



2nd Lung Science & Health

SYMPOSIUM

-2023-

ABSTRACT BOOK

2nd Lung Science and Health
Symposium 2023

THEME

**Occupational Lung Health:
Protecting our lungs while we work**



MAKERERE UNIVERSITY

THURSDAY, 30TH
NOVEMBER,
2023

SKYZ HOTEL
NAGURU
Kampala





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CONTENTS

CONTENTS

WELCOME REMARKS: DIRECTOR, MLI	VI
WELCOME REMARKS: CHAIR,	VII
ORGANIZING COMMITTEE	VIII
SYMPOSIUM PROGRAM	VIII

LIST OF PUBLICATIONS 2022/23 X

Delay in healthcare seeking for young children with severe pneumonia at Mulago National Referral Hospital, Uganda: A mixed methods cross-sectional study	1
Mycobacterium tuberculosis infection and cytogenetic abnormalities among people with HIV	2
HIV-related lung cancer in Uganda: a cohort study	3
A systematic review of strategies adopted to scale up COVID-19 testing in low-, middle- and high-income countries	4
Strategies to resolve the gap in Adolescent Tuberculosis care at four health facilities in Uganda: The TEEN TB pilot project	5
Evaluation of circulating serum cathelicidin levels as a potential biomarker to discriminate between active and latent tuberculosis in Uganda	7
Association of circulating serum free bioavailable and total vitamin D with cathelicidin levels among active TB patients and household contacts	8
Distinguishing pulmonary rehabilitation from chest physiotherapy in the African context	9
Risk factors for disruptions in tuberculosis care in Uganda during the COVID-19 pandemic	10
Leveraging the structures of the COVID-19 pandemic response for successful control of Ebola in Uganda	11

Implication of the Global Initiative for Chronic Obstructive Lung Disease 2023 report for resource-limited settings: tracing the G in the GOLD	12
--	----

Cross-sectional validation of the COPD Assessment Test (CAT) among chronic obstructive pulmonary disease patients in rural Uganda	14
---	----

Respiratory Health and Cities	15
-------------------------------	----

Cost of treatment support for multidrug-resistant tuberculosis using patient-centred approaches in Ethiopia: a model-based method	16
---	----

Barriers to childhood asthma care in sub-Saharan Africa: a multicountry qualitative study with children and their caregivers.	17
---	----

Unmet Diagnostic and Therapeutic Opportunities for Chronic Obstructive Pulmonary Disease in Low- and Middle-Income Countries.	18
---	----

A cross-country qualitative analysis of teachers' perceptions of asthma care in sub-Saharan Africa	20
--	----

Clinical features, resistance patterns and treatment outcomes of drug-resistant extra-pulmonary tuberculosis: A scoping review	22
--	----

LIST OF PUBLICATIONS 2021/22 24

The availability, cost, and affordability of essential medicines for asthma and COPD in low-income and middle-income countries: a systematic review	25
---	----

Impact of on-site Xpert on TB diagnosis and mortality trends in Uganda	26
--	----

Facilitators and barriers to the implementation of improved solid fuel cookstoves and clean fuels in low-income and middle-income countries:	
--	--

an umbrella review	27	Ultra before MDRT-TB treatment initiation: A case report from Uganda	39
Systematic Review of Physical Activity, Sedentary Behaviour and Sleep Among Adults Living with Chronic Respiratory Disease in Low- and MiddleIncome Countries	28	Impact of socio-economic factors on Tuberculosis treatment outcomes in north-eastern Uganda: a mixed methods study	40
Molecular characterisation of second-line drug resistance among drug resistant tuberculosis patients tested in Uganda: a two and a half-year's review	29	Feasibility of using a mobile App to monitor and report COVID-19 related symptoms and people's movements in Uganda	41
Asthma care in sub-Saharan Africa: Mind the gap!	30	The rural Uganda non-communicable disease (RUNCD) study: prevalence and risk factors of self-reported NCDs from a cross sectional survey	42
Hypovitaminosis D among newly diagnosed pulmonary TB patients and their household contacts in Uganda	31	Music and dance in respiratory disease management in Uganda: a qualitative study of patient and healthcare professional perspectives.	43
Factors Associated with Linkage to HIV Care Among Oral Self-Tested HIV Positive Adults in Uganda	32	Adoption of evidence-informed guidelines in prescribing protease inhibitors for HIV-Tuberculosis co-infected patients on rifampicin and effects on HIV treatment outcomes in Uganda	44
Safety and efficacy of hydroxychloroquine for treatment of non-severe COVID-19 among adults in Uganda: a randomized open label phase II clinical trial	33	Undernutrition and Treatment Success in Drug Resistant Tuberculosis in Uganda	45
Prevalence of Aspergillus fumigatus skin positivity in adults without an apparent/known atopic disease in Uganda	34	Efficacy of convalescent plasma for treatment of COVID-19 in Uganda	46
Vitamin D binding protein gene polymorphism and its association with free serum bioavailability among tuberculosis patients and household contacts	35	Association of fluvoxamine with mortality and symptom resolution among inpatients with COVID-19 in Uganda: a prospective interventional open-label cohort study	48
Patient level barriers to accessing TB care services during the COVID-19 pandemic in Uganda, a mixed methods study. (Under review by BMC Health Services Research journal)	36	Prevalence, risk factors and outcome in Ugandan children infected with <i>Mycoplasma pneumoniae</i> : a prospective study	49
Perceptions of Adolescents and Health Workers Towards Adolescents' TB Diagnosis in Central Uganda: A Cross-Sectional Qualitative Study	38	COVID-19 vaccine acceptance among high-risk populations in Uganda	50
Rifampicin susceptibility discordance between Xpert MTB/RIF G4 and Xpert		Impact of the bacillary load on the accuracy of rifampicin resistance results by Xpert® MTB/RIF	51
		Gaps related to screening and	

