M., & W.J. Morgan. Asthma and wheezing in the first six years of life. The Group Health Medical Associates. *N. Engl. J. Med.* **332**, 133–138 (1995).

v. Global Initiative for Asthma: Global Strategy for Asthma Management and Prevention, 2016. Available from www.ginasthma.org. Accessed July 2016

vi. Nantanda, R., Tumwine, J. K., Ndeezi, G., & Ostergaard, M. S., Asthma and Pneumonia among children less than five years in Mulago hospital Uganda: evidence of under-diagnosis of asthma. *PLoS One* **8**, e81562 (2013).

vii. Agusti, A., Bel, E., Thomas, M., Vogelmeier, C., Brusselle, G., Holgate, S., et al. Treatable traits: toward precision medicine of chronic airway diseases. *Eur. Respir. J.* **47**, 410–419 (2016).

Table 2. Parents interpretation of children's respiratory symptoms.⁶

A study in the East end of London, invited parents (first language English, Urdu, Bengali (Sylheti), or Turkish) to view a video of children's respiratory symptoms:

- A third of parents use other words for wheeze; a third falsely label other sounds as wheeze
- Compared to other respiratory sounds, parents are more likely to label wheeze correctly
- Parents are better able to locate sounds than to label them
- There was no significant difference between parents of wheezers and non-wheezers in accuracy of labelling of location
- Parents are better at labelling if English is their first language

Defining 'wheeze' is not always simple

Wheezing is usually associated with airflow obstruction and is central to the diagnosis of asthma. In older children, airflow obstruction and reversibility can be documented objectively on spirometry or peak flow measurements, but lung function measurements in children younger than 4–5 years are usually not feasible in clinical practice. This places much greater emphasis on the history of wheezing provided by the parents/caregivers, which is problematic because what parents and doctors mean by 'wheezing' is often very different.^{6, 7} (See Table 2). Furthermore, the word 'wheeze' does not exist in some languages. Because of this most guidelines emphasise that if a doctor hears wheezing on auscultation, it is an important observation to record.

All that wheezes is not asthma

Not all wheezing is due to asthma or viral infections. There are rare but important differential diagnoses.⁸ Persistent wheezing in young children, wet cough, vomiting, failure to thrive and a poor response to anti-asthma medications may be important clues to alternative diagnoses such as cystic fibrosis.

Viral wheezing and asthma

Viruses have been found in at least 80% of wheezing episodes in children.⁹ With the exception of respiratory syncytial virus (RSV) in infants hospitalised with bronchiolitis, human rhinovirus (HRV) is

by far the most common virus isolated in children over 12 months.¹⁰ HRV-C is the most common rhinovirus species in wheezing children, and, compared to other viruses, is more often associated with recurrent acute wheezing attacks severe enough to result in children presenting to hospital.¹¹ In the follow up of a high-risk birth cohort (one parent with positive skin prick test to an aeroallergen and/or asthma) the persistence of asthma at age 13 years was most strongly associated with rhinovirus-associated wheezing illnesses and with aero-allergen sensitisation in early life.¹² Evidence suggests that some children are more susceptible and have more severe rhinovirus infections because of a subtle defect in innate anti-viral immunity.¹³

Bronchiolitis and the link with asthma

In the first year of life, bronchiolitis (usually defined as the first episode of wheezing in children less than 2 years old)¹⁴ due to RSV infection is the commonest lower respiratory tract illness with wheezing, affecting around 1 in 3 children.¹⁵ On auscultation there is wheezing and/or fine crackles. The disease is usually mild with only 2–3% of children being hospitalised.¹⁴

An association between bronchiolitis and asthma has been noted in many studies. However, while longitudinal follow-up suggests that RSV infections in early childhood are associated with an increased risk of wheezing, this association subsides with age and becomes insignificant by 13 years, unlike rhinovirus infections where the association with wheezing persists.¹⁶

Will symptoms persist in the long term (the prognosis)?

For some children, early wheezing will translate into long-term asthma. This is particularly the case for those with early rhinovirus infections, with sensitisation to aeroallergens and with reduced lung function. The problem is that we cannot, with complete certainty, identify those in whom symptoms will persist and those in whom they will remit. Nevertheless, in the child in our case study, the early frequent and severe episodes in a child with a maternal history of hay fever and possible exposure to environmental smoke may point to a more protracted course of the respiratory symptoms.

Although not widely used in clinical practice, several asthma prediction scores have been developed and published in the last decade,¹⁷ and may usefully inform the history that the healthcare professional needs to take. The clinical asthma prediction score (CAPS), designed specifically for use in general practice, is based on five parameters: age, family history of asthma or allergy, wheezing-induced sleep disturbances, wheezing in the absence of colds, and (if available) specific Immunoglobulin E.¹⁸ The score ranges from 0 to 11 points; CAPS <3 signifies a negative predictive value of 78% while CAPS ≥7 signifies a positive predictive value of 74%. Measurement of specific IgE provides additional value, though the downside is the need for a blood test in a young child.

Prognosis for the 3 year old boy in the case study

Based on the available information, the score in this boy will be at least three (asthma probability 30% at school age) but, with additional information on specific IgE and sleep disturbances, could be as high as nine (asthma probability of 82% at school age). These CAPS scores suggest a policy of either watchful waiting (asthma probability 30–60%) or initiating formal asthma management (asthma probability of 60% or higher).¹⁸ The wide range reflects the current difficulties in predicting prognosis.

WHAT TREATMENT WILL REDUCE OUR SON'S SYMPTOMS—AND, IF POSSIBLE, PREVENT LONG-TERM ASTHMA?

At present, there is no treatment known to 'cure' asthma. Current treatments, however, can control symptoms and modify the chances of attacks.^{19, 20} Bronchodilators should be used when the child is wheezy, though discussion with parents is important to ensure they are interpreting sounds correctly and that the child responds to the bronchodilator. If asthma is probable, inhaled steroids are the most effective treatment for controlling symptoms and should be first-line treatment if attacks are frequent and severe and/or if there are interval symptoms. Perhaps the one clear 'fact' is that complete avoidance of exposure to environmental tobacco smoke is important.²¹

Does preventing RSV infection reduce risk of asthma?

Reflecting the observation that the persistence of wheezing beyond childhood is associated with rhinovirus infection (as opposed to RSV), prevention of RSV infection does not have a measurable effect on subsequent episodes of wheeze and asthma.²² Giving pre-term infants anti-RSV antibodies for the first year of life reduces RSV infections but not recurrent wheeze over the pre-school years.²³

Does early start of inhaled steroids prevent risk of asthma?

In 2006 three studies were published on the use of inhaled corticosteroids (ICS) in young children at high risk of developing asthma with one or more episodes of wheeze.^{24–26} Although some children had a temporary reduction in symptoms during ICS treatment, this did not prevent development of asthma. So, in our clinical case, it is important to discuss with the parents that the

early start of ICS is not needed as a primary prevention strategy but it might have an effect on the severity of the symptoms.

Relief of acute wheezy episodes

Let us consider that the consultation for this boy and his parents was triggered by a further attack of respiratory symptoms and wheeze. If there are no alarming symptoms, such as respiratory distress, requiring immediate intervention and/or referral, the use of a short acting beta₂ agonist (SABA) will be the drug of choice to relieve the acute wheeze.⁸ Symptom relief is the main goal; SABA do not alter the natural course of the wheeze episode.

SABA can be administered safely and effectively at all pre-school ages, including below the age of one. Inhalation is well tolerated and an effect can be expected within 10–15 min. If necessary, inhalation of SABA (with a face mask) during the consultation may provide prompt relief of symptoms, demonstrating both how inhaled medication should be delivered by a spacer (five breaths to one puff) and the rapid symptom response that can result. A dose of a SABA may be needed every 3–6 hours for one or more days until the symptoms of wheeze disappear.

It is essential to ask the parents to revisit your practice at the end of the episode of respiratory symptoms (normally 1–2 weeks after the first visit). During this review the effect of the medication can be evaluated, and in case of complete remission of the symptoms medication should be stopped in order to prevent unnecessary use and overtreatment with SABA in the future. Furthermore, the parents can be advised on when to visit the practice again in case new symptoms appear.

Prevention in children with frequent wheezy episodes or a higher probability of asthma

The indication for treatment with ICS (step 2 in GINA; see Fig. 1) is based on the frequency and severity of symptoms, and the probability that the child has asthma. The older the child, the presence of a multiple trigger wheeze and the presence of a positive specific IgE test to house dust mite, cat or dog allergens (or a positive family history for asthma and /or allergy) will increase the chances of a response to regular treatment with an ICS.

Treatment with ICS should be started as a carefully monitored diagnostic trial,²⁷ and the clinical effect evaluated after 4–8 weeks.²⁸ If the child responds well to a treatment with ICS, it is recommended, in discussion with parents, to reduce and ultimately withdraw the medication to exclude natural resolution of symptoms. If symptoms recur during or after withdrawal, restart treatment and consider on-going treatment.^{8, 29} If there is no response to treatment, the ICS should be stopped and alternative diagnoses should be reconsidered.

The use of ICS in children with viral induced episodes of wheeze, without symptoms or triggers in between episodes, is more controversial. The effect on symptoms is at best limited, but a recent meta-analysis has shown that short-term (7–10 days) high dose ICS, starting at the first sign of an URTI, may reduce the risk of severe exacerbations.²⁰

A follow-up consultation in general practice is essential when inhalation medication is started in any child irrespective of the indication. During this review, the parents can be informed about the short and long-term prognosis and the action to take during a subsequent episode. Prevention of overtreatment of children with ICS and the (in)correct labelling of wheeze as asthma is as important as overlooking an asthma diagnosis and not treating with ICS. Until an asthma diagnosis is confirmed by a physician, requests for repeat prescriptions of SABA or ICS in preschool children should trigger a review of current status.

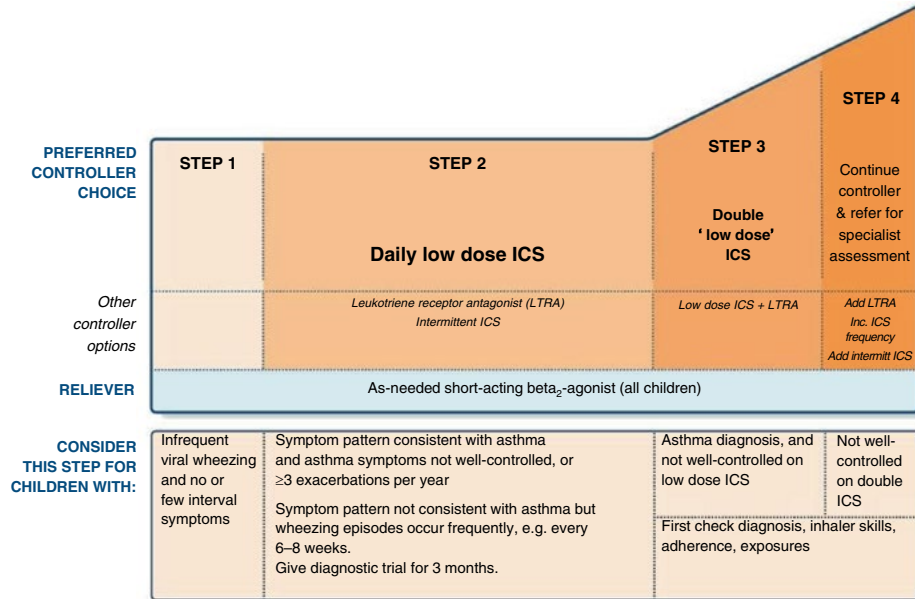


Fig. 1 Stepwise approach to pharmacotherapy in children under 5 years. Reproduced with permission from the GINA guidelines.⁸

Other medication that may be considered

Oral steroids during attacks do not seem to be effective in preschool children with viral induced wheezing of moderate severity.^{30, 31} They should be used only in children with severe wheeze, and even then the evidence is not robust.¹⁹

A recent Cochrane review revealed no benefit from the use of leukotriene receptor antagonists (LTRAs) in pre-school children with viral induced wheeze. However, identifying these phenotypes is challenging, and individual children may warrant a carefully monitored trial of a LTRA.³² Long acting beta₂-agonists (LABA) have been studied in older children with persistent asthma as add-on therapy to ICS. There are no studies on the use of LABA in preschool children with recurrent wheeze and therefore their use cannot be recommended.³³

Management strategy in the 3 year old boy in the case study

In this particular case, the GP will need more than one review visit before a clear clinical picture will emerge and before the parents can be informed about the likely prognosis of the respiratory symptoms in their child. The parents reported that inhaled steroids did not have a convincing effect, but parental expectations need to be discussed (e.g. ICS will not reduce the frequency of viral upper respiratory tract infections), and inhaler technique and compliance with the trial of treatment needs to be checked and discussed (see below). If the child is currently symptomatic a further carefully monitored trial of ICS should be considered, if they are asymptomatic a wait-and-see strategy may be appropriate. In either situation, even after reassurance of the parents either by the General Practitioner (GP) and the practice nurse, a referral to a specialist may sometimes be appropriate as the most effective way to reassure the parents. Depending on resources in

primary care, however, a paediatrician may not have more diagnostic or therapeutic possibilities in preschool children than a general practitioner.

SUPPORTING WORRIED PARENTS

Diagnostic uncertainty & dealing with parental anxiety

It is recognised that approximately one in three children has at least one episode of wheeze before their third birthday,^{1, 3} with the expectation that the majority of children will outgrow their symptoms between age 3 and 8 years.^{1, 3, 34, 35} This however provides little comfort to a parent whose child is exhibiting symptoms and experiencing exacerbations (see a perspective from a parent in Table 3). It is important to explain that diagnosis is based on the clinical history, symptoms and response to treatment, and that these will need to be carefully observed and re-considered over time.

Treatment has to be tailored to the individual child. Parental acceptance that not all asthma therapies will prove effective in reducing exacerbations can be hard to achieve. Explanations of pharmacological treatment limitations may help to achieve more realistic expectations. Some parents may need longer consultations or will benefit from a referral to other members of the healthcare team such as the health visitor, asthma educator, respiratory nurse, physiotherapist, or community health worker. Education needs to be provided in plain language, using pictures or models to illustrate, and tailored to the parents' current understanding and beliefs. Parents may also benefit from speaking to other parents who have been in a similar situation and they may seek this type of support via social media such as Facebook or Twitter. Parents should always be cautioned

Table 3. Perspective from a parent

Getting a diagnosis

It started with bronchiolitis in autumn when my son was under 2 years old however he had subsequent wheezy episodes over winter and spring and the diagnosis changed to viral induced wheeze. Depending on who we see, either in accident and emergency, GP practice or hospital consultant some say he may have asthma and others say he is too young to have asthma. That has left us as parents frustrated. We have a family history of asthma so it could be that.

Medications

When my son has a wheezy episode we have a plan to follow which was given to us by the respiratory nurse specialists at the hospital. It gives us guidance on what to do when he gets a cold and when we need to see someone. Prednisolone seems to work but he has had so many courses over the last year some of the doctors have started to admit him and monitor him instead without giving steroids.

Giving the inhaler through the spacer with mask has been challenging. Sometimes nurses don't do it correctly or are in a rush to give all 10 puffs. This has scared my son in the past but he got used to it over time. We know that if he is crying or upset he won't get a full dose so it is important to keep him calm. We learned some distraction techniques from the nurse specialists and they have been helpful.

Impact on family life

We have been to see our general practitioner, accident and emergency department, or hospital consultant on many occasions. The unpredictability of the episodes has made it difficult for us to make family plans especially for a holiday. We ended up in hospital on two occasions when we were away from home. We have had to take time off when he is unwell as he cannot go to nursery and this has had an impact on our jobs. Medical staff keep saying it will get better as he gets older.

Table 4. Useful websites for families of wheezy children

Organisation	Website	Description
Asthma UK	www.asthma.org.uk	Advice and support parents need to help their child stay well with their asthma
Chest Heart & Stroke Scotland.	www.mylungsmylife.org	Information, tips and advice to help parents make choices about their child's asthma
Children and Young Peoples Allergy Network Scotland	www.cyans.org.uk	The 'families' section gives basic information on the different types of allergy and how to manage allergies
European Lung Foundation	http://www.europeanlung.org	Reliable information about a range of lung diseases and their risk factors

about the use of less reputable sources of self-help and encouraged to discuss strategies for self-management with their own doctor or nurse. Table 4 lists some useful websites for families.

Inhaler technique

The first experience of administering inhaled medication via a spacer can have an impact upon the child's acceptance of future treatment. The spacer is often used for the first time when the child is experiencing difficulty breathing. Having a facemask placed over their nose and mouth can be frightening. Prior to first use the child should have an opportunity to handle the spacer and build up to the facemask being kept in position for up to 10 s dependant on taught technique. Between wheezy episodes parents should ensure their child remains familiar with the spacer to try and avoid future distress. Although actively accepting an inhaler should be the goal, administering treatment while a child is sleeping is a practical strategy that may help in some situations. Small children should never be chastised or wrapped in blankets or towels to aid with inhaler administration and these methods should be replaced with praise and distraction techniques. Holding techniques should be demonstrated and parents should be signposted to websites with demonstration videos as reminders (for example: Asthma UK 'Using your inhalers' <https://www.asthma.org.uk/advice/inhalers-medicines-treatments/using-inhalers>). Inhalers (and spacers) should only be prescribed after patients have received training in the use of the device and have demonstrated satisfactory technique.²⁷ If this is difficult in a time-limited consultation, arrangements may be made with a local community pharmacist, healthcare assistant, health educator or practice nurse to check inhaler technique when inhalers have been prescribed.

Self management

There is a paucity of evidence about effective self-management strategies for parents of pre-school children.²⁷ Parents often report that their child's condition seems to decline rapidly, but it is important to discuss symptoms or behaviours exhibited in the day (s) prior to previous exacerbations. On reflection, parents may be able to identify non-specific signs (such as decreased dietary intake, runny nose) as a precursor to an attack. Recognition of the signs of increased work of breathing should be discussed with parents and thresholds set for medical review. This may need to be adapted dependant on family dynamics, geographical location and severity of previous attacks. Safety is paramount and parents should not be made to feel they are over reacting or seeking too many medical reviews; they must feel confident to seek help at crucial times.

CREATING A HEALTHY ENVIRONMENT

This is a 3-year old child with recurrent episodes of wheezing. The health care professional has a responsibility to help parents create a healthy environment by addressing any modifiable risk factors such as tobacco and biomass smoke, in-door allergens, house dampness and also to provide information about inevitable respiratory viral triggers of asthma exacerbations.

Environmental risk factors for asthma exacerbations

The link between the environment and exacerbation of asthma symptoms is a well-described entity.⁸ Many studies have described the role of air pollutants (indoor and outdoor) including biomass smoke and fumes from cars and factories, in triggering asthma symptoms.^{36, 37} The effect of environmental tobacco smoke, also known as second-hand smoking in causation

and exacerbation of asthma symptoms in children is also well-documented.^{38–40}

Children exposed to environmental tobacco smoke, experience more frequent and severe exacerbations of the asthma symptoms, even where medical treatment is adequate.^{37, 40} The dust and surfaces in a smoker's home have been found to be contaminated with tobacco smoke, even when parents avoid smoking in the house.⁴¹ Vapour phase nicotine and particulates have been also found in the home of smokers.^{42, 43} Generally, contamination and exposure to second-hand smoke are 5–7 times higher in the homes of 'smoking outdoor' people compared to non-smokers.⁴¹

Indoor air pollution, including use of biomass smoke from burning wood, animal dung and crop residues for cooking and heating, has been associated with an increased risk of asthma exacerbations in children and adults.³⁶ Therefore, improving air quality at home and reviewing some of the activities that may trigger attacks will be an important aspect of creating a health environment for this child.

Besides air pollution, a consistent association of dampness with respiratory symptoms is found among both atopic and non-atopic children. House dust mite exposure and sensitisation may contribute, but the link seems to be related principally to non-atopic mechanisms.⁴⁴ Moreover, indoor allergens from mouse, cats, pets, dust mite and mould have been described as important exposures that lead to exacerbation of asthma symptoms.^{44, 45}

What can be done to create a healthy environment for this child? As the diagnosis of asthma is increasingly likely, ICS along with addressing modifiable environmental risk factors for exacerbations (particularly tobacco smoke), can reduce hospital visits, avoid high healthcare costs and improve quality of life of the child and his parents.^{46, 47} The parents need to understand the benefits of the lifestyle changes and should be motivated to creating a smoke-free home, without exceptions for guests or friends.

Smoking cessation is a complex process and the parents will need support from family, friends and the healthcare system to be able to stop smoking. Key to this process is an understanding the barriers to smoking cessation such as; parental beliefs about second-hand smoke and readiness to quit smoking. Stress has been described as a major barrier to quitting because cigarette smoking is often used to give (temporary) relief from stress.⁴⁸ It is therefore important to discuss the sources of stress and coping strategies that are not harmful. It is also important to build on known motivators for smoking cessation including family support and the will to protect the child from the effects of tobacco smoke.⁴⁹

Reduction in exposure to biomass smoke can be achieved through use of alternative cooking and heating fuel such as liquefied gas or by using improved cookstoves.⁵⁰ However, the challenges in adopting such changes including costs involved and behavioural aspects must be discussed with the parents.⁵¹

Many children are sensitised to more than one allergen, and many households have damp rooms. Reducing exposure to damp and mould improves asthma control in adults, but the benefit of interventions such as regular cleaning, avoiding use of carpets, and withdrawing pets from the home,⁴⁵ is described as 'limited' in guidelines and can be 'expensive and complicated'.⁸

The story continues...

- The family doctor recognised that the parents needed time to discuss their concerns and to have answers to their questions. She spent the consultation listening to the story of admissions and on-going symptoms, and explained why there was uncertainty about the diagnosis and why the treatments that had been tried had not relieved all the symptoms. She arranged for the parents to meet with a specialist nurse who had expertise in managing pre-school children with asthma.

At the review, the nurse was able to reinforce the information provided by the doctor, review (self) management strategies, offer practical advice on delivery of inhaled therapy, and discuss reducing environmental triggers (including offering the father support with smoking cessation). At a follow-up appointment a month later, although their son continued to have occasional symptoms he was still thriving, and the parents decided against another trial of ICS at this time. The parents felt reassured and supported, and the decision about a referral to a hospital clinic was postponed.

AUTHOR CONTRIBUTIONS

J.P., P.B., A.McM., R.N., M.S. contributed sections of the text, commented on the collated document, and approved the final version. J.B. contributed the patient perspective supported by A.McN. The handling editor (Hilary Pincock) collated and edited the individual sections.

COMPETING INTERESTS

The authors declare that have no competing interests.

REFERENCES

- Henderson, J., Granel, R., Heron, J., Sherriff, A., Simpson, A. & Woodcock, A. et al. Associations of wheezing phenotypes in the first 6 years of life with atopy, lung function and airway responsiveness in mid-childhood. *Thorax* **63**, 974–980 (2008).
- Paton, J. British Thoracic Society National Paediatric Asthma Audit Summary Report (November). <https://www.brit-thoracic.org.uk/document-library/audit-and-quality-improvement/audit-reports/bts-paediatric-asthma-audit-report-2015>. Accessed December 2016 (2015).
- Martinez, F. D., Wright, A. L., Taussig, L. M., Holberg, C. J., Halonen, M. & Morgan, W. J., for the Group Health Medical Associates. Asthma and wheezing in the first six years of life. *N. Engl. J. Med.* **332**, 133–138 (1995).
- Granel, R., Henderson, A. J. & Sterne, J. A. Associations of wheezing phenotypes with late asthma outcomes in the Avon longitudinal study of parents and children: a population-based birth cohort. *J. Allergy Clin. Immunol.* doi:10.1016/j.jaci.2016.01.046 (2016).
- Garden, F. L., Simpson, J. M., Mellis, C. M. & Marks, G. B. Change in the manifestations of asthma and asthma-related traits in childhood: a latent transition analysis. *Eur. Respir. J.* **47**, 499–509 (2016).
- Cane, R. S. & McKenzie, S. A. Parents' interpretations of children's respiratory symptoms on video. *Arch. Dis. Child.* **84**, 31–34 (2001).
- Lowe, L., Murray, C. S., Martin, L., Deas, J., Cashin, E. & Poletti, G. et al. Reported versus confirmed wheeze and lung function in early life. *Arch. Dis. Child.* **89**, 540–543 (2004).
- Global Initiative for Asthma. Global Strategy For Asthma Management and Prevention. www.ginasthma.org. Accessed July 2016 (2016).
- Jackson, D. J., Sykes, A., Mallia, P. & Johnston, S. L. Asthma exacerbations: origin, effect, and prevention. *J. Allergy Clin. Immunol.* **128**, 1165–1174 (2011).
- Turunen, R., Koistinen, A., Vuorinen, T., Arku, B., Söderlund-Venermo, M. & Ruuskanen, O. et al. The first wheezing episode: respiratory virus etiology, atopic characteristics, and illness severity. *Pediatr. Allergy Immunol.* **25**, 796–803 (2014).
- Cox, D. W., Bizzintino, J., Ferrari, G., Khoo, S. K., Zhang, G. & Whelan, S. et al. Human rhinovirus species C infection in young children with acute wheeze is associated with increased acute respiratory hospital admissions. *Am. J. Respir. Crit. Care Med.* **188**, 1358–1364 (2013).
- Rubner, F. J., Jackson, D. J., Evans, M. D., Gangnon, R. E., Tisler, C. J., Pappas, T. E., et al. Early life rhinovirus wheezing, allergic sensitization, and asthma risk at adolescence. *J. Allergy Clin. Immunol.* **139**, 501–507. doi:10.1016/j.jaci.2016.03.049 (2017). Epub 10 May 2016.
- Hewitt, R., Farne, H., Ritchie, A., Luke, E., Johnston, S. L. & Mallia, P. The role of viral infections in exacerbations of chronic obstructive pulmonary disease and asthma. *Thor. Adv. Respir. Dis.* **10**, 158–174 (2016).
- National Collaborating Centre for Women's and Children's Health. *Bronchiolitis: diagnosis and management of bronchiolitis in children*, (London, 2015).
- Geerdink, R. J., Pillay, J., Meynard, L. & Bont, L. Neutrophils in respiratory syncytial virus infection: a target for asthma prevention. *J. Allergy. Clin. Immunol.* **136**, 838–847 (2015).
- Stein, R. T., Sherriff, D., Morgan, W. J., Holberg, C. J., Halonen, M. & Taussig, L. M. et al. Respiratory syncytial virus in early life and risk of wheeze and allergy by age 13 years. *Lancet* **354**, 541–545 (1999).

17. Luo, G., Nkoy, F. L., Stone, B. L., Schmick, D. & Johnson, M. D. A systematic review of predictive models for asthma development in children. *BMC Med. Inform. Decis. Mak.* **15**, 99 (2015).
18. van der Mark, L. B., van Wonderen, K. E., Mohrs, J., van Aalderen, W. M., ter Riet, G. & Bindels, P. J. E. Predicting asthma in preschool children at high risk presenting in primary care: development of a clinical asthma prediction score. *Prim. Care Respir. J.* **23**, 52–59 (2014).
19. Brand, P. L., Caudri, D., Eber, E., Gaillard, E. A., Garcia-Marcos, L. & Hedlin, G. *et al.* Classification and pharmacological treatment of preschool wheezing: changes since 2008. *Eur. Respir. J.* **43**, 1172–1177 (2014).
20. Kaiser, S. V., Huynh, T., Bacharier, L. B. & Rosenthal, J. L. Preventing exacerbations in preschoolers with recurrent wheeze: a meta-analysis. *Pediatrics* **137**, 1–15 (2016).
21. Tinuoye, O., Pell, J. P. & Mackay, D. F. Meta-analysis of the association between secondhand smoke exposure and physician-diagnosed childhood asthma. *Nicotine Tob. Res.* **15**, 1475–1483 (2013).
22. Meissner, H. C. Viral Bronchiolitis in children. *N. Engl. J. Med.* **374**, 62–72 (2016).
23. O'Brien, K. L., Chandran, A., Weatherholtz, R., Jafri, H. S., Griffin, M. P. & Bellamy, T. *et al.* Efficacy of motavizumab for the prevention of respiratory syncytial virus disease in healthy Native American infants: a phase 3 randomised doubleblind placebo-controlled trials. *Lancet Infect. Dis.* **15**, 1398–1408 (2015).
24. Guilbert, T. W., Morgan, W. J., Zeiger, R. S., Mauger, D. T., Boehmer, S. J. & Szeffer, S. J. *et al.* Long term inhaled corticosteroids in preschool children at high risk for asthma. *N. Eng. J. Med.* **354**, 1985–1992 (2006).
25. Bisgaard, H., Hermansen, M. N., Lohand, L., Halkjaer, L. V. & Buchwald, F. Inter-mittent inhaled corticosteroids in infants with episodic wheezing. *N. Eng. J. Med.* **354**, 1998–2005 (2006).
26. Murray, C. S., Woodcock, A., Langley, S. J., Morris, J. & Custovic, A., for the IFWIN study team. Secondary prevention of asthma by the use of Inhaled Fluticasone propionate in Wheezy Infants (IFWIN): double-blind, randomised, controlled study. *Lancet* **368**, 754–762 (2006).
27. British Thoracic Society/Scottish Intercollegiate Guidelines Network. British guideline on the management of asthma. *Thorax* **69**, (Suppl 1), 1–192 (2016). Update 2016 <http://sign.ac.uk/guidelines/fulltext/153/index.html>. Accessed September 2016.
28. Bush, A., Grigg, J. K. & Saglani, S. Managing wheeze in preschool children. *BMJ* **348**, g15 (2014).
29. Brand, P. L., Baraldi, E., Bisgaard, H., Boner, A. L., Castro-Rodriguez, J. A. & Custovic, A. *et al.* Definition, assessment and treatment of wheezing disorders in preschool children: an evidence-based approach. *Eur. Respir. J.* **32**, 1096–1110 (2008).
30. Panicker, J., Lakhanpaul, M., Lambert, P. C., Kenia, P., Stephenson, T. & Smyth, A. *et al.* Oral prednisolone for preschool children with acute virus-induced wheezing. *N. Engl. J. Med.* **360**, 329–338 (2009).
31. Jartti, T., Nieminen, R., Vuorinen, T., Lehtinen, P., Vahlberg, T. & Gem, J. *et al.* Short- and long-term efficacy of prednisolone for first acute rhinovirus-induced wheezing episode. *J. Allergy Clin. Immunol.* **135**, 691–698 (2015).
32. Brodli, M., Gupta, A., Rodriguez-Martinez, C. E., Castro-Rodriguez, J. A., Ducharme, F. M. & McKean, M. C. Leukotriene receptor antagonists as maintenance and intermittent therapy for episodic viral wheeze in children. *Cochrane Database Syst. Rev.* **19**(10). Art. No.: CD008202. doi:10.1002/14651858.CD008202.pub2 (2015).
33. Chauhan, B. F., Chartrand, C., Ni Chroinin, M., Milan, S. J. & Ducharme, F. M. Addition of long-acting beta₂-agonists to inhaled corticosteroids for chronic asthma in children. *Cochrane Database Syst. Rev.* Issue 11. Art. No.: CD007949. doi:10.1002/14651858.CD007949.pub2 (2015).
34. Savenije, O. E., Kerkhof, M., Koppelman, G. H. & Postma, D. S. Predicting who will have asthma at school age among preschool children. *J. Allergy Clin. Immunol.* **130**, 325–331 (2012).
35. Pescatore, A. M., Dogaru, C. M., Duembgen, L., Silverman, M., Gaillard, E. A. & Spycher, B. D. *et al.* A simple asthma prediction tool for preschool children with wheeze or cough. *J. Allergy Clin. Immunol.* **133**, 111–118 (2014).
36. Laumbach, R. J. & Kipen, H. M. Respiratory health effects of air pollution: update on biomass smoke and traffic pollution. *J. Allergy Clin. Immunol.* **129**, 3–11 (2012).
37. Dick, S., Doust, E., Cowie, H., Ayres, J. G. & Turner, S. Associations between environmental exposures and asthma control and exacerbations in young children: a systematic review. *BMJ Open.* **4**, e003827 (2014).
38. Farber, H. J., Groner, J., Walley, S. & Nelson, K. Protecting children from tobacco, nicotine, and tobacco smoke. *Pediatrics* **136**, e1439–e1467 (2015).
39. Chilmonczyk, B. A., Salmun, L. M., Megathlin, K. N., Neveu, L. M., Palomaki, G. E. & Knight, G. J. *et al.* Association between exposure to environmental tobacco smoke and exacerbations of asthma in children. *N. Engl. J. Med.* **328**, 1665–1669 (1993).
40. Moore, F. *Literature review: second-hand smoke prevention*, (NHS Health Scotland, 2009).
41. Matt, G. E., Quintana, P. J., Hovell, M. F., Bernert, J. T., Song, S. & Novianti, N. *et al.* Households contaminated by environmental tobacco smoke: sources of infant exposures. *Tob. Control* **13**, 29–37 (2004).
42. Kanchnongkittiphon, W., Gaffin, J. M. & Phipatanakul, W. The indoor environment and inner-city childhood asthma. *Asian Pac. J. Allergy Immunol.* **32**, 103–110 (2014).
43. Kanchnongkittiphon, W., Mendell, M. J., Gaffin, J. M., Wang, G. & Phipatanakul, W. Indoor environmental exposures and exacerbation of asthma: an update to the 2000 review by the institute of medicine. *Environ. Health Perspect.* **123**, 6–20 (2015).
44. Weinmayr, G., Gehring, U., Genuneit, J., Büchele, G., Kleiner, A. & Siebers, R. *et al.* Dampness and moulds in relation to respiratory and allergic symptoms in children: results from Phase Two of the International Study of Asthma and Allergies in Childhood (ISAAC Phase Two). *Clin. Exp. Allergy* **43**, 762–774 (2013).
45. Vicendese, D., Dharmage, S. C., Tang, M. L., Olenko, A., Allen, K. J. & Abramson, M. J. *et al.* Bedroom air quality and vacuuming frequency are associated with repeat child asthma hospital admissions. *J. Asthma* **52**, 727–731 (2015).
46. Yeatts, K., Shy, C., Sotir, M., Music, S. & Herget, C. Health consequences for children with undiagnosed asthma-like symptoms. *Arch. Pediatr. Adolesc. Med.* **157**, 540–544 (2003).
47. Oostenbrink, R., Jansingh-Piepers, E. M., Raat, H., Nuijsink, M., Landgraf, J. M. & Essink-Bot, M. L. *et al.* Health-related quality of life of pre-school children with wheezing illness. *Pediatr. Pulmonol.* **41**, 993–1000 (2006).
48. Farber, H. J., Knowles, S. B., Brown, N. L., Caine, L., Luna, V. & Qian, Y. *et al.* Secondhand tobacco smoke in children with asthma: sources of and parental perceptions about exposure in children and parental readiness to change. *Chest* **133**, 1367–1374 (2008).
49. Kegler, M. C., Escoffery, C., Groff, A., Butler, S. & Foreman, A. A qualitative study of how families decide to adopt household smoking restrictions. *Fam. Community Health* **30**, 328–341 (2007).
50. Thomas, E., Wickramasinghe, K., Mendis, S., Roberts, N. & Foster, C. Improved stove interventions to reduce household air pollution in low and middle income countries: a descriptive systematic review. *BMC Public Health* **15**, 650 (2015).
51. Rhodes, E. L., Dreibelbis, R., Klasen, E., Naithani, N., Baliddawa, J. & Menya, D. *et al.* Behavioral attitudes and preferences in cooking practices with traditional openfire stoves in Peru, Nepal, and Kenya: implications for improved cookstove interventions. *Int. J. Environ. Res. Public Health* **11**, 10310–10326 (2014).



This work is licensed under a Creative Commons Attribution 4.0 International License. The images or other third party material in this article are included in the article's Creative Commons license, unless indicated otherwise in the credit line; if the material is not included under the Creative Commons license, users will need to obtain permission from the license holder to reproduce the material. To view a copy of this license, visit <http://creativecommons.org/licenses/by/4.0/>

© The Author(s) 2017



RESEARCH ARTICLE

Open Access

The “child size medicines” concept: policy provisions in Uganda

Xavier Nsabagasani^{1*}, Jasper Ogwal-Okeng^{2†}, Anthony Mbonye^{3†}, Freddie Ssengooba^{4†}, Rebecca Nantanda^{1†}, Herbert Muyinda^{1†} and Ebba Holme Hansen^{5†}

Abstract

Background: In 2007, the World Health Organization (WHO) launched the ‘make medicines child size’ (MMCS) campaign by urging countries to prioritize procurement of medicines with appropriate strengths for children’s age and weight and, in child-friendly formulations of rectal and flexible oral solid formulations. This study examined policy provisions for MMCS recommendations in Uganda.

Methods: This was an in-depth case study of the Ugandan health policy documents to assess provisions for MMCS recommendations in respect to oral and rectal medicine formulations for malaria, pneumonia and diarrhea, the major causes of morbidity and mortality among children in Uganda- diseases that were also emphasized in the MMCS campaign. Asthma and epilepsy were included as conditions that require long term care. Schistosomiasis was included as a neglected tropical disease. Content analysis was used to assess evidence of policy provisions for the MMCS recommendations.

Results: For most medicines for the selected diseases, appropriate strength for children’s age and weight was addressed especially in the EMHSLU 2012. However, policy documents neither referred to ‘child size medicines’ concept nor provided for flexible oral solid dosage formulations like dispersible tablets, pellets and granules- indicating limited adherence to MMCS recommendations. Some of the medicines recommended in the clinical guidelines as first line treatment for malaria and pneumonia among children were not evidence-based.

Conclusion: The Ugandan health policy documents reflected limited adherence to the MMCS recommendations. This and failure to use evidence based medicines may result into treatment failure and or death. A revision of the current policies and guidelines to better reflect ‘child size’, child appropriate and evidence based medicines for children is recommended.

Keywords: Essential medicines, ‘Child size medicines’, Guidelines, Policy, Uganda

Introduction

The need for appropriate medicines for children has attracted attention worldwide [1-5]. It is argued that appropriate medicine formulations should be the basis for drug therapy for children to ensure efficacy and safety [5,6]. Unsuitable formulations may lead to the child not taking the medicines, or receiving inappropriate doses leading to adverse reactions or ineffective treatment [7], needless to mention death. Many formulations used for children, especially tablets, are inappropriate for dosing,

dispensing and administering [8]. For example, tablets for adults have traditionally been split and given to children, resulting in inaccurate doses in view of the children’s weight, age, physiological and cognitive conditions [9].

The World Health Organization in 2007, launched the ‘make medicines child size’ (MMCS) campaign to ensure that children receive the right medicine in the right dose. The MMCS initiative defined ‘child size medicines’ as those with: appropriate strengths and, child-friendly characteristics such as suppositories, solutions and flexible solid oral dosage formulations [10]. The United Nations (UN) member states were urged to make the procurement and supply of ‘child size medicines’ a priority and also ensure that there are corresponding legislative and

* Correspondence: dianatim2001@yahoo.co.uk

†Equal contributors

¹Child Health and Development Center, College of Health Sciences, Makerere University, Kampala, Uganda

Full list of author information is available at the end of the article



© 2015 Nsabagasani et al.; licensee BioMed Central. This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly credited. The Creative Commons Public Domain Dedication waiver (<http://creativecommons.org/publicdomain/zero/1.0/>) applies to the data made available in this article, unless otherwise stated.

RESEARCH ARTICLE

Open Access

Clinical outcomes of children with acute asthma and pneumonia in Mulago hospital, Uganda: a prospective study

Rebecca Nantanda^{1,3*}, Marianne S Ostergaard², Grace Ndeezi³ and James K Tumwine³

Abstract

Background: Little attention has been paid to asthma in 'under-fives' in Sub-Saharan Africa. In 'under-fives', acute asthma and pneumonia have similar clinical presentation and most children with acute respiratory symptoms are diagnosed with pneumonia according to the WHO criteria. The mortality associated with acute respiratory diseases in Uganda is high but improving, dropping from 24% in 2004 to 11.9% in 2012. We describe the immediate clinical outcomes of children with acute asthma and pneumonia and document the factors associated with prolonged hospitalization and mortality.