diagnosis of tuberculosis in care cascade in selected health facilities in East Africa countries: A retrospective study	53	high-risk populations in Uganda	64
Efficacy of convalescent plasma for treatment of COVID-19 in Uganda	54	Rising and falling prevalence of asthma symptoms	66
Adoption of evidence-informed guidelines in prescribing protease inhibitors for HIV-Tuberculosis co-infected patients on rifampicin and effects on HIV treatment outcomes in Uganda.	55	LIST OF PUBLICATIONS 2020/21	67
Chronic obstructive pulmonary disease prevalence and associated factors in an urban HIV clinic in a low income country	56	Assessing a transmission network of Mycobacterium tuberculosis in an African city using single nucleotide polymorphism threshold analysis	68
Health workers' perspectives of a mobile health tool to improve diagnosis and management of paediatric acute respiratory illnesses in Uganda: a qualitative study	57	Discordance of the Repeat GeneXpert MTB/RIF Test for Rifampicin Resistance Detection Among Patients Initiating MDR-TB Treatment in Uganda	69
Challenges in the Implementation of Chronic Obstructive Pulmonary Disease Guidelines in Low- and Middle-Income Countries	58	Feasibility of collecting and processing of COVID-19 convalescent plasma for treatment of COVID-19 in Uganda	70
Identifying Appropriate Delivery of and Referral to Pulmonary Rehabilitation in Uganda: A Survey Study of People Living with Chronic Respiratory Disease and Health Care Workers	60	Characteristics and outcomes of admitted patients infected with SARS-CoV-2 in Uganda	71
Study protocol for a randomised controlled trial assessing the impact of pulmonary rehabilitation on maximal exercise capacity for adults living with post-TB lung disease: Global RECHARGE Uganda	61	Health Workers' Practices in Assessment and Management of Children with Respiratory Symptoms in Primary Care Facilities in Uganda: A FRESH AIR Descriptive Study	72
Latent Tuberculosis Infection Status of Pregnant Women in Uganda Determined Using QuantiFERON TB Gold-Plus	62	Latent Tuberculosis Infection Status of Pregnant Women in Uganda Determined Using QuantiFERON TB Gold-Plus	74
Excess COVID-19 mortality among critically ill patients in Africa	63	Baseline Xpert MTB/RIF ct values predict sputum conversion during the intensive phase of anti-TB treatment in HIV infected patients in Kampala, Uganda: a retrospective study.	75
COVID-19 vaccine acceptance among		Africa's respiratory "Big Five"	76
		Fungal asthma among Ugandan adult asthmatics.	77
		Effectiveness of thermal screening in detection of COVID-19 among truck drivers at Mutukula Land Point of Entry, Uganda	78
		Skin prick reactivity among asthmatics in East Africa	80
		Variations in Trim5 α and Cyclophilin A genes among HIV-1 elite controllers	

and non controllers in Uganda: a laboratory-based cross-sectional study	81	for Chronic Obstructive Pulmonary Disease in Low- and Middle-Income Country Settings	94
Characteristics and outcomes of admitted patients infected with SARS-CoV-2 in Uganda	82	Gaps in COPD Guidelines of Low- and Middle-Income Countries: A Systematic Scoping Review	95
Dance for Respiratory Patients in Low-Resource Settings	83	National tuberculosis prevalence surveys in Africa, 2008–2016: an overview of results and lessons learned	96
illness representations of chronic obstructive pulmonary disease (COPD) to inform health education strategies and research design—learning from rural Uganda	84	LIST OF PUBLICATIONS 2019/20	98
Prevalence and Predictors of CD4+ T-Lymphocytopenia Among HIV-Negative Tuberculosis Patients in Uganda	85	Delays in diagnosis and treatment of pulmonary tuberculosis in patients seeking care at a regional referral hospital, Uganda: a cross sectional study	99
Households experiencing catastrophic costs due to tuberculosis in Uganda: magnitude and cost drivers	86	Feasibility and acceptability of a midwife-led health education strategy to reduce exposure to biomass smoke among pregnant women in Uganda, A FRESH AIR project	100
Accuracy and Incremental Yield of the Chest X-Ray in Screening for Tuberculosis in Uganda: A Cross-Sectional Study	87	Health seeking behaviour among individuals presenting with chronic cough at referral hospitals in Uganda; Missed opportunity for early tuberculosis diagnosis	101
Association between Blood Pressure and HIV Status in Rural Uganda: Results of Cross-Sectional Analysis	88	Comparison of GeneXpert cycle threshold values with smear microscopy and culture as a measure of mycobacterial burden in five regional referral hospitals of Uganda- A cross-sectional study	102
Incidence and predictors of COPD mortality in Uganda: A 2-year prospective cohort study	89	Burden of fungal asthma in Africa: A systematic review and meta-analysis	103
Back to Basics in Paediatric Pneumonia— Defining a Breath and Setting Reference Standards to Innovate Respiratory Rate Counting	90	Prevalence of chronic respiratory disease in urban and rural Uganda	105
Factors critical to implementation success of cleaner cooking interventions in low-income and middle-income countries: protocol for an umbrella review	91	Prevalence and factors associated with asthma among adolescents and adults in Uganda: a general population-based survey	106
Global RECHARGE: Establishing a standard international data set for pulmonary rehabilitation in low- and middle-income countries	92	Singing for Breathing Uganda: Group singing for people with chronic lung disease in Kampala	107
A Novel Case-Finding Instrument		Phenotypic characteristics and asthma severity in an East African cohort of	

adults and adolescents with asthma: findings from the African severe asthma project	108	Uganda: A Cross-Sectional Analysis of the 2016 Demographic and Health Survey	119
Diagnosis and treatment of acute respiratory illness in children under five in primary care in low-, middle-, and high-income countries: A descriptive FRESH AIR study	109	Accuracy of Xpert Ultra in Diagnosis of Pulmonary Tuberculosis among Children in Uganda: a Substudy from the SHINE Trial	121
The socioeconomic burden of chronic lung disease in low-resource settings across the globe – an observational FRESH AIR study	110	SYMPOSIUM ABSTRACTS	122
The role of epigenetics in respiratory health in urban populations in low and middle-income countries	112	Research to support disease outbreak response: Experience from the Ebola Vaccine trial (Tokomeza Ebola trial) in Uganda	123
Algorithm-aided diagnosis of chronic pulmonary aspergillosis in low- and middle-income countries by use of a lateral flow device.	113	Building robust laboratory systems for disease outbreak response: Lessons learnt from Uganda's laboratory response to COVID-19	124
Achieving Control of Asthma in Children in Africa (ACACIA): protocol of an observational study of children's lung health in six sub-Saharan African countries.	114	Computed Tomography and histopathological correlative Imaging of lung cancer in Uganda	125
Symptom-based screening tool for asthma syndrome among young children in Uganda	115	Is HIV-1 infection a risk factor for Lung Cancer initiation and progression in Uganda and Tanzania?	126
Training needs for Ugandan primary care health workers in management of respiratory diseases: a cross sectional survey	116	"Screening and Diagnostic Pathways for Lung Cancer Patients in two East African Countries: Experience from the Lung Cancer in East Africa in Relation To HIV-1 Infection project"	127
Chronic Obstructive Pulmonary Disease Prevalence and Associated Factors in a Setting of Well-Controlled HIV, A Cross-Sectional Study	117	Prevalence Of Pulmonary Tuberculosis Among Casual Labourers Working In Road Construction Sites In Central Uganda	128
High prevalence of phenotypic pyrazinamide resistance and its association with pncA gene mutations in <i>Mycobacterium tuberculosis</i> isolates from Uganda	118	Using a multi component Quality Improvement interventions to reduce TB/HIV mortality among admitted patients at a large tertiary care hospital.	129
Investigating the Association between Wood and Charcoal Domestic Cooking, Respiratory Symptoms and Acute Respiratory Infections among Children Aged Under 5 Years in		MLI - 2 ND LUNG SCIENCE AND HEALTH SYMPOSIUM COMMITTEES	130

Welcome remarks: Director, MLI



Prof. Bruce J. Kirenga, Director Makerere University Lung Institute

Dear Delegates and Guests

I am extremely delighted to host you here today for the 2nd Makerere University Lung Institute Science and Health Symposium 2023.