Methods: We enrolled 614 children aged 2 to 59 months with acute respiratory symptoms presenting at the emergency paediatric unit of Mulago hospital. Clinical histories, physical examination, blood and radiological tests were done. Children with asthma and bronchiolitis were collectively referred to as 'Asthma syndrome'. Hospitalized children were monitored every 12 hours for a maximum of 7 days. Survival analysis was done to compare outcome of children with asthma and pneumonia. Cox regression analysis was done to determine factors associated with prolonged hospitalization and mortality.

Results: Overall mortality was 3.6%. The highest case fatality was due to *pneumocystis jirovecii* pneumonia (2/4) and pulmonary tuberculosis (2/7). None of the children with asthma syndrome died. Children with 'asthma syndrome' had a significantly shorter hospital stay compared to those with pneumonia ($p < 0.001$). Factors independently associated with mortality included hypoxemia (HR = 10.7, 95% CI 1.4- 81.1) and severe malnutrition (HR = 5.7, 95% CI 2.1- 15.8). Factors independently associated with prolonged hospitalization among children with asthma syndrome included age less than 12 months (RR = 1.2, 95% CI 1.0-1.4), hypoxemia (RR = 1.4, 95% CI 1.2-1.7), and severe malnutrition (RR = 1.5 95% CI 1.3-1.8). Similar factors were associated with long duration of hospital stay among children with pneumonia.

Conclusion: This study identified a sharp decline in acute respiratory mortality compared to the previous studies in Mulago hospital. This may be related to focus on and treatment of asthma in this study, and will be analysed in a later study. Bacterial pneumonia is still associated with high case fatality. Hypoxemia, severe malnutrition, and being an infant were associated with poor prognosis among children with acute asthma and pneumonia and need to be addressed in the management protocols.

Keywords: Asthma, Pneumonia, 'Under-fives', Duration of hospitalization, Mortality

* Correspondence: nantanda@gmail.com

¹Child Health and Development Centre, Makerere University College of Health Sciences, Kampala, Uganda

³Department of Paediatrics and Child Health, Makerere University College of Health Sciences, Kampala, Uganda

Full list of author information is available at the end of the article



RESEARCH ARTICLE

Open Access

Clinical outcomes of children with acute asthma and pneumonia in Mulago hospital, Uganda: a prospective study

Rebecca Nantanda^{1,3*}, Marianne S Ostergaard², Grace Ndeezi³ and James K Tumwine³

Abstract

Background: Little attention has been paid to asthma in 'under-fives' in Sub-Saharan Africa. In 'under-fives', acute asthma and pneumonia have similar clinical presentation and most children with acute respiratory symptoms are diagnosed with pneumonia according to the WHO criteria. The mortality associated with acute respiratory diseases in Uganda is high but improving, dropping from 24% in 2004 to 11.9% in 2012. We describe the immediate clinical outcomes of children with acute asthma and pneumonia and document the factors associated with prolonged hospitalization and mortality.

Methods: We enrolled 614 children aged 2 to 59 months with acute respiratory symptoms presenting at the emergency paediatric unit of Mulago hospital. Clinical histories, physical examination, blood and radiological tests were done. Children with asthma and bronchiolitis were collectively referred to as 'Asthma syndrome'. Hospitalized children were monitored every 12 hours for a maximum of 7 days. Survival analysis was done to compare outcome of children with asthma and pneumonia. Cox regression analysis was done to determine factors associated with prolonged hospitalization and mortality.

Results: Overall mortality was 3.6%. The highest case fatality was due to *pneumocystis jirovecii* pneumonia (2/4) and pulmonary tuberculosis (2/7). None of the children with asthma syndrome died. Children with 'asthma syndrome' had a significantly shorter hospital stay compared to those with pneumonia ($p < 0.001$). Factors independently associated with mortality included hypoxemia (HR = 10.7, 95% CI 1.4- 81.1) and severe malnutrition (HR = 5.7, 95% CI 2.1- 15.8). Factors independently associated with prolonged hospitalization among children with asthma syndrome included age less than 12 months (RR = 1.2, 95% CI 1.0-1.4), hypoxemia (RR = 1.4, 95% CI 1.2-1.7), and severe malnutrition (RR = 1.5 95% CI 1.3-1.8). Similar factors were associated with long duration of hospital stay among children with pneumonia.

Conclusion: This study identified a sharp decline in acute respiratory mortality compared to the previous studies in Mulago hospital. This may be related to focus on and treatment of asthma in this study, and will be analysed in a later study. Bacterial pneumonia is still associated with high case fatality. Hypoxemia, severe malnutrition, and being an infant were associated with poor prognosis among children with acute asthma and pneumonia and need to be addressed in the management protocols.

Keywords: Asthma, Pneumonia, 'Under-fives', Duration of hospitalization, Mortality

* Correspondence: nantanda@gmail.com

¹Child Health and Development Centre, Makerere University College of Health Sciences, Kampala, Uganda

³Department of Paediatrics and Child Health, Makerere University College of Health Sciences, Kampala, Uganda

Full list of author information is available at the end of the article



Article

Lung Function of Children at Three Sites of Varying Ambient Air Pollution Levels in Uganda: A Cross Sectional Comparative Study

Bruce J. Kirenga^{1,2,3,*}, Rebecca Nantanda², Corina de Jong³, Levicatus Mugenyi², Qingyu Meng⁴, Gilbert Aniku⁵, Sian Williams⁶, Hellen Aanyu-Tukamuheba⁵, Moses Kanya¹, Stephan Schwander⁴, Thys van der Molen³ and Vahid Mohsenin⁷

¹ Department of Medicine, Makerere University, Kampala, Uganda; mkanya@infocom.co.ug

² Makerere University Lung Institute, Kampala, Uganda; rnantanda@gmail.com (R.N.);

lmugenyi005@gmail.com (L.M.)

³ GRIAC-Primary Care, Department of General Practice and Elderly Care, University of Groningen, University Medical Center Groningen, EB79 Groningen, The Netherlands; c.de.jong02@umcg.nl (C.d.J.); thys.v.molen@gsk.com (T.v.d.M.)

⁴ Departments of Urban-Global Public Health and Environmental and Occupational Health, School of Public Health, Rutgers University, The State University of New Jersey, Piscataway, NJ 08854, USA; Qingyu.Meng@dtsc.ca.gov (Q.M.); schwansk@sph.rutgers.edu (S.S.)

⁵ Department of Paediatrics and Child Health, Makerere University College of Health Sciences, Kampala, Uganda; gilbert.aniku@gmail.com (G.A.); hellen.aanyut@gmail.com (H.A.-T.)

⁶ International Primary Care Respiratory Group, Aberdeen AB32 9AE, UK; sian.health@gmail.com

⁷ Department of Medicine, Yale University School of Medicine, New Haven, CT 06520, USA; vahid.mohsenin@yale.edu

* Correspondence: brucekirenga@yahoo.co.uk; Tel.: +256-782-404-431

Received: 16 October 2018; Accepted: 15 November 2018; Published: 26 November 2018



Abstract: Air pollution is a major cause of sub-optimal lung function and lung diseases in childhood and adulthood. In this study we compared the lung function (measured by spirometry) of 537 Ugandan children, mean age 11.1 years in sites with high (Kampala and Jinja) and low (Buwenge) ambient air pollution levels, based on the concentrations of particulate matter smaller than 2.5 micrometres in diameter (PM_{2.5}). Factors associated with lung function were explored in a multiple linear regression model. PM_{2.5} level in Kampala, Jinja and Buwenge were 177.5 µg/m³, 96.3 µg/m³ and 31.4 µg/m³ respectively ($p = 0.0000$). Respectively mean forced vital capacity as % of predicted (FVC%), forced expiratory volume in one second as % of predicted (FEV₁%) and forced expiratory flow 25–75% as % of predicted (FEF_{25–75}%) of children in high ambient air pollution sites (Kampala and Jinja) vs. those in the low ambient air pollution site (Buwenge subcounty) were: FVC% (101.4%, vs. 104.0%, $p = 0.043$), FEV₁% (93.9% vs. 98.0, $p = 0.001$) and FEF_{25–75}% (87.8 vs. 94.0, $p = 0.002$). The proportions of children whose %predicted parameters were less than 80% predicted (abnormal) were higher among children living in high ambient air pollution than those living in lower low ambient air pollutions areas with the exception of FVC%; high vs. low: FEV₁ < 80%, %predicted (12.0% vs. 5.3%, $p = 0.021$) and FEF_{25–75} < 80%, %predicted (37.7% vs. 29.3%, $p = 0.052$) Factors associated with lung function were (coefficient, p -value): FVC% urban residence (−3.87, $p = 0.004$), current cough (−2.65, $p = 0.048$), underweight (−6.62, $p = 0.000$), and overweight (11.15, $p = 0.000$); FEV₁% underweight (−6.54, $p = 0.000$) and FEF_{25–75}% urban residence (−8.67, $p = 0.030$) and exposure to biomass smoke (−7.48, $p = 0.027$). Children in study sites with high ambient air pollution had lower lung function than those in sites with low ambient air pollution. Urban residence, underweight, exposure to biomass smoke and cough were associated with lower lung function.

Keywords: urbanization; lung function; air pollution; children; Uganda

RESEARCH

Open Access



Availability and affordability of medicines and diagnostic tests recommended for management of asthma and chronic obstructive pulmonary disease in sub-Saharan Africa: a systematic review

Davis Kibirige^{1,2*}, Richard E. Sanya², Rebecca Nantanda^{3,4}, William Worodria⁵ and Bruce Kirenga^{3,5}

Abstract

Background: Early accurate diagnosis and sustainable availability of affordable medicines and diagnostic tests is fundamental in optimal management of asthma and chronic obstructive pulmonary disease (COPD). We systematically reviewed original research articles about availability and affordability of medicines and diagnostic tests recommended for management of asthma and COPD in sub-Saharan Africa (SSA).

Methods: We searched PubMed, Scopus and African Journal Online for original research articles conducted in SSA between 2000 and March 2018 containing information about availability and affordability of any recommended medicine and diagnostic test for asthma and COPD.

Results: The search yielded 9 eligible research articles. Availability of short-acting beta agonists (SABA), inhaled corticosteroids (ICS) and short acting anti-muscarinic agents (SAMA) ranged between 19.9–100%, 0–45.5% and 0–14.3% respectively. Combination of ICS-long acting beta agonists (LABA) were available in 0–14.3% of facilities surveyed. There was absence of inhaled long acting anti-muscarinic agents (LAMA) and LAMA/LABA combinations. Spirometry and peak expiratory flow devices were available in 24.4–29.4% and 6.7–53.6% respectively. Affordability of SABA and ICS varied greatly, ranging from < 2 to 107 days' wages while ICS–LABA combinations, SAMA and oral theophylline plus leukotriene receptor antagonists cost 6.4–17.1, 13.7 and 6.9 days' wages respectively.

Conclusion: Availability and affordability of medicines and diagnostics recommended for the management of asthma and COPD is a big challenge in SSA. Research about this subject in this region is still limited. More robustly performed studies are required to further understand the magnitude of inequity in access to these medicines and diagnostic tests in SSA and also to formulate simple pragmatic solutions to address this challenge.

Keywords: Availability, Affordability, Essential medicines, Diagnostic tests, Asthma, Chronic obstructive pulmonary disorders, COPD, Sub-Saharan Africa, Africa

*Correspondence: kibirigedavis@gmail.com

¹ Department of Medicine, Uganda Martyrs Hospital Lubaga, P.O.BOX 14130, Kampala, Uganda

Full list of author information is available at the end of the article



© The Author(s) 2019. This article is distributed under the terms of the Creative Commons Attribution 4.0 International License (<http://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license, and indicate if changes were made. The Creative Commons Public Domain Dedication waiver (<http://creativecommons.org/publicdomain/zero/1.0/>) applies to the data made available in this article, unless otherwise stated.

RESEARCH ARTICLE

Open Access



Prevalence and factors associated with asthma among adolescents and adults in Uganda: a general population based survey

Bruce J. Kirenga^{1*}, Corina de Jong^{2,3}, Wincenslaus Katagira⁴, Samuel Kasozi⁴, Levicatus Mugenyi^{5,6}, Marike Boezen⁷, Thys van der Molen^{2,8} and Moses R. Kamya¹

Abstract

Background: Recent large-scale population data on the prevalence of asthma and its risk factors are lacking in Uganda. This survey was conducted to address this data gap.

Methods: A general population based survey was conducted among people ≥ 12 years. A questionnaire was used to collect participants socio-demographics, respiratory symptoms, medical history, and known asthma risk factors. Participants who reported wheeze in the past 12 months, a physician diagnosis of asthma or current use of asthma medications were classified as having asthma. Asthmatics who were ≥ 35 years underwent spirometry to determine how many had fixed airflow obstruction (i.e. post bronchodilator forced expiratory volume in one second/forced vital capacity (FEV₁/FVC) ratio < lower limit of normal (LLN). Descriptive statistics were used to summarize participants' characteristics. Prevalence of asthma was calculated as a proportion of asthmatics over total survey population. To obtain factors independently associated with asthma, a random-effects model was fitted to the data.

Results: Of the 3416 participants surveyed, 61.2% (2088) were female, median age was 30 years (IQR, 20–45) and 323 were found to have asthma. Sixteen people with asthma ≥ 35 years had fixed airflow obstruction. The prevalence of asthma was 11.0% (95% CI:8.9–13.2; males 10.3%, females 11.4%, urban 13.0% and rural 8.9%). Significantly more people with asthma smoked than non-asthmatics: 14.2% vs. 6.3%, $p < 0.001$, were exposed to biomass smoke: 28.0% vs. 20.0%, $p < 0.001$, had family history of asthma: 26.9% vs. 9.4%, $p < 0.001$, had history of TB: 3.1% vs. 1.30%, $p = 0.01$, and had hypertension: 17.9% vs. 12.0%, $p = 0.003$. In multivariate analysis smoking, (adjusted odds ratio (AOR), 3.26 (1.96–5.41, $p < 0.001$) family history of asthma, AOR 2.90 (98–4.22 $p < 0.001$), nasal congestion, AOR 3.56 (2.51–5.06, $p < 0.001$), biomass smoke exposure, AOR 2.04 (1.29–3.21, $p = 0.002$) and urban residence, AOR 2.01 (1.23–3.27, $p = 0.005$) were independently associated with asthma.

Conclusion: Asthma is common in Uganda and is associated with smoking, biomass smoke exposure, urbanization, and allergic diseases. Health care systems should be strengthened to provide asthma care. Measures to reduce exposure to the identified associated factors are needed.

Keywords: Asthma, Prevalence, Uganda

* Correspondence: brucekirenga@yahoo.co.uk

¹Makerere University Lung Institute & Division of Pulmonary Medicine, Department of Medicine, Makerere University College of Health Sciences, Kampala, Uganda

Full list of author information is available at the end of the article



© The Author(s). 2019 **Open Access** This article is distributed under the terms of the Creative Commons Attribution 4.0 International License (<http://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license, and indicate if changes were made. The Creative Commons Public Domain Dedication waiver (<http://creativecommons.org/publicdomain/zero/1.0/>) applies to the data made available in this article, unless otherwise stated.

RESEARCH ARTICLE

Diagnostic performance of blood inflammatory markers for tuberculosis screening in people living with HIV

Katherine Farr^{1,2}, Resmi Ravindran³, Luke Strnad^{4,5}, Emily Chang^{1,6}, Lelia H. Chaisson⁷, Christina Yoon¹, William Worodria^{8,9}, Alfred Andama^{10,11}, Irene Ayakaka^{11,12}, Priscilla Bbosa Nalwanga¹¹, Patrick Byanyima¹¹, Nelson Kalema¹³, Sylvia Kaswabuli¹¹, Wincelaus Katagira¹¹, Kyomugisha Denise Aman¹¹, Emmanuel Musisi^{11,14}, Nuwagaba Wallen Tumwine¹¹, Ingvar Sanyu¹¹, Robert Ssebunya¹¹, J. Lucian Davis^{15,16}, Laurence Huang^{1,6}, Imran H. Khan³*, Adithya Cattamanchi^{1,2}



1 Division of Pulmonary and Critical Care Medicine, University of California San Francisco and Zuckerberg San Francisco General Hospital, San Francisco, California, United States of America, **2** Curry International Tuberculosis Center, University of California San Francisco, San Francisco, California, United States of America, **3** Department of Pathology and Laboratory Medicine, University of California at Davis, Sacramento, California, United States of America, **4** Division of Infectious Diseases, Oregon Health & Science University, Portland, Oregon, United States of America, **5** Epidemiology Programs, Oregon Health & Science University-Portland State University School of Public Health, Portland, Oregon, United States of America, **6** Division of HIV, Infectious Diseases, and Global Medicine, Department of Medicine, University of California San Francisco and Zuckerberg San Francisco General Hospital, San Francisco, California, United States of America, **7** Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland, United States of America, **8** Department of Medicine, School of Medicine, Makerere University, Kampala, Uganda, **9** Division of Respiratory Medicine, Department of Medicine, Mulago Hospital, Kampala, Uganda, **10** Department of Medicine, Mulago Hospital, Makerere University, Kampala, Uganda, **11** Infectious Diseases Research Collaboration, Kampala, Uganda, **12** International Multidisciplinary Programme to Address Lung Health and TB in Africa, Liverpool School of Tropical Medicine, Liverpool, United Kingdom, **13** Infectious Diseases Institute, Department of Research, Makerere College Health Sciences, Makerere University, Kampala, Uganda, **14** Department of Biochemistry, College of Natural Sciences, Makerere University, Kampala, Uganda, **15** Department of Epidemiology of Microbial Diseases, Yale School of Public Health, New Haven, Connecticut, United States of America, **16** Section of Pulmonary, Critical Care, and Sleep Medicine, Yale School of Medicine, New Haven, Connecticut, United States of America

OPEN ACCESS

Citation: Farr K, Ravindran R, Strnad L, Chang E, Chaisson LH, Yoon C, et al. (2018) Diagnostic performance of blood inflammatory markers for tuberculosis screening in people living with HIV. *PLoS ONE* 13(10): e0206119. <https://doi.org/10.1371/journal.pone.0206119>

Editor: Juraj Ivanyi, King's College London, UNITED KINGDOM

Received: December 6, 2017

Accepted: October 8, 2018

Published: October 23, 2018

Copyright: © 2018 Farr et al. This is an open access article distributed under the terms of the [Creative Commons Attribution License](https://creativecommons.org/licenses/by/4.0/), which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Data Availability Statement: Data for this study are freely available from the UCSF MIND Study. Individuals interested in the data may contact the MIND Steering Committee and data will be released after reviewing that the intended use is consistent with study goals and that persons requesting the data have appropriate human subjects research training and approvals, if needed. Dr. Abdul Sessolo (Asessolo@idrc-uganda.org) is the focal point for the MIND Steering Committee.

☯ These authors contributed equally to this work.
* ihkhan@ucdavis.edu

Abstract

Background

Approaches to screening for active tuberculosis (TB) among people living with HIV are inadequate, leading to missed diagnoses and poor implementation of preventive therapy.

Methods

Consecutive HIV-infected adults hospitalized at Mulago Hospital (Kampala, Uganda) between June 2011 and July 2013 with a cough ≥ 2 weeks were enrolled. Patients underwent extensive evaluation for pulmonary TB. Concentrations of 43 cytokines/chemokines were measured at the same time point as C-reactive protein (CRP) in banked plasma samples using commercially-available multiplex kits. Advanced classification algorithms were used to rank cytokines/chemokines for their ability to identify TB, and to model the specificity

Funding: LS was supported by a training grant from the National Institutes of Health (5T32AI007641-12, <https://www.nih.gov/>). LHC was supported by a training grant from the National Institutes of Health (5T32AI102623, <https://www.nih.gov/>). JLD was supported by a grant from the National Institutes of Health (K23AI080147, <https://www.nih.gov/>). Patient enrollment and specimen collection was supported by grants from National Institutes of Health/National Heart, Lung, and Blood Institute to LH (K24HL087713 and R01HL090335, <https://www.nhlbi.nih.gov/>), and this sub-study was supported by a Pilot Award to AC from the National Institutes of Health/National Institute of Allergy and Infectious Diseases-funded UCSF Center for AIDS Research (P30-AI027763, <http://cfar.ucsf.edu/>).

Competing interests: The authors have declared that no competing interests exist.

of the top-ranked cytokines/chemokines individually and in combination with sensitivity constrained to $\geq 90\%$ as recommended for TB screening.

Results

The median plasma level of 5 biomarkers (IL-6, INF- γ , MIG, CRP, IL-18) was significantly different between patients with and without TB. With sensitivity constrained to 90%, all had low specificity with IL-6 showing the highest specificity (44%; 95% CI 37.4–49.5). Biomarker panels were found to be more valuable than any biomarker alone. A panel combining IFN- γ and IL-6 had the highest specificity (50%; 95% CI 46.7–53.3). Sensitivity remained high (>85%) for all panels among sputum smear-negative TB patients.

Conclusions

Direct measurement of unstimulated plasma cytokines/chemokines in peripheral blood is a promising approach to TB screening. Cytokine/chemokine panels retained high sensitivity for smear-negative TB and achieved improved specificity compared to individual cytokines/chemokines. These markers should be further evaluated in outpatient settings where most TB screening occurs and where other illnesses associated with systematic inflammation are less common.

RESEARCH

Open Access



The impact of HIV on the prevalence of asthma in Uganda: a general population survey

Bruce J. Kirenga^{1*}, Levicatus Mugenyi², Corina de Jong^{3,4}, J. Lucian Davis⁵, Wincelous Katigira⁶, Thys van der Molen^{3,4}, Moses R. Kanya⁷ and Marike Boezen⁸

Abstract

Background: HIV and asthma are highly prevalent diseases in Africa but few studies have assessed the impact of HIV on asthma prevalence in high HIV burden settings. The objective of this analysis was to compare the prevalence of asthma among persons living with HIV (PLHIV) and those without HIV participating in the Uganda National Asthma Survey (UNAS).

Methods: UNAS was a population-based survey of persons aged ≥ 12 years. Asthma was diagnosed based on either self-reported current wheeze concurrently or within the prior 12 months; physician diagnosis; or use of asthma medication. HIV was defined based on confidential self-report. We used Poisson regression with robust standard errors to estimate asthma prevalence and the prevalence ratio (PR) for HIV and asthma.

Results: Of 3416 participants, 2067 (60.5%) knew their HIV status and 103 (5.0%) were PLHIV. Asthma prevalence was 15.5% among PLHIV and 9.1% among those without HIV, PR 1.72, (95%CI 1.07–2.75, $p = 0.025$). HIV modified the association of asthma with the following factors, PLHIV vs. not PLHIV: tobacco smoking (12% vs. 8%, $p < 0.001$), biomass use (11% vs. 7%, $p < 0.001$), allergy (17% vs. 11%, $p < 0.001$), family history of asthma (17% vs. 11%, $p < 0.001$), and prior TB treatment (15% vs. 10%, $p < 0.001$).

Conclusion: In Uganda the prevalence of asthma is higher in PLHIV than in those without HIV, and HIV interacts synergistically with other known asthma risk factors. Additional studies should explore the mechanisms underlying these associations. Clinicians should consider asthma as a possible diagnosis in PLHIV presenting with respiratory symptoms.

Keywords: Asthma, HIV, Prevalence, Uganda

Background

Human Immunodeficiency Virus (HIV) and asthma are both highly prevalent diseases globally [1, 2]. An estimated 334 million people have asthma and 36.7 million people have HIV [1, 2]. Both diseases disproportionately affect Africa and other low and middle income countries (LMICs) [2, 3]. The weighted mean prevalence of asthma in Africa is 7.0% in the rural areas (2.5–11.5) and 9.6%

(3.9–15.2) in urban areas. The prevalence of asthma and HIV in Uganda is 10% and 6.2% respectively [4, 5].

Epidemiological studies have found increased prevalence of asthma among HIV infected persons [6–13]. However, the number of studies is small and most are either clinical or hospital based and most of them have been conducted in high income low HIV burden settings. Examples of available studies include a study that included 248 HIV infected and 236 HIV uninfected males. This study found that the prevalence of wheezing was 54.4%, vs. 21.2%, $p < 0.001$ [9]. In another study among 223 HIV patients in the USA, the prevalence of doctor diagnosed asthma was 20.6 compared to 8.2% in the general population [13]. In a study comparing 14,005

* Correspondence: brucekirenga@yahoo.co.uk

¹Makerere University Lung Institute & Division of Pulmonary Medicine, Department of Medicine, Makerere University College of Health Sciences, Kampala, Uganda

Full list of author information is available at the end of the article



© The Author(s). 2018 **Open Access** This article is distributed under the terms of the Creative Commons Attribution 4.0 International License (<http://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license, and indicate if changes were made. The Creative Commons Public Domain Dedication waiver (<http://creativecommons.org/publicdomain/zero/1.0/>) applies to the data made available in this article, unless otherwise stated.

Does pulmonary rehabilitation alter patients' experiences of living with chronic respiratory disease? A qualitative study

This article was published in the following Dove Press journal:
International Journal of COPD

Rupert Jones¹
Herbert Muyinda²
Grace Nyakoojo²
Bruce Kirenga²
Wincelaus Katagira²
Jillian Pooler¹

¹Clinical Trials and Population Studies, Plymouth University Peninsula Schools of Medicine and Dentistry, Plymouth, UK; ²Makerere University Lung Institute, College of Health Science, Makerere University, Kampala, Uganda

Purpose: Chronic respiratory disease (CRD) including COPD carries high and rising morbidity and mortality in Africa, but there are few available treatments. Pulmonary rehabilitation (PR) is a non-pharmacological treatment with proven benefits in improving symptoms and exercise capacity, which has not been tested in Africa. We aimed to evaluate the lived experience of people with CRD, including physical and psychosocial impacts, and how these are addressed by PR.

Patients and methods: A team of respiratory specialists, nurses, and physiotherapists implemented PR to meet the clinical and cultural setting. PR consisted of a 6-week, twice-weekly program of exercise and self-management education. Forty-two patients were recruited. Qualitative data were collected through interviews with patients at baseline and six weeks post-completion, focus group discussions, ethnographic observations, and brief interviews.

Results: Before and after PR, a total of 44 semi-structured interviews, 3 focus group discussions, and 4 ethnographic observations with brief interviews were conducted. Participants reported profound problems with respiratory symptoms, functional impairment, wide-reaching economic and psychological impacts, and social isolation. Patients who were debilitated by their condition before PR reported that PR addressed all their major concerns. It was reported that breathlessness, pain, immobility, weight loss, and other CRD-related symptoms were reduced, and social and intimate relationships were improved. Local materials were used to improvise the exercises, enabling some to be maintained at home. Recommendations for future PR programs included patient information to take home as a reminder of the exercises, and to show their families, and the support of a community health worker to help maintenance of exercises at home.

Conclusion: PR has the potential to restore the physical, mental, and social functioning in patients with CRD, whereas medication has much more narrow effects. PR offers a major new option for treatment of a neglected group of patients.

Keywords: exercise therapy, non-pharmacological treatment, self-management, stigma

Correspondence: Rupert Jones
Plymouth University Peninsula Schools
of Medicine & Dentistry, NI4, ITTC
Building, Plymouth Science Park,
Derriford, Plymouth PL6 8BX, UK
Tel +44 1752 764403
Email rupert.jones@plymouth.ac.uk

submit your manuscript | www.dovepress.com
Dovepress
   
<http://dx.doi.org/10.2147/COPD.S165623>

International Journal of COPD 2018:13 2375–2385

2375



© 2018 Jones et al. This work is published by Dove Medical Press Limited, and licensed under a Creative Commons Attribution License. The full terms of the License are available at <http://creativecommons.org/licenses/by/4.0/>. The license permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.



HHS Public Access

Author manuscript

S Afr Respir J. Author manuscript; available in PMC 2018 January 22.

Published in final edited form as:
S Afr Respir J. 2017 ; 23(4): 106–112.

Predictors and short-term outcomes of recurrent pulmonary tuberculosis, Uganda: a cohort study

Nelson Kalema^{1,2}, Christina Lindan³, Dave Glidden³, Samuel D. Yoo^{1,4}, Achilles Katamba², Andama Alfred¹, Wincelous Katagira¹, Patrick Byanyima¹, Emmanuel Musisi¹, Sylvia Kaswabuli¹, Sanyu Ingvar¹, Josephine Zawedde¹, Christina Yoon^{1,5}, Irene Ayakaka¹, J. Lucian Davis^{7,8}, Laurence Huang^{1,5,6}, William Worodria^{1,2}, and Adithya Cattamanchi^{1,3,5}

¹Infectious Disease Research Collaboration, Kampala, Uganda ²Department of Medicine, Mulago Hospital, Makerere University, Kampala, Uganda ³Department of Epidemiology and Biostatistics and Global Health Sciences, University of California San Francisco, San Francisco, CA ⁴Department of Internal Medicine, Jimma University, Jimma, Ethiopia ⁵Division of Pulmonary and Critical Care Medicine, Zuckerberg San Francisco General Hospital, University of California San Francisco, San Francisco, CA ⁶HIV, Infectious Diseases, and Global Medicine Division, Zuckerberg San Francisco General Hospital, University of California San Francisco, San Francisco, CA ⁷Yale School of Public Health, New Haven, CT ⁸Pulmonary, Critical Care, and Sleep Medicine Section, Yale School of Medicine, New Haven, CT

Abstract

Introduction—Recurrent tuberculosis (TB) occurring >2 years after completing treatment for a prior TB episode is most often due to reinfection with a new strain of *M. tuberculosis*.

Objectives—We determined the prevalence and outcome of late recurrent TB among hospitalized patients in Kampala, Uganda.

Methods—We conducted a retrospective analysis of patients admitted to Mulago Hospital who had cough of >2 weeks' duration and completed TB treatment >2 years prior to admission. All patients had mycobacterial culture performed on two sputum specimens and vital status ascertained 2-months post-enrollment. We performed logistic regression and Cox proportional hazards modelling to identify predictors of recurrent TB and survival, respectively.

Results—Among 234 patients, 84 (36%) had recurrent TB. Independent predictors included younger age (aOR=0.64, 95% CI=0.42-0.97, p=0.04), chest pain >2 weeks (aOR=3.32, 95%

Corresponding author: Nelson Kalema, MBChB, M. Med, Clinical Research Scholar, MAS Program UCSF, C/O Makerere University College of Health Sciences, Implementation Science Program, P. O Box 7072, Kampala Uganda, kalemanelson@gmail.com, Phone: +256782313109.

Author Contributions

Conceived and designed the experiments: NK WW AK AI JLD SDY LH AC.

Performed the experiments: SK EM PB AA.

Analyzed the data: NK DG AC JLD LH.

Contributed reagents/materials/analysis tools: LH AC JLD

Wrote the paper: NK DG KL SDY LH JLD WW AC.

Enrolled and cared for the patients included in this study: KW, NK, ZJ, SI.

Conflicts of interest: None

CI=1.38-8.02, $p=0.007$), severe weight loss ≥ 5 kilograms (aOR=4.88, 95% CI=1.66-14.29, $p=0.004$) and presence of ≥ 1 WHO danger sign of severe illness (aOR=3.55, 95% CI=1.36-9.29, $p=0.01$). Two-month mortality was 17.8% (95% CI=10.5-29.2%), and was higher among patients who were not initiated on TB treatment (aHR=16.67, 95% CI=1.18-200, $p=0.04$), those who were HIV-positive and not on antiretroviral treatment (aHR=16.99, 95% CI=1.17-246.47, $p=0.04$) and those with a history of smoking (aHR=1.20, 95% CI=1.03-1.40, $p=0.02$).

Conclusion—The high prevalence of late recurrent TB likely reflects high levels of TB transmission in Kampala. Increased use of empiric TB treatment and early ART treatment initiation if HIV-positive should be considered in patients with a prior history of TB, particularly if they are young, with weight loss ≥ 5 kgs, chest pain >2 weeks or ≥ 1 WHO danger sign of severe illness.

Keywords

Recurrent TB; survival; treatment; Africa; Uganda

INTRODUCTION

Recurrence of tuberculosis (TB) following completion of treatment is an important but understudied problem in high-burden countries.^[1-3] Recurrent TB can result from relapse of the original *M. tuberculosis* strain or from reinfection with a new strain.^[4] Relapse usually occurs because of inadequate treatment whereas reinfection reflects high rates of ongoing TB transmission in at risk populations.^[3, 5] Data show that the risk of recurrent TB due to reinfection is higher among HIV-positive than HIV-negative persons.^[6] Thus, assessing the burden of recurrent TB and its causes in high TB-HIV incidence settings can help TB control programs determine whether limited additional resources should be focused on enhanced treatment monitoring and adherence to reduce relapse, or on TB case finding and treatment to interrupt transmission.

Molecular genotyping is the gold standard for assessing whether recurrent TB is due to relapse versus reinfection. Unfortunately, however, only a few studies in high TB burden settings have described the burden of recurrent pulmonary TB using molecular genotyping. These studies indicate that the length of time between completion of treatment and recurrence is indicative of whether recurrent disease is a result of re-infection or relapse. A study in southern India found that among patients who developed recurrent pulmonary TB one to two years following completion of treatment, the recurrence was due to relapse in 91% of HIV-uninfected patients, and was due to reinfection in 88% of HIV-infected patients.^[7] In Uganda, relapse was determined to be the cause of recurrence in 80 of 98 (82%) patients presenting with another episode of TB one to two years following treatment of prior disease.^[8] In contrast, among patients who developed recurrent TB > 2 years after treatment completion, molecular genotyping studies have shown reinfection to be the predominant cause.^[9] In Cape Town, South Africa, a study in a predominantly HIV-uninfected population found that reinfection accounted for 12/16 (75%) cases of recurrent TB.^[10] Similarly, another study from South Africa found that reinfection accounted for 23/66 (34%) recurrent TB episodes among patients who completed treatment within the prior two years but for 43/66 (65%) of recurrent TB episodes among patients who had completed treatment > 2

A pre–post intervention study of pulmonary rehabilitation for adults with post-tuberculosis lung disease in Uganda

This article was published in the following Dove Press journal:
International Journal of COPD

Rupert Jones¹
Bruce J Kirenga²
Wincelsa Katagira²
Sally J Singh³
Jill Pooler⁴
Alphonse Okwera²
Richard Kasiita⁵
Doyo G Enki⁶
Siobhan Creanor⁶
Andy Barton⁴

¹Population Studies and Clinical Trials, Peninsula Schools of Medicine and Dentistry, Plymouth University, Plymouth, UK; ²Population Studies and Clinical Trials, Makerere Lung Institute, Makerere University College of Health Sciences, Mulago Hospital, Kampala, Uganda; ³Cardio-Respiratory Directorate, University Hospitals of Leicester NHS Trust, Leicester; ⁴Population Studies and Clinical Trials, Peninsula Schools of Medicine and Dentistry, Plymouth University, Plymouth, UK; ⁵Department of Physiotherapy, Mulago Hospital, Kampala, Uganda; ⁶Medical Statistics, Peninsula Schools of Medicine and Dentistry, Plymouth University, Plymouth, UK

Correspondence: Rupert Jones
Peninsula Schools of Medicine and Dentistry, Plymouth University, N14, ITTC Building, Plymouth PL6 8BX, UK
Tel +44 1752 76 4258
Email rupert.jones@plymouth.ac.uk

Setting: The study was conducted at Mulago Hospital, Kampala, Uganda.

Objective: As chronic respiratory disease (CRD) is a huge, growing burden in Africa, with few available treatments, we aimed to design and evaluate a culturally appropriate pulmonary rehabilitation (PR) program in Uganda for people with post-tuberculosis lung disorder (p-TBLD).

Design: In a pre–post intervention study, a 6-week, twice-weekly PR program was designed for people with p-TBLD. Outcome measures included recruitment, retention, the Clinical COPD Questionnaire (CCQ), tests of exercise capacity, and biometrics. Given this was a developmental study, no formal statistical significance testing was undertaken.

Results: In all, 34 participants started PR and 29 (85%) completed all data collection. The mean age of the 29 participants was 45 years, and 52% were female. The mean (95% confidence interval) CCQ score at baseline was 1.8 (1.5, 2.0), at the end of PR was 1.0 (0.8, 1.2), and at 6 weeks after the end of PR was 0.8 (0.7, 1.0). The Incremental Shuttle Walking Test (ISWT) was 299 m (268.5, 329.4) at baseline, 377 (339.6, 413.8) at the end of PR, and 374 (334.2, 413.5) at 6 weeks after the end of PR. Improvements were seen in measures of chest pain; 13/29 (45%) participants reported chest pain at baseline but only 7/29 (24%) at the end of PR, and in those with persistent pain, the mean pain scores decreased. Mild hemoptysis was reported in 4/29 (17%) participants at baseline and in 2/29 (7%) at the end of PR.

Conclusion: PR for people with p-TBLD in Uganda was feasible and associated with clinically important improvements in quality of life, exercise capacity, and respiratory outcomes. PR uses local resources, requires little investment, and offers a new, sustainable therapy for p-TBLD in resource-limited settings. With the rising global burden of CRD, further studies are needed to assess the value of PR in p-TBLD and other prevalent forms of CRD.

Keywords: tuberculosis, exercise training, self-management, nonpharmacological intervention

Introduction

The World Health Organization considers the control and management of noncommunicable diseases (NCDs) a top priority – NCDs cause more deaths than all other causes combined and are projected to increase from 38 million worldwide in 2012 to 52 million by 2030.¹ Lung diseases are preeminent, and COPD is now the third leading cause of death globally and the ninth highest cause of disability.¹ The burgeoning prevalence of chronic respiratory disease (CRD) is fueled by an aging population, the combination of respiratory infections such as tuberculosis (TB) with human immunodeficiency virus (HIV), tobacco smoking, household air pollution, and nutritional impairment.^{2–4}



HHS Public Access

Author manuscript

J Acquir Immune Defic Syndr. Author manuscript; available in PMC 2017 July 01.

Published in final edited form as:

J Acquir Immune Defic Syndr. 2016 July 1; 72(3): 297–303. doi:10.1097/QAI.0000000000000970.

Empiric TB treatment of severely ill patients with HIV and presumed pulmonary TB improves survival

Wincelaus Katagira, MBChB, MMED¹, Nicholas D. Walter, MD, MS^{1,4}, Saskia den Boon, Msc, PhD¹, Nelson Kalema, MBChB, MMED¹, Irene Ayakaka, MBChB, MPH¹, Eric Vittinghoff, PhD, MPH⁵, William Worodria, MBChB, MMED, PhD^{1,3}, Adithya Cattamanchi, MD, MAS^{1,2}, Laurence Huang, MD^{2,6}, and J. Lucian Davis, MD, MAS^{7,8}

¹ Makerere University – University of California, San Francisco (MU-UCSF) Research Collaboration, Kampala, Uganda ² Division of Pulmonary and Critical Care Medicine, San Francisco General Hospital, University of California San Francisco, San Francisco, CA, USA ³ College of Health Sciences, Makerere University, Kampala, Uganda ⁴ Division of Pulmonary Sciences and Critical Care Medicine, University of Colorado, Denver, Aurora, CO, USA ⁵ Department of Biostatistics and Epidemiology, University of California San Francisco, San Francisco, CA, USA ⁶ Division of HIV/AIDS, San Francisco General Hospital, University of California San Francisco, San Francisco, CA, USA ⁷ Department of Epidemiology of Microbial Diseases, School of Public Health, Yale University, New Haven, CT, USA ⁸ Pulmonary, Critical Care, and Sleep Medicine Section, School of Medicine, Yale University, New Haven, CT, USA

Abstract

Rationale—In 2007, WHO issued emergency recommendations on empiric treatment of sputum acid-fast bacillus (AFB) smear-negative patients with possible tuberculosis (TB) in HIV-prevalent areas, and called for operational research to evaluate their effectiveness. We sought to determine if early, empiric TB treatment of possible TB patients with abnormal chest radiography or severe illness as suggested by the 2007 WHO guidelines is associated with improved survival.