As the Institute marks eight years we are excited that you have joined us today to share the scientific achievements of the Lung Institute.

Vested in research to transform the world's lung health status, MLI boasts of a wide range of research and studies that we shall be able to share with you today. This one day symposium is expected to unveil studies conducted by Makerere University Lung Institute tailored to influence policies that will keep workers and their employees safe at their places of work and ensure healthy lungs.

At the symposium a scientific program has been prepared to share with participants findings and work conducted by the institute as we mark eight years in existence. With Occupation Lung Health cited as another time bomb, the day's discussions are expected to educate masses on what's at stake and for policy makers to equitably distribute resources to curb this.

As we mark eight years since MLI started we commit to invest in more research and lung health care to transform lives.

Welcome remarks: Chair, Organizing Committee

I extend a warm welcome to all the participants of the 2023 and second Lung Science and Health Symposium (LSH) of Makerere University Lung Institute (MLI).

Worldwide, lung-related conditions are the third leading cause of death. In Uganda, lung-related conditions account for over 9 million health facility out-patient visits annually and are the second commonest reason for hospitalization. However, 15%-30% of the lung conditions in adults stem from exposure to hazardous materials at the workplace, rendering them entirely preventable. To underscore the high, but entirely preventable burden of work-related (occupational) lung diseases, the theme for the 2023 symposium is **“Occupational Lung Health: Protecting our lungs while we work”**. The aim of the symposium is to catalyze a robust national multisectoral response towards occupational lung diseases; by providing the necessary evidence-base to drive the response. I extend my sincere gratitude to all the members of the organizing committee for this 2023 lung symposium. I am confident that participants will be enlightened about the public health significance of occupational lung diseases globally and nationally. The symposium should therefore serve as a turning point for improving occupational lung health in Uganda.

Dr. Simon Walusimbi is a Research Fellow and Public Health Physician at Makerere University Lung Institute/School of Public in the College of Health Sciences



Symposium Program



MAKERERE UNIVERSITY LUNG INSTITUTE SCIENCE SYMPOSIUM
Makerere University College of Health Sciences, Kampala Uganda

**SYMPOSIUM PROGRAM****2nd Lung Science and Health Symposium 2023**

Theme: Occupational Lung Health: Protecting our lungs while we work

THURSDAY, 30TH NOVEMBER, 2023 | SKYZ HOTEL NAGURU, Kampala

8:20 -8:50	Arrival and Registration	MLI Secretariat
8:50 - 9:00	Welcome Remarks by Chairperson, Organising Committee	Dr Simon Walusimbi
SESSION 1: Lung Cancer Chair: Dr Robert Lukande		
9:00 -9:15	Radiology-pathological correlation, validation of LUNG RADS and development of a lung cancer screening protocol in Uganda	Dr. Margret Mbabazi
9:15 -9:25	Screening and Diagnostic Pathways for Lung Cancer Patients in two East African Countries: Experience from the Lung Cancer in East Africa in Relation To HIV-1 Infection project	Dr. Treasure Ibingira
9:25 -9:35	HIV-related lung cancer in Uganda: a cohort study	Dr. Joseph Baluku
9:35 -9:40	Q & A	ALL
SESSION 2: Keynote Address and Opening Ceremony Chair: Dr Simon Walusimbi		
9:40-9:50	A case of occupational lung disease following work at a wheat milling company	M. Med Internal Medicine -Pulmonology, MakCHS
9:50 -10:30	Keynote lecture	Prof. William Worodria
10:30-10:35	Remarks by Director, MLI	Assoc. Prof Bruce Kirenga
10:35 -10:40	Remarks by the Chair, BOD MLI	Prof. Charles Ibingira
10:40 -10:45	Remarks by Principal, MakCHS	Prof. Damalie Nakanjako
10:45 -10:55	Remarks by Vice Chancellor, Mak	Prof. Barnabas Nawangwe
10:55 -11:10	Opening Ceremony	Minister of Gender, Labour & Social Development
11:10 – 11:25	Tea/Coffee Break	ALL
SESSION 3: Panel Discussion Chair: Zahra Namuli Sentongo		
11:25 -12:55	Occupational Lung Health: Implications for Practice, Policy, and Research	
SESSION 4: Paediatric Lung Health Chair: Prof Nicolette Nabukeera-Barungi		
12:55 -13:05	Delayed healthcare seeking for young children with severe pneumonia at Mulago Hospital	Dr. Phiona Ekyaruhanga
13:05 -13:15	Severe pneumonia is associated with worse neurocognitive function among infants living with HIV	Dr. Damalie Nalwanga
13:15 -13:20	Q & A	ALL