Methods—We prospectively enrolled consecutive HIV-seropositive inpatients at Mulago Hospital in Kampala, Uganda, from 2007 to 2011 with cough ≥ 2 weeks. We retrospectively examined the effect of empiric TB treatment before discharge on eight-week survival among those with and without a WHO-defined “danger sign,” including fever $>39^{\circ}\text{C}$, tachycardia >120 beats-per-minute, or tachypnea >30 breaths-per-minute. We modeled the interaction between empiric TB treatment and danger signs and their combined effect on eight-week survival and adjusted for relevant covariates.

Results—Among 631 sputum smear-negative patients, 322(51%) had danger signs. Cumulative eight-week survival of patients with danger signs was significantly higher with empiric TB

Corresponding Author: J. Lucian Davis, MD, MAS, Epidemiology of Microbial Diseases, Yale School of Public Health Pulmonary, Critical Care, and Sleep Medicine, Yale School of Medicine, P.O. Box 208034, 60 College Street, LEPH 442, New Haven, CT 06520, Office 203.785.2912, Fax 203.785.4782, Lucian.Davis@yale.edu.

Conflicts of Interest: None declared

The data in this manuscript was presented at the ATS 2012 as a poster presentation.

treatment(80%) than without(64%, $p<0.001$). After adjusting for duration of cough and concurrent hypoxemia, patients with danger signs who received empiric TB treatment had a 44% reduction in eight-week mortality(Risk Ratio 0.54, 95%CI 0.32-0.91, $p=0.020$).

Conclusions—Empiric TB treatment of HIV-seropositive, smear-negative, presumed pulmonary TB patients with one or more danger signs is associated with improved eight-week survival. Enhanced implementation of the 2007 WHO empiric-treatment recommendations should be encouraged whenever and wherever rapid and highly sensitive diagnostic tests for TB are unavailable.

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

RESEARCH ARTICLE

A Clinical Predictor Score for 30-Day Mortality among HIV-Infected Adults Hospitalized with Pneumonia in Uganda

Catherine A. Koss^{1*}, Leah G. Jarlsberg², Saskia den Boon³, Adithya Cattamanchi^{2,3}, J. Lucian Davis^{2,3}, William Worodria^{3,4,5}, Irene Ayakaka³, Ingvar Sanyu³, Laurence Huang^{2,3,6}, International HIV-associated Opportunistic Pneumonias (IHOP) Study[†]

1 Department of Medicine, University of California, San Francisco, San Francisco, California, United States of America, **2** Division of Pulmonary and Critical Care Medicine, Department of Medicine, San Francisco General Hospital, University of California San Francisco, San Francisco, California, United States of America, **3** Makerere University–University of California San Francisco Research Collaboration, Kampala, Uganda, **4** Department of Medicine, Makerere University College of Health Sciences, Kampala, Uganda, **5** Department of Medicine, Mulago National Referral and Teaching Hospital, Kampala, Uganda, **6** HIV/AIDS Division, Department of Medicine, San Francisco General Hospital, University of California San Francisco, San Francisco, California, United States of America

[†] Membership of the IHOP Study Team is provided in the Acknowledgements.
* catherine.koss@ucsf.edu



OPEN ACCESS

Citation: Koss CA, Jarlsberg LG, den Boon S, Cattamanchi A, Davis JL, Worodria W, et al. (2015) A Clinical Predictor Score for 30-Day Mortality among HIV-Infected Adults Hospitalized with Pneumonia in Uganda. *PLoS ONE* 10(5): e0126591. doi:10.1371/journal.pone.0126591

Academic Editor: Julian W. Tang, Alberta Provincial Laboratory for Public Health/ University of Alberta, CANADA

Received: November 11, 2014

Accepted: April 5, 2015

Published: May 11, 2015

Copyright: © 2015 Koss et al. This is an open access article distributed under the terms of the [Creative Commons Attribution License](https://creativecommons.org/licenses/by/4.0/), which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Data Availability Statement: All relevant data are within the paper.

Funding: This research was supported by grants from the National Institutes of Health (K24 087713, L.H. and R01 090335, L.H.) and the Mount Zion Global Health Project Fund (C.A.K.). The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Competing Interests: I have read the journal's policy and the authors of this manuscript have the following

Abstract

Background

Pneumonia is a major cause of mortality among HIV-infected patients. Pneumonia severity scores are promising tools to assist clinicians in predicting patients' 30-day mortality, but existing scores were developed in populations infected with neither HIV nor tuberculosis (TB) and include laboratory data that may not be available in resource-limited settings. The objective of this study was to develop a score to predict mortality in HIV-infected adults with pneumonia in TB-endemic, resource-limited settings.

Methods

We conducted a secondary analysis of data from a prospective study enrolling HIV-infected adults with cough ≥ 2 weeks and < 6 months and clinically suspected pneumonia admitted to Mulago Hospital in Kampala, Uganda from September 2008 to March 2011. Patients provided two sputum specimens for mycobacteria, and those with Ziehl-Neelsen sputum smears that were negative for mycobacteria underwent bronchoscopy with inspection for Kaposi sarcoma and testing for mycobacteria and fungi, including *Pneumocystis jirovecii*. A multivariable best subsets regression model was developed, and one point was assigned to each variable in the model to develop a clinical predictor score for 30-day mortality.

competing interests: L.H. has received a one-time consultation fee from MiniVax and has other grants from the National Institutes of Health. Neither of these are conflicts of interest for this study. The authors have declared that no other competing interests exist. This does not alter the authors' adherence to PLOS ONE policies on sharing data and materials.

Results

Overall, 835 patients were studied (mean age 34 years, 53.4% female, 30-day mortality 18.2%). A four-point clinical predictor score was identified and included heart rate >120 beats/minute, respiratory rate >30 breaths/minute, oxygen saturation <90%, and CD4 cell count <50 cells/mm³. Patients' 30-day mortality, stratified by score, was: score 0 or 1, 12.6%, score 2 or 3, 23.4%, score 4, 53.9%. For each 1 point change in clinical predictor score, the odds of 30-day mortality increased by 65% (OR 1.65, 95% CI 1.39-1.96, $p < 0.001$).

Conclusions

A simple, four-point scoring system can stratify patients by levels of risk for mortality. Rapid identification of higher risk patients combined with provision of timely and appropriate treatment may improve clinical outcomes. This predictor score should be validated in other resource-limited settings.

Rates of asthma exacerbations and mortality and associated factors in Uganda: a 2-year prospective cohort study

Bruce J Kirenga,^{1,2} Corina de Jong,^{3,4} Levicatus Mugenyi,^{1,5} Wincelous Katagira,² Abdallah Muhofa,² Moses R Kanya,¹ H Marike Boezen,⁶ Thys van der Molen^{3,4}

► Additional material is published online only. To view please visit the journal online (<http://dx.doi.org/10.1136/thoraxjnl-2017-211157>).

¹Makerere University Lung Institute, Makerere University College of Health Sciences, Kampala, Uganda

²Department of Medicine, Makerere University College of Health Sciences, Kampala, Uganda

³GRIAC-Primary Care, Department of General Practice and Elderly Care, University of Groningen, University Medical Center Groningen (UMCG), Groningen, The Netherlands

⁴Groningen Research Institute for Asthma and COPD (GRIAC), University of Groningen, University Medical Center Groningen (UMCG), Groningen, The Netherlands

⁵Center for Statistics, Interuniversity Institute for Biostatistics, and Statistical Bioinformatics, Hasselt University (UHasselt), Groningen, The Netherlands

⁶Department of Epidemiology, University of Groningen, Groningen, The Netherlands

Correspondence to
Dr Bruce J Kirenga, Makerere University Lung Institute, Mulago Hospital, Kampala 7072, Uganda;
brucekirenga@yahoo.co.uk

Received 16 October 2017
Revised 6 April 2018
Accepted 16 April 2018
Published Online First
11 May 2018



► <http://dx.doi.org/10.1136/thoraxjnl-2018-211718>



To cite: Kirenga BJ, de Jong C, Mugenyi L, *et al.* *Thorax* 2018;**73**:983–985.

ABSTRACT

Data on asthma treatment outcomes in Africa are limited. 449 patients with asthma (age 5–93 years) in Uganda were followed up for 2 years to determine rates of exacerbations and mortality and associated factors. During follow-up the median number of exacerbations per patient was 1 (IQR 0–5) and 17 patients died (3.7%, 27.3 deaths per 1000 person years). Considering only the first year of follow-up, 59.6% of the patients experienced at least one exacerbation, 32.4% experienced three or more exacerbations. A multivariable model showed that the likelihood of experiencing at least one exacerbation in the first year of follow-up was lower with better baseline asthma control (higher asthma control test (ACT) score), with OR 0.87 (95% CI: 0.82 to 0.93, P=0.000), and was higher with more exacerbations in the year prior to enrolment (OR for log number of exacerbations 1.28, 95% CI: 1.04 to 1.57, P=0.018). Better asthma control (OR 0.93, 95% CI: 0.88 to 0.99, P=0.021) and number of baseline exacerbations (OR 1.35, 95% CI: 1.11 to 1.66, P=0.005) were also the only factors that were independently associated with experiencing three or more exacerbations during the first year of follow-up. The only factor found to be associated with all-cause mortality was FEV₁, with higher recent FEV₁ associated with lower all-cause mortality (OR 0.30, 95% CI: 0.14 to 0.65; P=0.002). Rates of asthma exacerbations and mortality are high in Uganda and are associated with poor asthma control. Health systems should be strengthened to care for asthma patients.

RESEARCH ARTICLE

Accuracy of different Xpert MTB/Rif implementation strategies in programmatic settings at the regional referral hospitals in Uganda: Evidence for country wide roll out

Winters Muttamba^{1,2✉*}, Willy Ssengooba^{2✉}, Rogers Sekibira¹, Bruce Kirenga¹, Achilles Katamba³, Moses Joloba²

1 Makerere University Lung Institute, College of Health Sciences, Makerere University, Kampala, Uganda, **2** Department of Medical Microbiology, College of Health Sciences, Makerere University, Kampala, Uganda, **3** School of Medicine, College of Health Sciences, Makerere University, Kampala, Uganda

✉ These authors contributed equally to this work.

* muttamba@gmail.com



OPEN ACCESS

Citation: Muttamba W, Ssengooba W, Sekibira R, Kirenga B, Katamba A, Joloba M (2018) Accuracy of different Xpert MTB/Rif implementation strategies in programmatic settings at the regional referral hospitals in Uganda: Evidence for country wide roll out. PLoS ONE 13(3): e0194741. <https://doi.org/10.1371/journal.pone.0194741>

Editor: Seyed Ehtesham Hasnain, Indian Institute of Technology Delhi, INDIA

Received: December 18, 2017

Accepted: March 8, 2018

Published: March 22, 2018

Copyright: © 2018 Muttamba et al. This is an open access article distributed under the terms of the [Creative Commons Attribution License](https://creativecommons.org/licenses/by/4.0/), which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Data Availability Statement: All relevant data are within the paper and its Supporting Information files.

Funding: This study was funded by the World Bank under the East Africa Public Health Laboratory Networking Project (EAPHLNP). The funder had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Abstract

Background

Xpert MTB/RIF assay is a highly sensitive test for TB diagnosis, but still costly to most low-income countries. Several implementation strategies instead of frontline have been suggested; however with scarce data. We assessed accuracy of different Xpert MTB/RIF implementation strategies to inform national roll-out.

Methods

This was a cross-sectional study of 1,924 adult presumptive TB patients in five regional referral hospitals of Uganda. Two sputum samples were collected, one for fluorescent microscopy (FM) and Xpert MTB/RIF examined at the study site laboratories. The second sample was sent to the Uganda Supra National TB reference laboratory for culture using both Lowenstein Jensen (LJ) and liquid culture (MGIT). We compared the sensitivities of FM, Xpert MTB/RIF and the incremental sensitivity of Xpert MTB/RIF among patients negative on FM using LJ and/or MGIT as a reference standard.

Results

A total 1924 patients were enrolled of which 1596 (83%) patients had at least one laboratory result and 1083 respondents had a complete set of all the laboratory results. A total of 328 (30%) were TB positive on LJ and/or MGIT culture. The sensitivity of FM was n (%; 95% confidence interval) 246 (63.5%; 57.9–68.7) overall compared to 52 (55.4%; 44.1–66.3) among HIV positive individuals, while the sensitivity of Xpert MTB/RIF was 300 (76.2%; 71.7–80.7) and 69 (71.6%; 60.5–81.1) overall and among HIV positive individuals respectively. Overall incremental sensitivity of Xpert MTB/RIF was 60 (36.5%; 27.7–46.0) and 20 (41.7%; 25.5–59.2) among HIV positive individuals.

Competing interests: The authors have declared that no competing interests exist.

Conclusion

Xpert MTB/RIF has a higher sensitivity than FM both in general population and HIV positive population. Xpert MTB/RIF offers a significant increase in terms of diagnostic sensitivity even when it is deployed selectively i.e. among smear negative presumptive TB patients. Our results support frontline use of Xpert MTB/RIF assay in high HIV/TB prevalent countries. In settings with limited access, mechanisms to refer smear negative sputum samples to Xpert MTB/RIF hubs are recommended.

RESEARCH ARTICLE

Open Access



Access to affordable medicines and diagnostic tests for asthma and COPD in sub Saharan Africa: the Ugandan perspective

Davis Kibirige^{1,2*}, Leaticia Kampiire³, David Atuhe⁴, Raymond Mwebaze⁵, Wincelous Katagira⁶, Winters Muttamba⁶, Rebecca Nantanda^{6,7}, William Worodria⁸ and Bruce Kirenga^{6,8}

Abstract

Background: Equitable access to affordable medicines and diagnostic tests is an integral component of optimal clinical care of patients with asthma and chronic obstructive pulmonary disease (COPD). In Uganda, we lack contemporary data about the availability, cost and affordability of medicines and diagnostic tests essential in asthma and COPD management.

Methods: Data on the availability, cost and affordability of 17 medicines and 2 diagnostic tests essential in asthma and COPD management were collected from 22 public hospitals, 23 private and 85 private pharmacies. The percentage of the available medicines and diagnostic tests, the median retail price of the lowest priced generic brand and affordability in terms of the number of days' wages it would cost the least paid public servant were analysed.

Results: The availability of inhaled short acting beta agonists (SABA), oral leukotriene receptor antagonists (LTRA), inhaled LABA-ICS combinations and inhaled corticosteroids (ICS) in all the study sites was 75%, 60.8%, 46.9% and 45.4% respectively. None of the study sites had inhaled long acting anti muscarinic agents (LAMA) and inhaled long acting beta agonist (LABA)-LAMA combinations. Spirometry and peak flow-metry as diagnostic tests were available in 24.4% and 6.7% of the study sites respectively. Affordability ranged from 2.2 days' wages for inhaled salbutamol to 17.1 days' wages for formoterol/budesonide inhalers and 27.8 days' wages for spirometry.

Conclusion: Medicines and diagnostic tests essential in asthma and COPD care are not widely available in Uganda and remain largely unaffordable. Strategies to improve access to affordable asthma and COPD medicines and diagnostic tests should be implemented in Uganda.

Keywords: Access, Medicines, Diagnostic tests, Asthma, COPD, Sub Saharan Africa, Uganda

Background

Globally, chronic respiratory diseases pose a major public health threat. Notably, the burden of asthma and chronic obstructive pulmonary disease (COPD) is steadily increasing in both developed and developing countries. According to recent World Health Organisation (WHO) estimates, about 235 million people have asthma

and 65 million people have moderate to severe COPD. High rates of mortality due to both conditions have been documented in low-and middle income countries (LMIC). In 2012, > three million people died of COPD, which accounted for about 6% of the all the deaths globally. An estimated 90% of these deaths occurred in LMIC [1].

In Uganda, a similar growing trend of mortality related to asthma and COPD has been described. A descriptive retrospective study conducted at an urban national referral hospital reported the burden of asthma and COPD of 70.6% and 21.6% respectively in 558 patients admitted to

* Correspondence: kibirigedavis@gmail.com

¹Department of Medicine, Uganda Martyrs Hospital Lubaga, P.O. BOX 7146, Kampala, Uganda

²Medical unit, GlaxoSmithKline Pharmaceutical Kenya Limited, Kampala, Uganda

Full list of author information is available at the end of the article



© The Author(s). 2017 **Open Access** This article is distributed under the terms of the Creative Commons Attribution 4.0 International License (<http://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license, and indicate if changes were made. The Creative Commons Public Domain Dedication waiver (<http://creativecommons.org/publicdomain/zero/1.0/>) applies to the data made available in this article, unless otherwise stated.

Association between Household Air Pollution Exposure and Chronic Obstructive Pulmonary Disease Outcomes in 13 Low- and Middle-Income Country Settings

Trishul Siddharthan^{1,2*}, Matthew R. Grigsby^{1,2*}, Dina Goodman^{1,2}, Muhammad Chowdhury³, Adolfo Rubinstein⁴, Vilma Irazola⁴, Laura Gutierrez⁴, J. Jaime Miranda^{5,6}, Antonio Bernabe-Ortiz^{5,6}, Dewan Alam⁷, Bruce Kirenga⁸, Rupert Jones⁹, Frederick van Gemert¹⁰, Robert A. Wise¹, and William Checkley^{1,2}

¹Division of Pulmonary and Critical Care and ²Center for Global Non-Communicable Diseases, School of Medicine, Johns Hopkins University, Baltimore, Maryland; ³Centre for Control of Chronic Diseases, icddr, Dhaka, Bangladesh; ⁴Institute for Clinical Effectiveness and Health Policy, Buenos Aires, Argentina; ⁵CRONICAS Centre of Excellence in Chronic Diseases and ⁶Departamento de Medicina, Facultad de Medicina, Universidad Peruana Cayetano Heredia, Lima, Peru; ⁷School of Kinesiology and Health Science, Faculty of Health, York University, Toronto, Ontario, Canada; ⁸Makerere Lung Institute, Makerere University, Kampala, Uganda; ⁹Plymouth University, Plymouth, United Kingdom; and ¹⁰University of Groningen, University Medical Centre Groningen, Harlingen, the Netherlands

ORCID IDs: 0000-0001-9914-1839 (T.S.); 0000-0001-7311-8673 (M.R.G.); 0000-0003-1106-8812 (W.C.).

Abstract

Rationale: Forty percent of households worldwide burn biomass fuels for energy, which may be the most important contributor to household air pollution.

Objectives: To examine the association between household air pollution exposure and chronic obstructive pulmonary disease (COPD) outcomes in 13 resource-poor settings.

Methods: We analyzed data from 12,396 adult participants living in 13 resource-poor, population-based settings. Household air pollution exposure was defined as using biomass materials as the primary fuel source in the home. We used multivariable regressions to assess the relationship between household air pollution exposure and COPD outcomes, evaluated for interactions, and conducted sensitivity analyses to test the robustness of our findings.

Measurements and Main Results: Average age was 54.9 years (44.2–59.6 yr across settings), 48.5% were women (38.3–54.5%), prevalence of household air pollution exposure was 38% (0.5–99.6%), and 8.8% (1.7–15.5%) had COPD. Participants with household air pollution exposure were 41% more likely to have COPD (adjusted odds ratio, 1.41; 95% confidence interval, 1.18–1.68) than those without the exposure, and 13.5% (6.4–20.6%) of COPD prevalence may be caused by household air pollution exposure, compared with 12.4% caused by cigarette smoking. The association between household air pollution exposure and COPD was stronger in women (1.70; 1.24–2.32) than in men (1.21; 0.92–1.58).

Conclusions: Household air pollution exposure was associated with a higher prevalence of COPD, particularly among women, and it is likely a leading population-attributable risk factor for COPD in resource-poor settings.

Keywords: COPD; air pollution, indoor/adverse effects; biomass

(Received in original form September 13, 2017; accepted in final form January 11, 2018)

*Joint first authorship.

This study was sponsored and funded by the NHLBI, a division of the NIH in the United States, under contract numbers HHSN268200900033C and HHSN26820900032C. In addition, W.C. is supported under UM1HL134590. T.S. is supported by a National Research Service Award through the National Institute of Environmental Health Sciences of the NIH (1F32ES028577). A.R. was supported by the NIH Office of the Director, Fogarty International Centre, and NHLBI through the International Clinical Research Fellows Program at Vanderbilt University (R24 TW007988) and the American Relief and Recovery Act.