13:20 -13:40	Poster Viewing	ALL
13:40 -14:20	Lunch Break	ALL
SESSION 5: Chronic Obstructive Lung Diseases: Chair: Dr. Ivan Kimuli		
14:40 – 12:55	COPD in Uganda and implications for primary prevention	Dr. Patricia Alupo
14:55– 15:05	Tuberculosis Associated Chronic Lung Disease status and Transforming Growth Factor Beta-1 in post-TB HIV infected cohort in Uganda	Dr. Ahmed Ddungu
15:05 – 15:15	Burden of Severe Asthma in SSA: Findings from the ASAP Project	Dr. Wincelous Katagira
15:15 -15:20	Q & A	ALL
SESSION 6: Air pollution and Lung Health Chair: Prof. Engineer Bainomugisha		
15:20 – 15:35	Understanding the interplay between air pollution and occupation health	Dr. Ivan Kimuli
15:35 -15:45	Prevalence of PTB among casual labourers working in road construction sites in Central Uganda	Ivan Ahimbisibwe
15:45 – 15:50	Q&A	ALL
SESSION 7: Tuberculosis Chair: Dr. Stavia Turyahabwe		
15:50 -16:00	Impact of socioeconomic factors on Tuberculosis treatment outcomes in North-Eastern Uganda: a mixed methods study	Dr. Jasper Nidoi
16:00 -16:10	Overcoming disruptions to health care delivery systems: Lessons from TB programming during the pandemic	Mr. Mudarshiru Bbuye
16:10 -16:20	Impact of on-site Xpert on TB diagnosis and mortality trends in Uganda	Ms. Irene Najjingo
16:20 – 16:40	Strategies to resolve the gap in adolescent TB (TEEN TB Project)	Mr. Samson Omongot
16:40 -16:50	Using a multi component Quality Improvement intervention to reduce TB/HIV mortality among admitted patients at a large tertiary care hospital.	Dr. Praise Akatukunda
16:50 – 16:55	Q & A	ALL
16:55- 17:10	Tea/ Coffee Break	ALL
SESSION 8: Lung Infections, Immunity and Epidemics Chair: Dr. Misaki Wayengera		
17:10 – 17:20	Sputum microbiome and chronic obstructive pulmonary disease in a rural Ugandan cohort of well-controlled HIV infection	Dr. Alex Kayongo
17:20 – 17:30	Characterizing patients presenting with COVID-19-related symptoms following national roll out of COVID-19 vaccination in Uganda.	Dr. Loryndah Namakula
17:30-17:35	Q & A	ALL
17:35-17:40	Closing Remarks	Prof. Charles Ibingira
18:00	Cocktail	

LIST OF
PUBLICATIONS
2022/23

Delay in healthcare seeking for young children with severe pneumonia at Mulago National Referral Hospital, Uganda: A mixed methods cross-sectional study

Phiona EkyaruhangalD^{1,2*}, Rebecca Nantanda², Hellen T. Aanyu³, John Mukisa⁴, Judith Amutuhaire SsemasaazilD⁵, Mukeere John¹, Palma Aceng¹, Joseph Rujumba

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Link: <https://doi.org/10.1371/journal.pone.0291387>

BACKGROUND: Globally, pneumonia is the leading infectious cause of under-five mortality, and this can be reduced by prompt healthcare seeking. Data on factors associated with delays in seeking care for children with pneumonia in Uganda is scarce.

OBJECTIVES: The study aimed to determine the prevalence, factors associated with delay, barriers, and facilitators of prompt healthcare seeking for children under five years of age with severe pneumonia attending Mulago National Referral Hospital (MNRH) Uganda.

METHODS: A mixed methods cross-sectional study was conducted among 384 caregivers of children with severe pneumonia at MNRH. Quantitative data was collected using interviewer-administered structured questionnaires and qualitative data through focus group discussions with caregivers. Descriptive statistics were used to determine the prevalence of delay in care seeking. Logistic regression analysis was used to determine the factors that were independently associated with delay in seeking healthcare. Content thematic analysis was used to analyze for barriers and facilitators of prompt healthcare seeking.

RESULTS: The prevalence of delay in seeking healthcare was 53.6% (95% CI: 48.6–58.6). Long distance to a hospital (AOR = 1.94, 95% CI 1.22–3.01, p value = 0.003), first seeking care elsewhere (AOR = 3.33, 95% CI 1.85–6.01, p value = 0.001), and monthly income 100,000 UGX (28 USD) (AOR = 2.27, 95% CI 1.33–3.86, p value = 0.003) were independently associated with delay in seeking healthcare. Limited knowledge of symptoms, delayed referrals, self-medication, and low level of education were barriers to prompt healthcare seeking while recognition of symptoms of severe illness in the child, support from spouses, and availability of money for transport were key facilitators of early healthcare seeking.

Mycobacterium tuberculosis infection and cytogenetic abnormalities among people with HIV

Joseph Baruch Baluku^{a, b}, Sharon Namiiri^c, Brenda Namanda^b, Shamim Katusabe^b, Dinah Namusoke^d, Reagan Nkongeb^b, Tonny Okecha^d, Carol Nassaza^{id}, Nixon Niyonzima^d, Naghib Bogere^d, Edwin Nuwagira^e, Martin Nabwana^f, Phillip Ssekamatte^g, Irene Andia-Biraro^c, William Worodria^{a, c}, Robert Salata^h, Sayoki Mfinangaⁱ, Stanton Gerson^j, Bruce Kirenga^a

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- j. School of Medicine, Case Western Reserve University, USA

Link: <https://doi.org/10.1016/j.mrgentox.2023.503640>

OBJECTIVE: To compare cytogenetic abnormalities among people living with HIV (PLWH) with and without previous exposure to Mycobacterium tuberculosis (Mtb) (both latent tuberculosis infection [LTBI] and active tuberculosis [TB]).

METHODS: Adult PLWH (≥18 years) were randomly selected at three HIV clinics in Uganda. Previous active TB was confirmed in the clinics' TB records. LTBI was defined as a positive QuantiFERON-TB Gold Plus assay. Participants' buccal mucosal exfoliated cells were examined (per 2000 cells) using the buccal micronucleus assay for chromosomal aberrations (micronuclei and/or nuclear buds), cytokinetic defects (binucleated cells), proliferative potential (normal differentiated cells and basal cell frequency) and/or cell death (condensed chromatin, karyorrhexis, pyknotic and karyolytic cells).

RESULTS: Among 97 PLWH, 42 (43.3%) had exposure to Mtb; 16 had previous successfully treated active TB and 26 had LTBI. PLWH with exposure to Mtb had a higher median number of normal differentiated cells (1806.5 [1757.0 – 1842.0] vs. 1784.0 [1732.0 – 1843.0], $p = 0.031$) and fewer karyorrhectic cells (12.0 [9.0 – 29.0] vs. 18.0 [11.0 – 30.0], $p = 0.048$) than those without. PLWH with LTBI had fewer karyorrhectic cells than those without (11.5 [8.0 – 29.0] vs. 18.0 [11 – 30], $p = 0.006$).

CONCLUSION: We hypothesized that previous exposure to Mtb is associated with cytogenetic damage among PLWH. We found that exposure to Mtb is associated with more normal differentiated cells and less frequent karyorrhexis (a feature of apoptosis). It is unclear whether this increases the propensity for tumorigenesis.

HIV-related lung cancer in Uganda: a cohort study

Joseph Baruch Baluku^{1,2}, Naghib Bogere³, Sharon Namiiro¹, Victoria Walusansa³, Irene Andia-Biraro⁴, William Worodria^{4,5} & Bruce Kirenga^{1,4}

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- 5 Mulago National Referral Hospital, Kampala, Uganda

Link: <https://doi.org/10.1186/s13027-022-00439-x>

BACKGROUND: There are few reports on lung cancer among people with HIV (PWH) in Sub-Saharan Africa. In this report, we describe a cohort of PWH and lung cancer at the Uganda Cancer Institute.

METHODS: This retrospective cohort of PWH and lung cancer was managed at the Uganda Cancer Institute between 2008 and 2018. Sociodemographic and clinical data were abstracted from the patient charts. The median survival from diagnosis to death, loss-to-follow up or 31st December 2018, was estimated.

RESULTS: There were 18 people with HIV and lung cancer. The median (interquartile range, IQR) age was 49.5 (38.8–56.0) years, 11 (61.1%) were women and 5 (27.8%) were smokers. Of the 18 PWH, 13 (72.2%) were on antiretroviral therapy and the median (IQR) CD4 count (n=13) was 380 (243.5–595) cells per mm³. Difficulty in breathing (88.9%), chest pain (78.6%, n=11), cough (76.5%, n=17) and weight loss (72.2%) were the commonest symptoms while pleural effusions were observed in 12 (66.7%). In this cohort, 8 (44.4%) were presumptively treated for tuberculosis before the diagnosis of lung cancer. Seven (38.9%) had an Eastern Cooperative Oncology Group performance status of 3. Non-small cell lung cancer was the predominant histological type observed in 17 (94.4%) of whom 14 (82.4%) had adenocarcinoma. Majority of PWH had stage IV disease (88.9%). The median (IQR) survival was 3.3 (1.1–13.2) months and all were either dead (72.2%) or lost-to-follow up (27.8%) at five years from diagnosis.

CONCLUSION: People with HIV and lung cancer in Uganda report low rates of smoking, present with advanced disease and post very poor survival rates. There is need for biomarkers for early detection of lung cancer in HIV.

A systematic review of strategies adopted to scale up COVID-19 testing in low-, middle- and high-income countries

Winters Muttamba,^{1,2} Bernadette Ann-Marie O'Hare,¹ Vibhor Saxena,¹ Mudarshiru Bbuye,² Parul Tyagi,¹ Andrew Ramsay,¹ Bruce Kirenga,² Wilber Sabiiti¹

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Link: <https://doi.org/10.1136/bmjopen-2022-060838>

OBJECTIVE: We undertook a systematic review of strategies adopted to scale up COVID-19 testing in countries across income levels to identify successful approaches and facilitate learning.

METHODS: Scholarly articles in English from PubMed, Google scholar and Google search engine describing strategies used to increase COVID-19 testing in countries were reviewed. Deductive analysis to allocate relevant text from the reviewed publications/reports to the a priori themes was done.

MAIN RESULTS: The review covered 32 countries, including 11 high-income, 2 upper-middle-income, 13 lower-middle-income and 6 low-income countries. Most low- and middle-income countries (LMICs) increased the number of laboratories available for testing and deployed sample collection and shipment to the available laboratories. The high-income countries (HICs) that is, South Korea, Germany, Singapore and USA developed molecular diagnostics with accompanying regulatory and legislative framework adjustments to ensure the rapid development and use of the tests. HICs like South Korea leveraged existing manufacturing systems to develop tests, while the LMICs leveraged existing national disease control programmes (HIV, tuberculosis, malaria) to increase testing. Continent-wide, African Centres for Disease Control and Prevention-led collaborations increased testing across most African countries through building capacity by providing testing kits and training.

CONCLUSION: Strategies taken appear to reflect the existing systems or economies of scale that a particular country could leverage. LMICs, for example, drew on the infectious disease control programmes already in place to harness expertise and laboratory capacity for COVID-19 testing. There however might have been strategies adopted by other countries but were never published and thus did not appear anywhere in the searched databases.

Strategies to resolve the gap in Adolescent Tuberculosis care at four health facilities in Uganda: The TEEN TB pilot project

Samson Omongot^{*1,6}, Winters Muttamba^{1,2}, Irene Najjingo¹, Joseph Baruch Baluku^{1,3}, Sabrina Kitaka⁴, Stavia Turyahabwe⁵, Bruce Kirenga^{1,6}

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INTRODUCTION: In 2021, an estimated 10.6 million people fell ill with tuberculosis (TB) globally, 1.2 million of these were children. About 40% of them aged between 5 and 14 years with TB are missed annually. In Uganda, 44% of adolescents with chronic cough of ≥ 2 weeks do not seek care from health facilities. Therefore, strategies to promote health care-seeking behaviour among adolescents are urgently needed. We piloted a project (TEEN TB project) aimed at improving uptake of tuberculosis (TB) care services among adolescents at Ugandan health facilities.

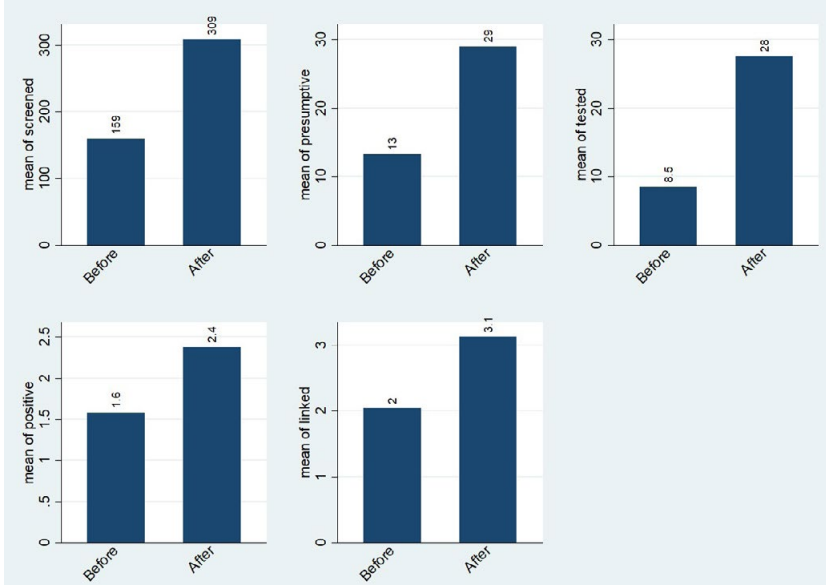
METHODOLOGY: We developed an adolescent TB awareness and screening package using the human centred design. This technique puts real people at the centre of the development process. The package consisted of 3 interventions (TB screening cards, adolescent-TB awareness poster messages and a local TB awareness song) deployed in the project health facilities and their surrounding communities. Data on socio-demographic and clinical characteristics of adolescents were collected for the period between October 2021 and March 2022 at 4 project health facilities (Kawolo, Iganga, Gombe and Kiwoko). We collected before and after intervention data from facility level records to determine the effect of the package.