Author Contributions: Conception and design, T.S., M.R.G., and W.C. Analysis and interpretation, T.S., M.R.G., D.G., and W.C. Drafting the manuscript for important intellectual content, T.S., M.R.G., D.G., L.G., J.J.M., A.B.-O., D.A., B.K., R.J., M.C., V.I., A.R., F.v.G., R.A.W., and W.C.

Correspondence and requests for reprints should be addressed to William Checkley, M.D., Ph.D., Division of Pulmonary and Critical Care, School of Medicine, Johns Hopkins University, 1830 Monument Street, Room 555, Baltimore, MD 21205. E-mail: wcheckl1@jhmi.edu.

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

Am J Respir Crit Care Med Vol 197, Iss 5, pp 611–620, Mar 1, 2018

Copyright © 2018 by the American Thoracic Society

Originally Published in Press as DOI: 10.1164/rccm.201709-1861OC on January 11, 2018

Internet address: www.atsjournals.org

RESEARCH

Open Access



Availability and affordability of medicines and diagnostic tests recommended for management of asthma and chronic obstructive pulmonary disease in sub-Saharan Africa: a systematic review

Davis Kibirige^{1,2*}, Richard E. Sanya², Rebecca Nantanda^{3,4}, William Worodria⁵ and Bruce Kirenga^{3,5}

Abstract

Background: Early accurate diagnosis and sustainable availability of affordable medicines and diagnostic tests is fundamental in optimal management of asthma and chronic obstructive pulmonary disease (COPD). We systematically reviewed original research articles about availability and affordability of medicines and diagnostic tests recommended for management of asthma and COPD in sub-Saharan Africa (SSA).

Methods: We searched PubMed, Scopus and African Journal Online for original research articles conducted in SSA between 2000 and March 2018 containing information about availability and affordability of any recommended medicine and diagnostic test for asthma and COPD.

Results: The search yielded 9 eligible research articles. Availability of short-acting beta agonists (SABA), inhaled corticosteroids (ICS) and short acting anti-muscarinic agents (SAMA) ranged between 19.9–100%, 0–45.5% and 0–14.3% respectively. Combination of ICS-long acting beta agonists (LABA) were available in 0–14.3% of facilities surveyed. There was absence of inhaled long acting anti-muscarinic agents (LAMA) and LAMA/LABA combinations. Spirometry and peak expiratory flow devices were available in 24.4–29.4% and 6.7–53.6% respectively. Affordability of SABA and ICS varied greatly, ranging from <2 to 107 days' wages while ICS–LABA combinations, SAMA and oral theophylline plus leukotriene receptor antagonists cost 6.4–17.1, 13.7 and 6.9 days' wages respectively.

Conclusion: Availability and affordability of medicines and diagnostics recommended for the management of asthma and COPD is a big challenge in SSA. Research about this subject in this region is still limited. More robustly performed studies are required to further understand the magnitude of inequity in access to these medicines and diagnostic tests in SSA and also to formulate simple pragmatic solutions to address this challenge.

Keywords: Availability, Affordability, Essential medicines, Diagnostic tests, Asthma, Chronic obstructive pulmonary disorders, COPD, Sub-Saharan Africa, Africa

*Correspondence: kibirigedavis@gmail.com

¹ Department of Medicine, Uganda Martyrs Hospital Lubaga, P.O.BOX 14130, Kampala, Uganda

Full list of author information is available at the end of the article



© The Author(s) 2019. This article is distributed under the terms of the Creative Commons Attribution 4.0 International License (<http://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license, and indicate if changes were made. The Creative Commons Public Domain Dedication waiver (<http://creativecommons.org/publicdomain/zero/1.0/>) applies to the data made available in this article, unless otherwise stated.

RESEARCH ARTICLE

Open Access



Prevalence and factors associated with asthma among adolescents and adults in Uganda: a general population based survey

Bruce J. Kirenga^{1*}, Corina de Jong^{2,3}, Wincenslaus Katagira⁴, Samuel Kasozi⁴, Levicatus Mugenyi^{5,6}, Marike Boezen⁷, Thys van der Molen^{2,8} and Moses R. Kamya¹

Abstract

Background: Recent large-scale population data on the prevalence of asthma and its risk factors are lacking in Uganda. This survey was conducted to address this data gap.

Methods: A general population based survey was conducted among people ≥ 12 years. A questionnaire was used to collect participants socio-demographics, respiratory symptoms, medical history, and known asthma risk factors. Participants who reported wheeze in the past 12 months, a physician diagnosis of asthma or current use of asthma medications were classified as having asthma. Asthmatics who were ≥ 35 years underwent spirometry to determine how many had fixed airflow obstruction (i.e. post bronchodilator forced expiratory volume in one second/forced vital capacity (FEV₁/FVC) ratio < lower limit of normal (LLN). Descriptive statistics were used to summarize participants' characteristics. Prevalence of asthma was calculated as a proportion of asthmatics over total survey population. To obtain factors independently associated with asthma, a random-effects model was fitted to the data.

Results: Of the 3416 participants surveyed, 61.2% (2088) were female, median age was 30 years (IQR, 20–45) and 323 were found to have asthma. Sixteen people with asthma ≥ 35 years had fixed airflow obstruction. The prevalence of asthma was 11.0% (95% CI:8.9–13.2; males 10.3%, females 11.4%, urban 13.0% and rural 8.9%). Significantly more people with asthma smoked than non-asthmatics: 14.2% vs. 6.3%, $p < 0.001$, were exposed to biomass smoke: 28.0% vs. 20.0%, $p < 0.001$, had family history of asthma: 26.9% vs. 9.4%, $p < 0.001$, had history of TB: 3.1% vs. 1.30%, $p = 0.01$, and had hypertension: 17.9% vs. 12.0%, $p = 0.003$. In multivariate analysis smoking, (adjusted odds ratio (AOR), 3.26 (1.96–5.41, $p < 0.001$) family history of asthma, AOR 2.90 (98–4.22 $p < 0.001$), nasal congestion, AOR 3.56 (2.51–5.06, $p < 0.001$), biomass smoke exposure, AOR 2.04 (1.29–3.21, $p = 0.002$) and urban residence, AOR 2.01 (1.23–3.27, $p = 0.005$) were independently associated with asthma.

Conclusion: Asthma is common in Uganda and is associated with smoking, biomass smoke exposure, urbanization, and allergic diseases. Health care systems should be strengthened to provide asthma care. Measures to reduce exposure to the identified associated factors are needed.

Keywords: Asthma, Prevalence, Uganda

* Correspondence: brucekirenga@yahoo.co.uk

¹Makerere University Lung Institute & Division of Pulmonary Medicine, Department of Medicine, Makerere University College of Health Sciences, Kampala, Uganda

Full list of author information is available at the end of the article



© The Author(s). 2019 **Open Access** This article is distributed under the terms of the Creative Commons Attribution 4.0 International License (<http://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license, and indicate if changes were made. The Creative Commons Public Domain Dedication waiver (<http://creativecommons.org/publicdomain/zero/1.0/>) applies to the data made available in this article, unless otherwise stated.

Validation of the Saint George's Respiratory Questionnaire in Uganda

Brooks W Morgan,^{1,2} Matthew R Grigsby,^{1,2} Trishul Siddharthan,^{1,2} Robert Kalyesubula,³ Robert A Wise,^{1,2} John R Hurst,⁴ Bruce Kirenga,³ William Checkley^{1,2,5}

To cite: Morgan BW, Grigsby MR, Siddharthan T, et al. Validation of the Saint George's Respiratory Questionnaire in Uganda. *BMJ Open Respi Res* 2018;5:e000276. doi:10.1136/bmjresp-2018-000276

► Additional material is published online only. To view please visit the journal online (<http://dx.doi.org/10.1136/bmjresp-2018-000276>).

Received 10 January 2018

Revised 26 February 2018

Accepted 20 May 2018



¹Division of Pulmonary and Critical Care, School of Medicine, Johns Hopkins University, Baltimore, Maryland, USA

²Center for Global Non-Communicable Disease Research and Training, Johns Hopkins University, Baltimore, Maryland, USA

³College of Health Sciences, Makerere University, Kampala, Uganda

⁴UCL Respiratory, Division of Medicine, University College London, London, UK

⁵Program in Global Disease Epidemiology and Control, Bloomberg School of Public Health, Johns Hopkins University, Baltimore, Maryland, USA

Correspondence to Dr William Checkley; wcheckl1@jhmi.edu

ABSTRACT

Introduction Chronic obstructive pulmonary disease (COPD) will soon be the third leading global cause of death and is increasing rapidly in low/middle-income countries. There is a need for local validation of the Saint George's Respiratory Questionnaire (SGRQ), which can be used to identify those experiencing lifestyle impairment due to their breathing.

Methods The SGRQ was professionally translated into Luganda and reviewed by our field staff and a local pulmonologist. Participants included a COPD-confirmed clinic sample and COPD-positive and negative members of the community who were enrolled in the Lung Function in Nakaseke and Kampala (LiNK) Study. SGRQs were assembled from all participants, while demographic and spirometry data were additionally collected from LiNK participants.

Results In total, 103 questionnaires were included in analysis: 49 with COPD from clinic, 34 community COPD-negative and 20 community COPD-positive. SGRQ score varied by group: 53.5 for clinic, 34.4 for community COPD-positive and 4.1 for community COPD-negative ($p < 0.001$). The cross-validated c statistic for SGRQ total score predicting COPD was 0.87 (95% CI 0.75 to 1.00). SGRQ total score was associated with COPD severity (forced expiratory volume in 1 s per cent of predicted), with an r coefficient of -0.60 ($-0.75, -0.39$). SGRQ score was associated with dyspnoea (OR 1.05/point; 1.01, 1.09) and cough (1.07; 1.03, 1.11).

Conclusion Our Luganda language SGRQ accurately distinguishes between COPD-positive and negative community members in rural Uganda. Scores were correlated with COPD severity and were associated with odds of dyspnoea and cough. We find that it can be successfully used as a respiratory questionnaire for obstructed adults in Uganda.

BACKGROUND

Chronic obstructive pulmonary disease (COPD) accounted for more than 3 million deaths globally in 2015, 5.3% of the world's total.^{1 2} As the global burden of COPD increases, special attention must be paid to low/middle-income countries, which are experiencing a unique combination of risk factors: a growing elderly population, urbanisation and increasing tobacco smoking.^{3 4} Additionally, research investigating potential links between biomass fuel use and COPD is ongoing.^{5 6} It has been estimated that

Key messages

- Our Luganda translation of the Saint George's Respiratory Questionnaire effectively distinguished between those with chronic obstructed pulmonary disease and those without.
- SGRQ total scores were associated with COPD severity and self-reported dyspnoea and cough.

the African region experienced the second largest increase in COPD cases between 1990 and 2010 (+102.1%, behind only Eastern Mediterranean among WHO regions).⁷

Within this population, there is a need for a simple tool to identify those who are experiencing lifestyle impairment due to their breathing as part of a plan to diagnose and treat those experiencing chronic respiratory disease. The Saint George's Respiratory Questionnaire (SGRQ) was designed to evaluate the health impacts of chronic respiratory disease, specifically asthma and COPD.⁸ It is comprised of three sections covering symptoms, physical activities and psychosocial impacts over a set preceding time period and has been shown to correlate to tests of exercise, breathlessness and anxiety/depression.⁸ Thus far, the SGRQ has been validated in over 60 languages. We aimed to translate the 3-month recall version of the SGRQ to Luganda and validate its relationship to airway obstruction in three samples of the Ugandan population: those from the community with no obstruction, those from the community with spirometry-confirmed COPD and those with clinic-confirmed COPD. We further attempted to determine the efficacy of the SGRQ as a screening tool for COPD, indicating those who may require further care.

METHODS

Study setting

The data for this analysis were collected as part of the Lung Function in Nakaseke and Kampala (LiNK) study, for which the general

RESEARCH ARTICLE

Open Access

Predictors and outcomes of mycobacteremia among HIV-infected smear- negative presumptive tuberculosis patients in Uganda

Lydia Nakiyingi^{1,2*}, Willy Ssengooba^{2,3}, Damalie Nakanjako^{1,2}, Derek Armstrong⁴, Molly Holshouser⁴, Bruce J Kirenga², Maunank Shah⁴, Harriet Mayanja-Kizza², Moses L Joloba², Jerrold J Ellner⁵, Susan E Dorman⁴ and Yukari C Manabe^{1,4}

Abstract

Background: Sputum smear microscopy for tuberculosis (TB) diagnosis lacks sensitivity in HIV-infected symptomatic patients and increases the likelihood that mycobacterial infections particularly disseminated TB will be missed; delays in diagnosis can be fatal. Given the duration for MTB growth in blood culture, clinical predictors of MTB bacteremia may improve early diagnosis of mycobacteremia. We describe the predictors and mortality outcome of mycobacteremia among HIV-infected sputum smear-negative presumptive TB patients in a high prevalence HIV/TB setting.

Methods: Between January and November 2011, all consenting HIV-infected adults suspected to have TB (presumptive TB) were consecutively enrolled. Diagnostic assessment included sputum smear microscopy, urine Determine TB lipoarabinomannan (LAM) antigen test, mycobacterial sputum and blood cultures, chest X-ray, and CD4 cell counts in addition to clinical and socio-demographic data. Patients were followed for 12 months post-enrolment.

Results: Of 394 sputum smear-negative participants [female, 63.7%; median age (IQR) 32 (28–39) years], 41/394 (10.4%) had positive mycobacterial blood cultures (mycobacteremia); all isolates were *M. tuberculosis* (MTB). The median CD4 cell count was significantly lower among patients with mycobacteremia when compared with those without (CD4 31 versus 122 cells/ μ L, $p < 0.001$). In a multivariate analysis, male gender [OR 3.4, 95%CI (1.4–7.6), $p = 0.005$], CD4 count < 100 cells/ μ L [OR 3.1, 95% CI (1.1–8.6), $p = 0.030$] and a positive lateral flow urine TB LAM antigen test [OR 15.3, 95%CI (5.7–41.1), $p < 0.001$] were significantly associated with mycobacteremia. At 12 months of follow-up, a trend towards increased mortality was observed in patients that were MTB blood culture positive (35.3%) compared with those that were MTB blood culture negative (23.3%) ($p = 0.065$).

Conclusions: Mycobacteremia occurred in 10% of smear-negative patients and was associated with higher mortality compared with smear-negative patients without mycobacteremia. Advanced HIV disease (CD4 < 100 cells/ mm^3), male gender and positive lateral flow urine TB LAM test predicted mycobacteremia in HIV-infected smear-negative presumptive TB patients in this high prevalence TB/HIV setting.

Keywords: Predictors, Mortality, Mycobacterial infections, Bacteremia, Smear- negative, HIV, LAM, Sub-Saharan Africa

* Correspondence: lydikyingi@yahoo.com

¹Infectious Diseases Institute, Makerere University College of Health Sciences, Kampala, Uganda

²Makerere University College of Health Sciences, Kampala, Uganda

Full list of author information is available at the end of the article



RESEARCH ARTICLE

Open Access

Tuberculosis risk factors among tuberculosis patients in Kampala, Uganda: implications for tuberculosis control

Bruce J Kirenga^{1*}, Willy Ssengooba^{2,6}, Catherine Muwonge³, Lydia Nakiyingi¹, Stephen Kyaligonza³, Samuel Kasozi³, Frank Mugabe³, Martin Boeree⁴, Moses Joloba² and Alphonse Okwera⁵

Abstract

Background: Slow decline in the incidence of tuberculosis (TB) has been observed in most high TB burden countries. Knowledge of the prevalence of different TB risk factors can help expand TB control strategies. However with the exception of Human Immunodeficiency Virus (HIV) the prevalence of the other TB risk factors are poorly studied in Uganda. We aimed to determine the prevalence of different TB risk factors and TB disease presentation among TB patients in Kampala Uganda.

Methods: We assessed 365 adult TB patients and used descriptive statistics to summarize their socio-demographic, clinical, radiological, sputum mycobacteriology and TB risk factors (HIV, diabetes, TB contact, alcohol use, tobacco smoking, poverty and overcrowding) data.

Results: A total of 158 (43.3%) patients were male and the median age was 29 (IQR 28–30). Majority of the patients (89.2%) had pulmonary TB, 86.9% were new and 13.2% were retreatment. Wasting (i.e. body mass index of $<18.5 \text{ kg/m}^2$) was found in 38.5% of the patients and 63% presented with cough. Constitutional symptoms (fever, anorexia, night sweats and weight loss) were reported by 32.1%. Most patients (78.6%) presented with non-cavity lung parenchyma disease (infiltrates, nodules, masses) but 35.2% had cavity disease. Pleural disease was detected in 19.3% of patients. Positive smear microscopy and culture (irrespective of month of treatment) was found in 52.7% and 36.5% of patients respectively. Any drug resistance was detected in 21.1% of patients while multidrug resistance (MDR) TB defined as resistance to rifampicin and isoniazid was detected in 6.3% of patients. All MDR patients were new patients. The prevalence of TB risk factors were as follows: HIV 41.4%, diabetes 5.4%, close contact 11.5%, family history 17.5%, smoking 26.37%, poverty 39.5%, overcrowding 57.3% and alcohol use 50.7%. Overcrowding increased smear positive rate, prevalence ratio 1.22, $p = 0.09$ but all the other studied risk factors did not affect clinical, radiological and mycobacteriological study patient characteristics.

Conclusions: Among TB patients in Kampala, Uganda, there is high prevalence of the known TB risk factors. Targeting reducing their prevalence may lead to better TB control in the country. Tuberculosis, risk factors, Uganda.

Background

Uganda is one of the 22 high tuberculosis (TB) burden countries (HBC) in the world [1]. From an estimated population of 35 million people with national HIV prevalence of 7.3%, 45,546 TB patients were diagnosed in the in the year 2010 of which 54% were

HIV-infected [1-4]. Of these 56% were smear positive, 28% were smear negative and 11% had extra pulmonary TB [1].

Despite implementation of the WHO recommended directly observed therapy short course (DOTS) TB control strategy, the reductions in the incidence of TB have been minimal in HBC [5]. Because of this slow decline of TB incidence there is currently renewed interest in finding new TB control strategies. Focus has been on such strategies as adding to the current arsenal of TB drugs, finding a TB vaccine and designing shorter TB

* Correspondence: brucekirenga@yahoo.co.uk

¹Department of Medicine, Makerere University College of Health Sciences, P.O. Box 7072, Kampala, Uganda

Full list of author information is available at the end of the article

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



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

Summary

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

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

Findings Between April 13, and Aug 14, 2012, we invited 620 people to participate, of whom 588 provided acceptable spirometry and were analysed. Mean age was 45 years (SD 13.7); 297 (51%) were women. 546 (93%) were exposed to biomass smoke. The prevalence of COPD was 16.2% (15.4% in men, 16.8% in women). Prevalence was highest in people aged 30–39 years (17 [38%] of 45 men, 20 [40%] of 50 women). 20 (44%) of 45 men with COPD were current smokers (mean age 40 years, SD 7.5), 11 (24%) were former smokers (mean age 49 years, SD 11.0); four [8%] of 50 women were current smokers (mean age 52 years, SD 18.1), nine (18%) were former smokers (mean age 64 years, SD 16.2). Mean Clinical COPD Questionnaire score was 0.81 (SD 0.78), mean Medical Research Council dyspnoea score was 1.33 (SD 0.65); 28 (30%) of 95 patients had had one or more exacerbations past 12 months. COPD was associated with wheeze (odds ratio 2.17, 95% CI 1.09–4.34; p=0.028) and being a former smoker (1.96, 1.07–3.59; p=0.029).

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

Funding International Primary Care Respiratory Group.

Copyright © van Gemert et al. Open Access article distributed under the terms of CC BY.