RESULTS: A total of 394 adolescents were included and the majority (76%) were still in school. Overall, the intervention improved adolescent TB care in the four project health facilities. The average number of adolescents screened increased by 94% from 159 to 309, with an incidence rate ratio (IRR) of 1.9 (95% CI: 1.9- 2.0, $p < 0.001$), there was a 2-fold increase among those presumed to have TB; from 13 to 29, IRR of 2.2 (95% CI: 1.9-2.5, $p < 0.001$) and those tested with GeneX-pert and microscopy increased more than 3 times from 8 to 28, IRR of 3.3 (95% CI: 2.8-3.8, $p < 0.001$). There was a minimal increase in the average monthly number of adolescents with a positive result from 1.6 to 2.4 and linkage to TB care services from 2 to 3.1. These were not statistically significant at $p=0.170$ and $p=0.154$ respectively.

CONCLUSION: The project improved uptake of TB services among adolescents along the TB care cascade (screening, TB testing and linkage to care). We recommend a robust and fully powered randomized controlled trial to evaluate the effectiveness of

the package.

Figure 1. Bar graph showing the overall six months average scores for adolescents screened, presumptive, tested, positive and linked to treatment and care before & after the intervention.



Evaluation of circulating serum cathelicidin levels as a potential biomarker to discriminate between active and latent tuberculosis in Uganda

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Link: <https://doi.org/10.1371/journal.pone.0272788>

BACKGROUND: Tuberculosis remains a major public health problem worldwide accounting for 1.4 million deaths annually. LL-37 is an effector molecule involved in immunity with both antimicrobial and immunomodulatory properties. The purpose of this study was to compare LL-37 circulatory levels among participants with active and latent tuberculosis and to determine its ability to discriminate between the two infectious states.

METHODS: A cross-sectional study was performed among 56 active tuberculosis patients, 49 latent tuberculosis individuals, and 43 individuals without tuberculosis infection. The enzyme-linked immunosorbent assay was used to assess LL-37 levels. Data analysis was performed using STATA software and Graph pad Prism version 8. Mann-Whitney U test was used for correlation between variables with two categories and the Kruskal-Wallis test for three or more categories.

RESULTS: The study had more female participants than males, with similar median ages across the three groups, 29.5, 25.0, and 23.0 years respectively. Active tuberculosis patients had significantly higher LL-37 levels compared to those with latent tuberculosis and without tuberculosis. The median/interquartile ranges were 318.8 ng/ml (157.9–547.1), 242.2 ng/ml (136.2–579.3), 170.9 ng/ml (129.3–228.3); $p = 0.002$ respectively. Higher LL-37 was found in the male participant with median/interquartile range, 424.8 ng/ml (226.2–666.8) compared to the females 237.7 ng/ml (129.6–466.6); $p = 0.045$. LL-37 had better discriminatory potential between active tuberculosis and no tuberculosis (AUC = 0.71, sensitivity 71.4% specificity = 69.8%) than with latent tuberculosis (AUC = 0.55, sensitivity = 71.4%, specificity = 44.9%). There was moderate differentiation between latent tuberculosis and no tuberculosis (AUC = 0.63, sensitivity = 44.9% specificity = 90.7%).

CONCLUSION: Significantly higher LL-37 levels were observed among active tuberculosis patients than those without tuberculosis infection and were, therefore able to discriminate between active tuberculosis and other tuberculosis infectious states, especially with no tuberculosis. Further assessment of this biomarker as a screening tool to exclude tuberculosis is required.

Association of circulating serum free bioavailable and total vitamin D with cathelicidin levels among active TB patients and household contacts

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Link: <https://www.nature.com/articles/s41598-023-32543-2>

ABSTRACT

The free hormone hypothesis postulates that the estimation of free circulating 25 (OH)D may be a better marker of vitamin D status and is of clinical importance compared to total vitamin D fraction. The unbound fraction is involved in biological activities since it is able to penetrate into the cell. Studies have shown that cathelicidin/LL-37 inhibits the growth of *Mycobacterium tuberculosis* in a vitamin D-dependent manner and therefore adequate vitamin D is required for its expression. The study aimed to determine the association between serum bioavailable and total vitamin D with LL-37 levels in ATB patients, LTBI, and individuals with no TB infection. This was a cross-sectional study in which bioavailable vitamin D and LL-37 levels were measured using competitive ELISA kits and total vitamin D was measured using electrochemiluminescence and consequently determined their association. The mean (SD) bioavailable vitamin D levels of the study participants were 3.8 ng/mL (2.6) and the median (IQR) of LL-37 levels were 320 ng/mL (160, 550 ng/mL). The mean (SD) of total vitamin D levels was 19.0 ng/mL (8.3) ng/mL. Similar weak correlations were observed between the bioavailable and total vitamin D with LL-37 levels, therefore, deviating from our hypothesis.

Distinguishing pulmonary rehabilitation from chest physiotherapy in the African context

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Link: https://dx.doi.org/10.25259/JPATS_1_2023

ABSTRACT

Chronic respiratory diseases (CRDs) are highly prevalent in low- and middle-income countries. In Africa, the burden of CRDs is set to worsen due to an increase in smoking prevalence and household air pollution. Chest physiotherapy (CP) and pulmonary rehabilitation (PR) are used to manage CRDs in Africa, but distinguishing between these terms is not clear common among health-care professionals (HCPs) and patients. Here, we provide clarity on the differences between PR and CP to facilitate a greater understanding of PR and remove barriers to research and implementation of PR across Africa. CP is a treatment aimed at clearing secretions within airways of the lungs, while PR, through exercise training, education and self-management, treats extrapulmonary or systemic impairments. We know that there is a need for PR among people living with CRDs in Africa. However, health professionals' knowledge and training in PR remains insufficient. To implement PR services for people with CRDs in Africa, a strong understanding of what PR is, and its evidence base are needed. The development of PR in Africa will start by filling the gaps in knowledge, awareness, advocacy, and training.