Lancet Glob Health 2015;
3: e44–51

See [Comment](#) page e6

University of Groningen,
University Medical Centre
Groningen, Harlingen,
Netherlands (F van Gemert MD,
I Tsiligianni PhD, C de Jong PhD,
Prof T van der Molen PhD);
Makerere University, Mulago
Hospital, Kampala, Uganda
(B Kirenga MMed,
Prof M Kanya PhD,
S Luzige MMed,
P Musinguzi MMed); Leiden
University Medical Centre,
Leiden, Netherlands
(N Chavannes PhD); District
Health Office, Masindi, Uganda
(J Turyagaruka MPH); Peninsula
Medical School, University of
Plymouth, Plymouth, UK
(R Jones MD); and International
Primary Care Respiratory
Group, Edinburgh, UK
(S Williams MSc)

Correspondence to:
Frederik van Gemert,
Department of General Practice,
University of Groningen,
University Medical Centre
Groningen, PO Box 196,
9700 AD Groningen,
Netherlands
frgemert@xs4all.nl

ARTICLE OPEN

Socio-economic factors, gender and smoking as determinants of COPD in a low-income country of sub-Saharan Africa: FRESH AIR Uganda

Frederik van Gemert¹, Niels Chavannes², Bruce Kirenga³, Rupert Jones⁴, Sian Williams⁵, Ioanna Tsiligianni¹, Judith Vonk⁶, Janwillem Kocks¹, Corina de Jong¹ and Thys van der Molen¹

In Uganda, biomass smoke seems to be the largest risk factor for the development of COPD, but socio-economic factors and gender may have a role. Therefore, more in-depth research is needed to understand the risk factors. The aim of this study was to investigate the impact of socio-economic factors and gender differences on the COPD prevalence in Uganda. The population comprised 588 randomly selected participants (> 30 years) who previously completed the FRESH AIR Uganda study. In this *post hoc* analysis, the impact of several socio-economic characteristics, gender and smoking on the prevalence of COPD was assessed using a logistic regression model. The main risk factors associated with COPD were non-Bantu ethnicity (odds ratio (OR) 1.73, 95% confidence interval (CI) 1.06–2.82, $P=0.030$), biomass fuel use for heating (OR 1.76, 95% CI 1.03–3.00, $P=0.038$), former smoker (OR 1.87, 95% CI 0.97–3.60, $P=0.063$) and being unmarried (OR 0.087, 95% CI 0.93–2.95, $P=0.087$). A substantial difference in the prevalence of COPD was seen between the two ethnic groups: non-Bantu 20% and Bantu 12.9%. Additional analysis between these two groups showed significant differences in socio-economic circumstances: non-Bantu people smoked more (57.7% vs 10.7%), lived in tobacco-growing areas (72% vs 14.8%) and were less educated (28.5% vs 12.9% had no education). With regard to gender, men with COPD were unmarried (OR 3.09, 95% CI 1.25–7.61, $P=0.015$) and used more biomass fuel for heating (OR 2.15, 95% CI 1.02–4.54, $P=0.045$), and women with COPD were former smokers (OR 3.35, 95% CI 1.22–9.22, $P=0.019$). Only a few socio-economic factors (i.e., smoking, biomass fuel use for heating, marital status and non-Bantu ethnicity) have been found to be associated with COPD. This applied for gender differences as well (i.e., for men, marital status and biomass fuel for heating, and for women being a former smoker). More research is needed to clarify the complexity of the different risk factors.

npj Primary Care Respiratory Medicine (2016) 26, 16050; doi:10.1038/npjpcrm.2016.50; published online 1 September 2016

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a major health problem in low- and middle-income countries (LMICs).¹ In 2010, COPD was the fourth leading cause of death globally, and it was expected to be the third by 2030.^{2,3} Unfortunately, the prediction has been overtaken by reality: at this moment, COPD is the third leading cause of mortality worldwide.^{4,5} Approximately 90% of COPD deaths occur in LMICs.⁶ Despite these high numbers, COPD is an unknown disease in most of the rural areas of sub-Saharan Africa, both in terms of public awareness and in public health planning. The people are unaware of the potential damage to respiratory and non-respiratory health caused by tobacco and biomass smoke.^{7–9} Biomass fuel use is the third largest contributor to the global burden of disease.¹⁰

Although the development of COPD is multifactorial, biomass smoke is probably the largest risk factor for COPD in LMICs.^{11–13} Worldwide, around 3 billion people, most of them living in LMICs, rely on the use of open fires and burning of biomass fuels (wood, animal dung, crop residues, straw and charcoal) for

cooking and heating in poorly ventilated conditions.¹⁴ Solid fuel burning is incomplete and produces high levels of household air pollution with a range of more than 250 health-damaging pollutants, including carbon monoxide, nitrogen and sulphur oxides, as well as a variety of pollutants, irritants, carcinogens, co-carcinogens and free radicals.^{12,13,15}

Until recently, data on the prevalence of COPD, the risk factors and socio-economic determinants in LMICs were scarce.^{9,16,17} In 2012, a prospective cross-sectional observational study (FRESH AIR Uganda) was conducted to assess the prevalence of COPD and its risk factors in a rural district of Uganda. Among adults above the age of 30 years, the prevalence of spirometry-based COPD was 16.2% (52.6% women), as defined according to the methods used in FRESH AIR Uganda.¹⁸ The prevalence of COPD was remarkably high (39%) among adults aged 30–39 years, both for men (37%) and for women (40%). In addition to tobacco smoking, particularly by young men, >90% of the participants were exposed to smoke caused by biomass fuel use.¹⁸

The FRESH AIR Uganda study was conducted in rural Masindi district (population 350,000) of Uganda, a low-income country

¹Department of General Practice, Groningen Institute for Asthma and COPD (GRIAC), University of Groningen, University Medical Center Groningen, Groningen, The Netherlands;

²Department of Public Health and Primary Care, Leiden University Medical Center, Leiden, The Netherlands; ³Division of Pulmonary Medicine, Makerere University Lung Institute, Mulago Hospital, Makerere University, Kampala, Uganda; ⁴Centre for Clinical Trials and Population Studies, Plymouth University Peninsula School of Medicine and Dentistry, Plymouth, UK; ⁵Executive Office, International Primary Care Respiratory Group, London, UK and ⁶Department of Epidemiology, Groningen Research Institute for Asthma and COPD (GRIAC), University of Groningen, University Medical Center Groningen, Groningen, The Netherlands.

Correspondence: F van Gemert (fvgemert@xs4all.nl)

Received 10 September 2015; revised 6 June 2016; accepted 17 June 2016



Rapid assessment of the demand and supply of tobacco dependence pharmacotherapy in Uganda

B. J. Kirenga,^{1,2} R. Jones,^{2,3} A. Muhofa,² G. Nyakoojo,² S. Williams⁴

<http://dx.doi.org/10.5588/pha.15.0070>

Tobacco dependence pharmacotherapy (TDP) plays a major role in smoking cessation. We conducted a rapid assessment of current smoking, availability of TDP and the willingness to quit and to pay for TDP among 56 patients with tobacco-attributable diseases and 38 pharmacies in Uganda. Of the 56 patients, 63% were current smokers, 77.4% wanted to quit and 37% were willing to pay. Drugs were largely unavailable: nicotine replacement products were available in only seven pharmacies (18%) and bupropion in three (8%); these cost respectively US\$15.7 and US\$17.1 for a 1-month supply. Improving supplies and lowering prices could facilitate access to TDP in Uganda.

Tobacco smoking is one of the leading risk factors for premature mortality. Smoking prevalence in Uganda is 7.9%,¹ but could be higher in some sections of the population, such as among patients with an established tobacco-attributable disease (TAD). It is known that continued smoking negatively impacts the outcome of TADs, while smoking cessation improves outcomes.²⁻⁴ According to the results of the Global Adult Tobacco Survey (GATS), 60% of Ugandan smokers wish to quit, but access to cessation support is extremely limited.¹ Article 14 of the World Health Organization Framework Convention on Tobacco Control (WHO FCTC) states that 'each Party shall develop and disseminate appropriate, comprehensive and integrated guidelines based on scientific evidence and best practices, taking into account national circumstances and priorities, and shall take effective measures to promote cessation of tobacco use and adequate treatment for tobacco dependence'.⁵ For the framework to be implemented, tobacco dependence pharmacotherapy (TDP) should be made available, particularly for those with the most to gain, such as patients with a TAD. The importance of the price of TDPs as a barrier to use in low- and middle-income countries (LMICs) is not well documented.

Current smoking prevalence among patients with TADs is not known in Uganda, nor is the willingness of these patients to quit smoking. Furthermore, the availability of TDP is not known. The aim of this study was to determine the prevalence of current smoking among in-patients with a TAD at a tertiary hospital in Uganda. We also aimed to investigate the supply of TDP through a survey of pharmacies licensed to import medicines into the country and to explore whether the cost of TDP products is a barrier to their use.

ASPECT OF INTEREST

This pilot study looked at both the demand and the supply of TDP. We conducted a cross-sectional survey of 1) medicine importers in the country and 2) patients with TADs admitted to Mulago Hospital, Kampala, Uganda, from 1 June to 13 June 2015.

To qualify for inclusion, patients had to have any of the following TADs: chronic obstructive pulmonary disease (COPD), lung cancer, asthma, cardiovascular disease, stroke or diabetes. A medical officer performed daily rounds for 1 week on the wards to recruit patients. All consenting patients with a TAD were included. Data collected from the patients included smoking status, duration of smoking, products smoked and willingness to quit and to pay for TDP. We did not collect data on number of cigarettes smoked/day due to the heterogeneity of the products smoked.

We used descriptive statistics to summarise the characteristics of the study populations (pharmacies and patients). We calculated the proportions of patients who were current smokers, willing to quit and to pay for drugs. The proportions of pharmacies with each individual medicine available were calculated as well as the mean monthly cost of available drugs.

The survey was approved by the Mulago Hospital Research and Ethics Committee, Kampala, Uganda. All patients provided informed consent to participate.

We assessed 38 pharmacies. Of 66 patients invited to participate, 56 were interviewed; exclusions included 6 patients without a target diagnosis and 4 who were unwilling to participate. Of the 56 patients, 40 (71%) were male; the mean age was 57.5 years (SD 16.4). Twenty-three patients (41%) had been hospitalised with COPD, 8 (14%) with stroke, 8 (14%) with cardiovascular disease, 7 (13%) with asthma, 7 (13%) with diabetes and 3 (5%) with lung cancer. Thirty five patients (63%) were current smokers, 20 (36%) were former smokers and one had never smoked. The median duration of smoking was 31.5 years (interquartile range 12.5–47.5 years).

Of the 35 current smokers, 18 (54.6%) reported smoking cigarettes, 15 (45.4%) reported smoking other forms of tobacco and 2 gave no response. Of the current smokers, 24 (77.4%) desired to quit and 10 (37.0%) were willing to pay for TDP.

Of the 38 pharmacies surveyed, one was public, one was private (not for profit) and 36 were private. The TDPs available are shown in the Table. Only seven (18%) pharmacies had ≥ 1 type of nicotine replacement

AFFILIATIONS

- 1 Division of Pulmonary Medicine, Department of Medicine, Makerere University College of Health Sciences, Kampala, Uganda
- 2 Lung Institute, Makerere University College of Health Sciences, Kampala, Uganda
- 3 Peninsula Medical School, University of Plymouth, Plymouth, UK
- 4 International Primary Care Respiratory Group, Edinburgh, UK

CORRESPONDENCE

Bruce J Kirenga
Division of Pulmonary Medicine
Makerere University College of Health Sciences
P O Box 7072
Kampala 256
Uganda
e-mail: brucekirenga@yahoo.co.uk, brucekirenga@gmail.com

ACKNOWLEDGEMENTS

The authors thank D Senfuka and J Ntaganzirwe for managing the data, and the patients, pharmacists and pharmacy owners for their participation in this survey. This study was funded by Lung Consortium International at Makerere University College of Health Sciences, Mulago Hospital, Kampala, Uganda. Funding was also received from the Global Bridges Project, Mayo Clinic, Rochester, MN, USA. Conflicts of interest: none declared.

KEY WORDS

pharmacotherapy; Uganda; tobacco dependence

Received 2 November 2015
Accepted 12 January 2016
First published online
17 February 2016

PHA 2016; 6(1): 35–37
© 2016 The Union

TABLE Availability and cost of tobacco dependence pharmacotherapy in the surveyed pharmacies

Name of drug	Pharmacies with drug in stock n (%)	Average monthly cost of drug UGX (USD)
Any nicotine replacement product*	7 (18.4)	55 000 (15.7)
Bupropion	3 (7.9)	60 000 (17.1)
Nortriptyline	1 (2.6)	

*Gum, lozenge, spray, patch.
UGX = Uganda shilling; USD = United States dollar.

therapy (NRT), of which three had bupropion only and one had nortriptyline only. The mean cost for a monthly course of NRT was US dollars (US\$15.7). Neither varenicline nor cytisine, two common TDPs, were found in stock in any of the pharmacies surveyed. The only pharmacy that stocked nortriptyline could not provide a cost.

DISCUSSION

This study established that 63% of patients with TADs in Mulago Hospital were current smokers, of whom 77.4% wanted to quit and 37% were willing to pay for TDP. This paper also shows that the inverse care law applies to TDP, with low availability and high prices.

Although Uganda has signed up to the WHO FCTC, smoking cessation services are not yet well developed in Uganda. There are few formal smoking cessation clinics and few staff trained in smoking cessation interventions such as behavioural change or drug therapies, and there is no telephone quit line for smokers. The 63% smoking rate among patients with TADs is comparable to those in other studies, such as the 72% rate cited by Khot et al. and Garcia-Aymerich et al.^{6,7}

The proportion of patients wishing to quit in this study could be higher than the 60% reported in the GATS, due to the effect of the current illness on the patients and the known opportunities for quitting smoking on admission.¹ The cost of about US\$15.7 for a monthly course of NRT is about 18.1% of the Ugandan average monthly income of US\$86.7.⁸ In comparison, a smoker in the United Kingdom (UK) spends an estimated 65 pounds sterling (GBP; US\$92 at the time of publication) on NRT per month, approximately 3.5% of the average estimated monthly income of GBP 1848 (US\$2615) in the UK.^{9,10}

Public Health Action

Le traitement pharmaceutique de la dépendance au tabac (TDP) joue un rôle majeur dans l'arrêt du tabac. Nous avons réalisé une évaluation rapide de la disponibilité du TDP et la volonté d'arrêter et de payer pour le TDP parmi 56 patients atteints de maladies attribuables au tabac et 38 pharmacies en Ouganda. Soixante-trois pourcent des patients étaient des fumeurs actuels, 77,4% souhaitaient

El tratamiento farmacológico de la dependencia al tabaco (TDP) cumple una función primordial en la deshabituación tabáquica. Se llevó a cabo una evaluación breve sobre el tabaquismo actual, la disponibilidad del TDP y la buena disposición al abandono del hábito y a sufragar el costo del tratamiento en 56 pacientes aquejados de enfermedades atribuibles al tabaquismo y 38 farmacias de Uganda. El 63% de los pacientes eran fumadores actuales, 77,4% deseaban

The findings of this paper should be interpreted with caution, as this was a small study in a single centre, involving patients admitted to hospital over a few days, thus rendering it vulnerable to selection bias. As they are from a self-reported questionnaire, the data on items such as willingness to pay for TDP are untested and may not reflect true behaviour in practice.

CONCLUSION

Governments should make TDP available for patients with TADs, and clinicians should be trained in smoking cessation as a component of the response to the rising tide of non-communicable diseases. Larger studies with more diverse populations are required to better understand the supply and demand for TDP as well as qualitative studies to investigate the drivers of TDP unavailability.

References

- World Health Organization. Global Adult Tobacco Survey in Uganda. Fact Sheet 2013. Brazzaville, Republic of Congo: WHO Regional Office for Africa, 2013. <http://www.afro.who.int/en/clusters-a-programmes/hpr/health-risk-factors/tobacco/country-profiles.html> Accessed January 2016.
- Yusuf S, Hawken S, Ounpuu S, et al. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. *Lancet* 2004; 364: 937–952.
- Siroux V, Pin I, Orszyszyn M, Le Moual N, Kauffmann F. Relationships of active smoking to asthma and asthma severity in the EGEA study. Epidemiological study on the genetics and environment of asthma. *Eur Respir J* 2000; 15: 470–477.
- Slama K, Chiang C-Y, Enarson D, et al. Tobacco and tuberculosis: a qualitative systematic review and meta-analysis. *Int J Tuberc Lung Dis* 2007; 11: 1049–1061.
- World Health Organization. WHO Framework Convention on Tobacco Control. Geneva, Switzerland: WHO, 2005. <http://www.who.int/ctc/about/en/> Accessed January 2016.
- Khot U N, Khot M B, Bajzer C T, et al. Prevalence of conventional risk factors in patients with coronary heart disease. *JAMA* 2003; 290: 898–904.
- Garcia-Aymerich J, Barreiro E, Farrero E, Marrades R, Morera J, Anto J. Patients hospitalized for COPD have a high prevalence of modifiable risk factors for exacerbation (EFRAM study). *Eur Respir J* 2000; 16: 1037–1042.
- Uganda Bureau of Statistics. Uganda national household surveys report 2009/2010: main source of household earning. Kampala, Uganda: Uganda Bureau of Statistics, 2010. <http://www.ubos.org/UNHS0910/chapter7.Average%20Monthly%20Household%20Income.html> Accessed January 2016.
- UK Office for National Statistics. Statistical bulletin: UK labour market, July 2015. Average weekly earnings. London, UK: Office for National Statistics, 2015. <http://www.ons.gov.uk/ons/rel/lms/labour-market-statistics/july-2015/statistical-bulletin.html#tab-6--Average-weekly-earnings> Accessed January 2016.
- Action on Smoking and Health. Nicotine replacement therapy. UK Market Review. London, UK: ASH, 2005. http://www.ash.org.uk/files/documents/ASH_429.pdf Accessed March 2016

arrêter et 37% étaient prêts à payer. Généralement, les médicaments étaient indisponibles : les substituts de la nicotine ne se trouvaient que dans sept pharmacies (18%) et le bupropion dans trois pharmacies (8%) et coûtaient US\$15,7 et US\$17,1, respectivement, pour un traitement d'un mois. Améliorer l'approvisionnement et réduire les prix pourrait faciliter l'accès au TDP en Ouganda.

abandonar el hábito y 37% estaban dispuestos a pagar por el TDP. En general, los medicamentos no estaban al alcance; solo siete farmacias contaban con productos de sustitución de la nicotina (18%) con un costo mensual de US\$15,7 y tres farmacias ofrecían bupropión (8%) con un costo de US\$17,1 por la dosis mensual. Mejorar el suministro y disminuir los precios, podría favorecer el acceso al TDP en Uganda.

Public Health Action (PHA) The voice for operational research. Published by The Union (www.theunion.org). PHA provides a platform to fulfil its mission, 'Health solutions for the poor'. PHA publishes high-quality scientific research that provides new knowledge to improve the accessibility, equity, quality and efficiency of health systems and services.

e-ISSN 2220-8372
Editor-in-Chief: Dermot Maher, MD, Switzerland
Contact: pha@theunion.org
PHA website: <http://www.theunion.org/what-we-do/journals/pha>
Article submission: <http://mc.manuscriptcentral.com/pha>

International research and guidelines on post-tuberculosis chronic lung disorders: a systematic scoping review

Sanne C van Kampen,¹ Amanda Wanner,¹ Miles Edwards,¹ Anthony D Harries,^{2,3} Bruce J Kirenga,⁴ Jeremiah Chakaya,^{2,5} Rupert Jones¹

BMJ Glob Health: first published as 10.1136/bmjgh-2018-000745 on 23 July 2018. Downloaded from <http://gh.bmj.com/> on 18 April 2019 by guest. Protected by copyright.

To cite: van Kampen SC, Wanner A, Edwards M, *et al*. International research and guidelines on post-tuberculosis chronic lung disorders: a systematic scoping review. *BMJ Glob Health* 2018;**3**:e000745. doi:10.1136/bmjgh-2018-000745

Handling editor Alberto L Garcia-Basteiro

► Additional material is published online only. To view please visit the journal online (<http://dx.doi.org/10.1136/bmjgh-2018-000745>).

Received 30 January 2018
Revised 18 May 2018
Accepted 28 May 2018



© Author(s) (or their employer(s)) 2018. Re-use permitted under CC BY-NC. No commercial re-use. See rights and permissions. Published by BMJ.

For numbered affiliations see end of article.

Correspondence to
Dr Sanne C van Kampen;
sanne.vankampen@gmail.com

ABSTRACT

Introduction Pulmonary tuberculosis (TB) is an important risk factor for chronic respiratory disease due to residual lung damage. Yet, the WHO End TB strategy does not mention post-TB chronic lung disorders (PTBLDs) and programmatic interventions to address PTBLD are lacking. This study assessed the scope of current guidelines and evidence on PTBLD to inform policy and research action.