Risk factors for disruptions in tuberculosis care in Uganda during the COVID-19 pandemic

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During the COVID-19 pandemic, TB mortality increased while diagnoses decreased, likely due to care disruption. In March, 2020, Uganda—a country with high TB burden, implemented a COVID-19 lockdown with associated decrease in TB diagnoses. This study aims to examine patient level risk factors for disruption in TB care during the COVID-19 pandemic in Uganda. This retrospective cross-sectional cohort study included six TB clinics in Uganda. Clustered sampling included phases of TB care and three time-periods: pre-lockdown, lockdown and post-lockdown. Characteristics of patients with TB care disruption (TBCD), defined as those with > 2 months of symptoms prior to diagnosis or who missed a TB clinic, and those without TB care disruption (non-TBCD) were analyzed between time-periods. 1,624 charts were reviewed; 1322 were contacted, 672 consented and completed phone interview; pre-lockdown (n = 213), lockdown (n = 189) and post-lockdown (n = 270). TBCD occurred in 57% (385/672) of patients. There was an increase in the proportion of urban patients in the TBCD and non-TBCD groups during post-lockdown (p <0.001). There was no difference in demographics, HIV co-infection, socioeconomic status, or distance to TB clinic between TBCD and non-TBCD groups or within TBCD by time-period. There were few differences amongst TBCD and all TB patients by time-period. The increase in urban patients' post-lockdown may represent a portion of urban patients who delayed care until post-lockdown. Insignificant trends suggesting more TBCD amongst those who lived further from clinics and those without HIV-coinfection require more investigation.

Leveraging the structures of the COVID-19 pandemic response for successful control of Ebola in Uganda

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Abstract

This epidemic presented unique challenges that the Uganda government had not faced before. Mubende district — the epicenter of the epidemic — is traversed by a major highway that connects Uganda to the neighboring countries of Democratic Republic of Congo (DRC), Rwanda, Tanzania, and Kenya. Mubende district is also only 150 kilometers (a 3-hour drive) from the capital city, Kampala (population 3.8 million), which eventually experienced spread of the virus. This connectivity required unique approaches to stop transmission in the densely populated urban and peri-urban areas, and to avert international spread through the highly active air and ground transportation networks. The epicenter also has mining activities and diverse communities from neighboring countries, which presented cultural challenges for risk communication and community engagement, and further increased the potential for regional spread. These factors led the WHO to classify the threat as category 3, warning that the epidemic was likely to spread across international borders⁷. The successful control of the epidemic within 113 days, without locking down the capital city, was guided by two factors: lessons from the COVID-19 pandemic, and recent successes in responding to EVD epidemics in DRC.

Implication of the Global Initiative for Chronic Obstructive Lung Disease 2023 report for resource-limited settings: tracing the G in the GOLD

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Link: <https://doi.org/10.1183/13993003.00484-2023>

Abstract

The new Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2023 report provides a very useful synthesis of available scientific evidence to guide COPD management, research and prevention, as always. Important changes include the revision of the definition of the condition and the replacement of groups C and D with E, which highlights the importance of exacerbations in COPD. We reviewed the report to examine how well it addresses the issues surrounding COPD in Africa and other resource-limited settings. We commend the report for highlighting that COPD not related to cigarette smoking constitutes half of all COPD globally. In resource-limited settings, exposure to biomass smoke while cooking, outdoor air pollution and occupational exposure are the biggest drivers of COPD, especially among women. Pulmonary tuberculosis and HIV are also notable risk factors for COPD in this setting, with over 20% of COPD patients reporting having had a history of pulmonary tuberculosis. In a study in rural Uganda, only 8% of women with COPD were current smokers, 84% had never smoked and >90% of people in the cohort had biomass exposure throughout their lives [4]. The report could have included more details on the importance of reducing or eliminating household air pollution exposure. Furthermore, the report points out the role of poverty-related exposures as another significant contributor to COPD in resource-limited settings. There are, however, other poverty-related factors associated with COPD in these settings, such as nutrition and infection, especially in early childhood. The report identifies childhood factors that impair lung growth and result in COPD in adulthood. Identified factors include prematurity, low birth weight, maternal smoking during pregnancy, repeated respiratory infections and poor nutrition, among others. We believe that household air pollution should be mentioned here as well. Young children (even before birth when a pregnant woman is cooking) are exposed to high levels of household air pollution, probably causing lifelong harm. The report states that spirometry is needed to confirm the diagnosis of COPD, but spirometry is rarely available in Africa. Given the prevalence of COPD, resources need to be made

available to make the diagnosis. Screening questionnaires or peak expiratory flow testing are better than nothing. Our group used symptom and risk factor screening followed by peak expiratory flow testing and found it to be fairly accurate and feasible [6]. The report now recommends a combination of long-acting β -agonist (LABA) and long-acting muscarinic antagonist (LAMA) for all patients in groups B and E, with a possibility of adding inhaled corticosteroids to those with high peripheral blood eosinophils. Generally, inhaled medications are hard to access in most of Africa. LAMA/LABAs are not widely available. Cheaper and more available alternatives should be included as alternatives in low-resource settings. However, other affordable interventions should be prominently promoted in resource-limited settings, including vaccinations for respiratory infections, pulmonary rehabilitation and surgical treatments.

In conclusion, the report is an excellent resource for understanding COPD and how best to manage it now. However, we agree with TABYSHOVA et al. that COPD guidelines still have blind spots for low-resource.

Cross-sectional validation of the COPD Assessment Test (CAT) among chronic obstructive pulmonary disease patients in rural Uganda

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Abstract

Measuring quality of life is a key component in the management of Chronic Obstructive Pulmonary Disease (COPD). The COPD assessment test (CAT), an easy to administer and shorter instrument than the standard Saint George's respiratory questionnaire (SGRQ), could be an alternative tool for measuring the quality of life of COPD patients in rural Uganda. A cross-sectional study was conducted between June and August 2022, consecutively recruiting 113 COPD patients aged > 40 years from the Low-Dose Theophylline for the management of Biomass-associated COPD (LODOT-BCOPD) study. Upon obtaining consent, participants answered an interviewer administered social demographic, CAT and SGRQ questionnaire. Internal consistency for both SGRQ and CAT was determined using Cronbach's alpha coefficient and values > 0.7 were considered acceptable while correlations were determined using Spearman's rank correlation. Limits of Agreement were visualised using Bland Altman and pair plots. Of the 113 participants, 51 (45.1%) were female. The mean age was 64 ± 12 years, 19 (16.8%) had history of smoking while majority (112 (99.1%)) reported use of firewood for cooking. There was a strong correlation of 0.791 (p < 0.001) between the CAT and SGRQ total scores with a high internal consistency of CAT, Cronbach's alpha

coefficient of 0.924 (0.901–0.946). The agreement between the absolute CAT scores and the SGRQ scores was good with a mean difference of -0.932 (95% Confidence Interval: -33.49–31.62). In summary, CAT has an acceptable validity and can be used as an alternative to the SGRQ to assess the quality of life of COPD patients in rural Uganda.