Methods A systematic literature search was conducted following Preferred Reporting Items for Systematic Review and Meta-Analysis guidelines. Eight databases (TRIP, International Guideline Library, MEDLINE/PubMed, EMBASE, Web of Science, Global Health, Cochrane Library) were searched for records on PTBLD published between 1 January 1990 and 1 December 2017. Non-English records, case series, conference abstracts and letters to editors were excluded. Data were extracted and charted on publication year, location, PTBLD condition(s) and main study outcome.

Results A total of 212 guidelines and 3661 articles were retrieved. After screening, only three international TB guidelines mentioned TB sequelae, but none described how to identify or manage the condition. A total of 156 articles addressed PTBLD: 54 (35%) mentioned unspecified TB sequelae; 47 (30%) specific post-TB conditions including aspergillosis, bronchial stenosis or bronchiectasis; 52 (33%) post-TB obstructive disorders or lung function impairment; and 20 (13%) post-TB respiratory symptoms or chest X-ray abnormalities. The first two groups mostly assessed surgery or ventilation techniques for patient management, while the last two groups typically assessed prevalence or predictors of disease.

Conclusion This is the first review to provide a comprehensive overview of the current literature on PTBLD. The scope of evidence around the burden of PTBLD warrants inclusion and recognition of the problem in international TB guidelines. Research is now needed on early detection of PTBLD and patient management options that are suitable for high-burden TB countries.

Key questions

What is already known?

- Pulmonary tuberculosis (TB) is an important risk factor for chronic respiratory disease due to residual lung damage.
- The scope of current guidelines and evidence on post-TB chronic lung disorders (PTBLDs) is unknown.

What are the new findings?

- Out of 212 international TB guidelines, only three mentioned TB sequelae and none described how to identify or manage the condition.
- Of 156 scientific articles on PTBLD, around two-thirds addressed treatment by surgery or ventilation techniques and one-third addressed prevalence or predictors of the condition.

What do the new findings imply?

- While the scope of evidence on the burden of PTBLD justifies inclusion in international guidelines, more research is needed on patient management options that are suitable for high-burden TB countries.

Trishul Siddharthan et al.

Urbanization and chronic respiratory disease, Uganda

This online first version has been peer-reviewed, accepted and edited,
but not formatted and finalized with corrections from authors and proofreaders.

Prevalence of chronic respiratory disease in urban and rural Uganda

Trishul Siddharthan,^a Matthew Grigsby,^a Brooks Morgan,^a Robert Kalyesubula,^b Robert A Wise,^a Bruce Kirenga^b & William Checkley^a

^a Division of Pulmonary and Critical Care, School of Medicine, Johns Hopkins University, 1830 E. Monument Street, Room 555, Baltimore, Maryland, MD 21287, United States of America.

^b College of Health Sciences, Makerere University, Kampala, Uganda.

Correspondence to William Checkley (email: wcheckl1@jhmi.edu).

(Submitted: 16 May 2018 – Revised version received: 7 December 2018 – Accepted: 25 February 2019 – Published online: 26 March 2019)

Abstract

Objective To determine the prevalence of chronic respiratory diseases in urban and rural Uganda and to identify risk factors for these diseases.

Methods The population-based, cross-sectional study included adults aged 35 years or older. All participants were evaluated by spirometry according to standard guidelines and completed questionnaires on respiratory symptoms, functional status and demographic characteristics. The presence of four chronic respiratory conditions was monitored: chronic obstructive pulmonary disease (COPD), asthma, chronic bronchitis and a restrictive spirometry pattern.

Findings In total, 1502 participants (average age: 46.9 years) had acceptable, reproducible spirometry results: 837 (56%) in rural Nakaseke and 665 (44%) in urban Kampala. Overall, 46.5% (698/1502) were male. The age-adjusted prevalence of any chronic respiratory condition was 20.2%. The age-adjusted prevalence of COPD was significantly greater in rural than urban participants (6.1 versus 1.5%, respectively; $P < 0.001$), whereas asthma was significantly more prevalent in urban participants: 9.7% versus 4.4% in rural participants ($P < 0.001$). The age-adjusted prevalence of chronic bronchitis was similar in rural and urban participants (3.5 versus 2.2%, respectively; $P = 0.62$), as was that of a restrictive spirometry pattern (10.9 versus 9.4%; $P = 0.82$). For COPD, the population attributable risk was 51.5% for rural residence, 19.5% for tobacco smoking, 16.0% for a body mass index $< 18.5 \text{ kg/m}^2$ and 13.0% for a history of treatment for pulmonary tuberculosis.

Conclusion The prevalence of chronic respiratory disease was high in both rural and urban Uganda. Place of residence was the most important risk factor for COPD and asthma.

Guidance on the diagnosis and management of asthma among adults in resource limited settings

Bruce J Kirenga^{1,3}, Jeremy I Schwartz², Corina de Jong³, Thys van der Molen³, Martin Okot-Nwang¹

1. Pulmonology unit, Department of Medicine, Makerere University College of Health sciences/Mulago Hospital
2. Department of Internal Medicine, Yale School of Medicine
3. Department of General Practice, Groningen Research Institute for Asthma and COPD (GRIAC), University Medical Center Groningen, University of Groningen, Groningen, The Netherlands

Abstract

Background: Optimal management of asthma in resource limited settings is hindered by lack of resources, making it difficult for health providers to adhere to international guidelines. The purpose of this review is to identify steps for asthma diagnosis and management in resource limited settings.

Methods: Review of international asthma guidelines and other published studies on diagnosis and management of asthma.

Results: We establish that clinical diagnosis of asthma can be made if recurrent respiratory symptoms especially current wheeze or wheeze in the last 12 months are present. Presence of a trigger, other allergic diseases, personal or family history of asthma; clinical improvement and increase in the peak flow and forced expiratory volume in one second of $\geq 12\%$ after salbutamol administration increases the likelihood of asthma. At diagnosis severity grading, patient education, removal or reduction of trigger should be done. Follow up 2-6 weeks and assessment of control during therapy is essential. Therapy should be adjusted up or down depending on control levels. Patients should be instructed to increase the frequency of their bronchodilators and/or steroids therapy when they start to experience worsening symptoms.

Conclusion: Good quality asthma care can be achieved in resource limited settings by use of clinical data and simple tests.

Keywords: Asthma, diagnosis, treatment, management and resource limited settings.

DOI: <http://dx.doi.org/10.4314/ahs.v15i4.18>

Cite as: Kirenga BJ, Schwartz JI, de Jong C, der Molen Tn, Okot-Nwang M. Guidance on the diagnosis and management of asthma among adults in resource limited settings. *Afri Health Sci.* 2015;15(4):1189-99. <http://dx.doi.org/10.4314/ahs.v15i4.18>

Case scenario

"A 24-year-old woman presents with shortness of breath, wheezing especially at night for four weeks. She has had to stop her job of hawking fruits on the streets because of these symptoms. Her symptoms are worsened by cold weather, wood smoke and dust. There are cockroaches in her house but she says these do not cause her any problems.

Prior to the onset of these problems, she had never had any illness similar to this but reports recurrent nasal blockage and sneezing in the morning and evening since childhood. Her mother had

asthma all her life and her 1 year old baby has prolonged and recurrent attacks of cough. She has no other medical problems and her last normal menstrual period was two weeks ago.

Peak expiratory flow rate (PEFR) measurements are 200ml/min and 320ml/min before and after administration of salbutamol. Part of her spirometry results are as follows: pre-bronchodilator $FEV_1 = 2.8L$ (63% predicted) and post-bronchodilator $FEV_1 = 3.18$ (84% predicted).

Introduction

Asthma is a common chronic disorder of the airways that is characterized by variable and recurring symptoms, airflow obstruction, bronchial hyper-responsiveness, and an underlying inflammatory process.¹ Global prevalence of asthma is estimated at 10-20% of adults.² In Uganda, a retrospective chart review found that one in six patients receiving care at the Mulago hospital chest clinic had asthma.³

Corresponding author:

Bruce J Kirenga,
Pulmonology unit,
Department of Medicine,
Makerere University College of Health sciences
/Mulago Hospital
Email: brucekirenga@yahoo.co.uk
P.O. Box 7072, Kampala, Uganda

REVIEW ARTICLE OPEN

Treating tobacco dependence: guidance for primary care on life-saving interventions. Position statement of the IPCRG

O. C. P. Van Schayck¹, S. Williams², V. Barchilon³, N. Baxter^{2,4}, M. Jawad⁵, P. A. Katsaounou⁶, B. J. Kirenga⁷, C. Panaitescu⁸, I. G. Tsiligianni⁹, N. Zwar¹⁰ and A. Ostrem¹¹

Tobacco smoking is the world's leading cause of premature death and disability. Global targets to reduce premature deaths by 25% by 2025 will require a substantial increase in the number of smokers making a quit attempt, and a significant improvement in the success rates of those attempts in low, middle and high income countries. In many countries the only place where the majority of smokers can access support to quit is primary care. There is strong evidence of cost-effective interventions in primary care yet many opportunities to put these into practice are missed. This paper revises the approach proposed by the International Primary Care Respiratory Group published in 2008 in this journal to reflect important new evidence and the global variation in primary-care experience and knowledge of smoking cessation. Specific for primary care, that advocates for a holistic, bio-psycho-social approach to most problems, the starting point is to approach tobacco dependence as an eminently treatable condition. We offer a hierarchy of interventions depending on time and available resources. We present an equitable approach to behavioural and drug interventions. This includes an update to the evidence on behaviour change, gender difference, comparative information on numbers needed to treat, drug safety and availability of drugs, including the relatively cheap drug cytisine, and a summary of new approaches such as harm reduction. This paper also extends the guidance on special populations such as people with long-term conditions including tuberculosis, human immunodeficiency virus, cardiovascular disease and respiratory disease, pregnant women, children and adolescents, and people with serious mental illness. We use expert clinical opinion where the research evidence is insufficient or inconclusive. The paper describes trends in the use of waterpipes and cannabis smoking and offers guidance to primary-care clinicians on what to do faced with uncertain evidence. Throughout, it recognises that clinical decisions should be tailored to the individual's circumstances and attitudes and be influenced by the availability and affordability of drugs and specialist services. Finally it argues that the role of the International Primary Care Respiratory Group is to improve the confidence as well as the competence of primary care and, therefore, makes recommendations about clinical education and evaluation. We also advocate for an update to the WHO Model List of Essential Medicines to optimise each primary-care intervention. This International Primary Care Respiratory Group statement has been endorsed by the Member Organisations of World Organization of Family Doctors Europe.

npj Primary Care Respiratory Medicine (2017)27:38; doi:10.1038/s41533-017-0039-5

BACKGROUND: THE TOBACCO EPIDEMIC

This paper provides an update to the original paper IPCRG Consensus statement: Tackling the smoking epidemic—practical guidance for primary care of 2008 published in this journal.¹ Tobacco dependence is a deadly epidemic killing up to half its users.² There are currently one billion smokers in the world and 80% live in low and middle income countries.³ Tobacco use is the leading cause of premature death globally due to the many diseases, which are attributed wholly or partially to smoking resulting in nearly six million deaths a year.^{4, 5} This annual total is higher than the combined mortality from malaria, tuberculosis and human immunodeficiency virus (HIV).⁶ Based on current trends, tobacco is expected to be responsible for 10% of global deaths, or eight million deaths a year by 2030, 80% in low and

middle income countries: this includes a 9% decline in high income, but a doubling in low and middle income to 6.8 million.⁷ This is creating growing health inequalities at national and global levels due to the strong association of tobacco use with socio-economic deprivation.

There is a global commitment to tackle the epidemic. In 2011, the UN General Assembly adopted a political declaration that committed member states to the prevention and control of non-communicable diseases (NCDs). This included a target of a 25% reduction in premature mortality from NCDs by 2025 ("25 × 25") and targets for nine risk factors, including a 30% relative reduction in smoking prevalence.⁸ This is anticipated to bring most health and economic benefit to low and middle income countries and included modelling of smoking attributable diseases such as

¹Department of Family Medicine, CAPHRI, Maastricht University, Maastricht, The Netherlands; ²International Primary Care Respiratory Group, Aberdeen, UK; ³Andalusian Health Service (SAS), Tobacco group of GRAP (Primary Care Respiratory Group), Andalusia, Spain; ⁴Southwark Clinical Commissioning Group, London, UK; ⁵Faculty of Medicine, School of Public Health, Imperial College London, London, UK; ⁶Pulmonary Medicine, Medical School, National and Kapodistrian University of Athens, Evangelismos Hospital, Athens, Greece; ⁷Lung Institute and Division of Pulmonary Medicine, Makerere University College of Health Sciences, Kampala, Uganda; ⁸Family Medicine Solo Practice, RespiRo-Romanian Primary Care Respiratory Group, Bucharest, Romania; ⁹Clinic of Social and Family Medicine, Faculty of Medicine, University of Crete, Crete, Greece; ¹⁰School of Public Health and Community Medicine, UNSW Australia, Sydney, NSW, Australia and ¹¹General Practitioner, Gransdalen Legesenter, Oslo, Norway
Correspondence: O. C. P. Van Schayck (onno.vanschayck@maastrichtuniversity.nl)

Received: 8 November 2016 Revised: 29 March 2017 Accepted: 9 May 2017
Published online: 09 June 2017

PubMed

Format: Abstract

Full text links

Am J Trop Med Hyg. 2019 Feb;100(2):386-391. doi: 10.4269/ajtmh.18-0281.



Prevalence of Tuberculosis Risk Factors among Bacteriologically Negative and Bacteriologically Confirmed Tuberculosis Patients from Five Regional Referral Hospitals in Uganda.

Muttamba W¹, Kirenga B¹, Ssengooba W², Sekibira R¹, Katamba A³, Joloba ML².

Author information

Abstract

Understanding risk factors for tuberculosis (TB) and their prevalence helps guide early diagnosis. We determined their prevalence among bacteriologically negative and bacteriologically confirmed TB patients in five regional referral hospitals in Uganda. This cross-sectional study considered 1,862 adult presumptive TB participants. We performed fluorescent microscopy, Xpert MTB/RIF (Xpert), Lowenstein-Jensen culture, human immunodeficiency virus, and random blood sugar testing on recruited patients. Prevalence and prevalence ratios of risk factors were compared among bacteriologically negative and confirmed cases. Odds ratios and 95% confidence interval (CI) were determined for significant risk factors in bacteriologically confirmed patients. Of the 1,862 participants, 978 (55%) were male and the median age of the participants was 36 years (interquartile range: 27-48). Up to 273 (15%) had a positive result on all three TB tests. Most prevalent risk factors (prevalence ratio [PR] > 1.0) among bacteriologically negative and positive TB patients were cigarette smoking (9.3% versus 2.1%; PR = 2.1), biosmoke (24% versus 39.7%; PR = 1.7), contact (4.2% versus 6.5%; PR = 1.6), male gender (51.4% versus 72.5%; PR = 1.4), alcohol use (17.2% versus 24.4%; PR = 1.4), diabetes (0.7% versus 0.9%; PR = 1.3), and family history of TB (12.1% versus 13.7%; PR = 1.1). The risk factors and their adjusted prevalence rate ratios (95% CI) of being bacteriologically positive were male (1.8 [1.4-2.4]), biosmoke exposure (1.5 [1.2-2.0]), and history of cigarette smoking (1.6 [1.1-2.4]). Among bacteriologically confirmed patients in Uganda, cigarette smoking, biosmoke exposure, contact, male gender, alcohol use, diabetes, and family history of TB are important risk factors for TB. Interventions for TB control in people with these risk factors would help in TB control efforts.

PMID: 30594259 PMCID: [PMC6367623](https://pubmed.ncbi.nlm.nih.gov/30594259/) [Available on 2020-02-01] DOI: [10.4269/ajtmh.18-0281](https://doi.org/10.4269/ajtmh.18-0281)

LinkOut - more resources



History of Makerere University Lung Institute (MLI)

History of Makerere University Lung Institute

The Makerere University Lung Institute was established on 17th September 2015 following acceptance of a proposal to establish a lung institute by Lung Consortium International (LCI) by Makerere University (Mak). On the 23rd November 2015, the first governance structure comprising of the institute governance board, IGB, chaired by Prof. Charles Ibingira (Principal of the College of Health Sciences) and Institute Technical advisory Board, ITB, chaired by Prof. Isaac Okullo (Deputy Principal of the College of Health Sciences) and management team lead by the Director, Dr. Bruce Kirenga and Co- Director, Prof Rupert Jones were inaugurated by the Vice Chancellor in the Senior Common room in the Mak main building. LCI is a consortium of Ugandan and international lung health specialists.

The members of the LCI at the founding of the MLI were



Dr. Bruce J Kirenga

Senior Lecturer, Department of Medicine, School of Medicine, College of Health Sciences, Makerere University, Uganda



Dr. Frederik van Gemert

Department of General Practice and Elderly Care, University Medical Center, University of Groningen, Groningen, The Netherlands



Dr. William Worodria

Senior Consultant Physician, Mulago Hospital Uganda



Dr. Frank R Mugabe

Senior Medical Officer, Ministry of Health Uganda



Prof. Rupert Jones

Institute of Translational & Stratified Medicine, Faculty of Medicine and Dentistry, University of Plymouth UK



Dr. Alphonse Okwera

Department of Medical Microbiology, School of Biomedical Sciences, College of Health Sciences, Makerere University, Uganda



Prof Moses Joloba

Department of Medical Microbiology, School of Biomedical Sciences, College of Health Sciences, Makerere University, Uganda

Founding Institute Governing Board



Prof. Charles Ibingira



Prof. Nelson Sewankambo



Prof Thys van der Molen



Dr. B.B Byarugaba



Dr. Jacinto Amandua



Dr. Francis Adatu

Founding Institute Technical Board



Prof Isaac Okullo



Dr. Frederik van Gemert



Prof. Josephine Kasolo



Prof Moses Joloba



Dr. Alphonse Okwera



Dr. Frank R Mugabe



Dr. William Worodria



Dr. Anna Nakanwagi



Dr. Abel Nkolo



Dr. Okot Nwang



Dr. Simon Kasasa



Dr. Achilles Katamba



**Dr. Hellen Aanyu –
Tukamuhebwa**



Dr. Fred Nakwagala

Founding Fellows



**Dr. Wincelaus
Katagira**



Dr. Rebecca Nantanda



Dr. Simon Walusimbi



Dr. Patrick Musinguzi

Founding Administrators



Mr. Simon Mugambe



Ms. Juliet Ntaganzirwe



Ms. Shamim Buteme

Founding Data Officers



Denis Senfuka



Zefania Mangusho



Rogers Sekibira

Founding Medical officer



Dr. Abdallah Muhofa

Founding Quality Control Officer



Ms. Grace Nyakoojo

Founding Nurse



Sr. Grace Kintu

Founding Driver



Simon Onanyang

Founding Counsellor



Ms. Janet Nalwaya

First offices





About MLI

Makerere University Lung Institute is a champion in innovative lung health research that integrates disease prevention, clinical care and training in sub-Saharan Africa.

Sub-Saharan Africa is experiencing a convergence of communicable and non-communicable lung diseases such as Tuberculosis, Chronic Obstructive Pulmonary Disease, asthma and lung cancer. Lung diseases are not only among the top causes of ill health and deaths but also remain largely under-recognized, partly because of low awareness in the general population. Lung diseases greatly impact on the quality of life of the affected people and their families; lead to high healthcare costs to the individual and the country. In addition, they are associated with loss of productivity which hinders personal and national development.

Therefore, Makerere University Lung Institute is an academic response to this epidemic with the noble purpose of improving the health and life of those that need it the most.

Vision

An Africa with healthy lungs

Mission

To conduct high quality lung health research that integrates disease prevention, clinical care and training in Sub-Saharan Africa

Core Values

Innovation | Excellence | Integrity | Care | Effort norm

Contacts

Makerere University Lung Institute
Lung Institute Building
College of Health Sciences/ Mulago Hospital
New Mulago Hill Road
P.O. Box 7749, Kampala-Uganda
Tel: 04 14699134
Email: mli@chs.mak.ac.ug | Website: mli.mak.ac.ug