Respiratory Health and Cities

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Link: <https://doi.org/10.1164/rccm.202304-0759vp>

Abstract

We practice medicine in an ever-changing world. An increasing proportion of the global population lives in cities and other urban areas. What does this mean for the respiratory health of those living in cities and their clinicians? The challenges of living in rural areas have been well described and center on poor access to expert health care (1) because of fewer providers; workforce shortages; greater travel distances; and, therefore, increased costs. The greater likelihood of proximity to expertise in cities masks several problems that are particularly relevant to respiratory health. These need specific consideration if we are to advocate for appropriate healthcare for all. Some of these problems are shared across high-income countries and low- and middle-income countries (LMICs), but the greatest challenges relate to rapid urbanization in LMICs. In this Viewpoint, we discuss the challenges of urban respiratory health. We argue that our community must lobby for better respiratory health in cities to reduce the future burden of disease.

Cost of treatment support for multidrug-resistant tuberculosis using patient-centred approaches in Ethiopia: a model-based method

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BACKGROUND: Patient and health system costs for treating multidrug-resistant tuberculosis (MDR-TB) remain high even after treatment duration was shortened. Many patients do not finish treatment, contributing to increased transmission and antimicrobial resistance. A restructure of health services, that is more patient-centred has the potential to reduce costs and increase trust and patient satisfaction. The aim of the study is to investigate how costs would change in the delivery of MDR-TB care in Ethiopia under patient-centred and hybrid approaches compared to the current standard-of-care.

METHODS: We used published data, collected from 2017 to 2020 as part of the Standard Treatment Regimen of Anti-Tuberculosis Drugs for Patients with MDR-TB (STREAM) trial, to populate a discrete event simulation (DES) model. The model was developed to represent the key characteristics of patients' clinical pathways following each of the three treatment delivery strategies. To the pathways of 1000 patients generated by the DES model we applied relevant patient cost data derived from the STREAM trial. Costs are calculated for treating patients using a 9-month MDR-TB treatment and are presented in 2021 United States dollars (USD).

RESULTS: The patient-centred and hybrid strategies are less costly than the standard-of-care, from both a health system (by USD 219 for patient-centred and USD 276 for the hybrid strategy) and patient perspective when patients do not have a guardian (by USD 389 for patient-centred and USD 152 for the hybrid strategy). Changes in indirect costs, staff costs, transport costs, inpatient stay costs or changes in directly-observed-treatment frequency or hospitalisation duration for standard-of-care did not change our results.

CONCLUSION: Our findings show that patient-centred and hybrid strategies for delivering MDR-TB treatment cost less than standard-of-care and provide critical evidence that there is scope for such strategies to be implemented in routine care. These results should be used inform country-level decisions on how MDR-TB is delivered and also the design of future implementation trials.

Barriers to childhood asthma care in sub-Saharan Africa: a multicountry qualitative study with children and their caregivers.

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Link: <http://dx.doi.org/10.1136/> | <http://dx.doi.org/10.1136/bmjopen-2022-070784>

OBJECTIVES: This study identifies barriers and provides recommendations to improve asthma care in children across sub-Saharan Africa, where qualitative data is lacking despite high rates.

DESIGN: One of the aims of our National Institute for Health Research global health research group 'Achieving Control of Asthma in Children in Africa' was to use qualitative thematic analysis of transcribed audio recordings from focus group discussions (FGDs) to describe barriers to achieving good asthma control.

SETTING: Schools in Blantyre (Malawi), Lagos (Nigeria), Durban (South Africa), Kampala (Uganda) and Harare (Zimbabwe).

PARTICIPANTS: Children (n=136), 12–14 years with either asthma symptoms or a diagnosis and their caregivers participated in 39 FGDs. All were recruited using asthma control questions from the Global Asthma Network survey.

RESULTS: There were four key themes identified: (1) Poor understanding, (2) difficulties experienced with being diagnosed, (3) challenges with caring for children experiencing an acute asthma episode and (4) suboptimal uptake and use of

prescribed medicines. An inadequate understanding of environmental triggers, a hesitancy in using metred dose inhalers and a preference for oral and alternate medications were identified as barriers. In addition, limited access to healthcare with delays in diagnosis and an inability to cope with expected lifestyle changes was reported. Based on these findings, we recommend tailored education to promote access to and acceptance of metred dose inhalers, including advocating for access to a single therapeutic, preventative and treatment option. Furthermore, healthcare systems should have simpler diagnostic pathways and easier emergency access for asthma.

CONCLUSIONS: In a continent with rapidly increasing levels of poorly controlled asthma, we identified multiple barriers to achieving good asthma control along the trajectory of care. Exploration of these barriers reveals several generalisable recommendations that should modify asthma care plans and potentially transform asthma care in Africa.

Unmet Diagnostic and Therapeutic Opportunities for Chronic Obstructive Pulmonary Disease in Low- and Middle-Income Countries.

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Link: <https://doi.org/10.1164/rccm.202302-0289OC>

RATIONALE: Chronic obstructive pulmonary disease (COPD) is a prevalent and burdensome condition in low- and middle-income countries (LMICs). Challenges to better care include more effective diagnosis and access to affordable interventions. There are no previous reports describing therapeutic needs of populations with COPD in LMICs who were identified through screening.

OBJECTIVES: To describe unmet therapeutic need in screening-detected COPD in LMIC settings.

METHODS: We compared interventions recommended by the international Global Initiative for Chronic Obstructive Lung Disease COPD strategy document, with that received in 1,000 people with COPD identified by population screening at three LMIC sites in Nepal, Peru, and Uganda. We calculated costs using data on the availability and affordability of medicines.

MEASUREMENT AND MAIN RESULTS: The greatest unmet need for nonpharmacological interventions was for education and vaccinations (applicable to all), pulmonary rehabilitation (49%), smoking cessation (30%), and advice on biomass smoke exposure (26%). Ninety-five percent of the cases were previously undiagnosed, and few were receiving therapy (4.5% had short-acting β -agonists). Only three of 47 people (6%) with a previous COPD diagnosis had access to drugs consistent with recommendations. None of those with more severe COPD were accessing appropriate maintenance inhalers. Even when available, maintenance treatments were unaffordable, with 30 days of treatment costing more than a low-skilled worker's daily average wage.

CONCLUSIONS: We found a significant missed opportunity to reduce the burden of COPD in LMIC settings, with most cases undiagnosed. Although there is unmet need in developing novel therapies, in LMICs where the burden is greatest, better diagnosis combined with access to affordable interventions could translate to immediate benefit.

A cross-country qualitative analysis of teachers' perceptions of asthma care in sub-Saharan Africa

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Abstract

Asthma is the most common chronic respiratory disease among school-going adolescents worldwide. However, the burden of severe asthma is highest in Sub-Saharan Africa. This study aimed to explore teachers' perceptions of asthma care across six African countries. We conducted focus group discussions (FGDs) using a semi-structured interview guide. Interviews were audio-recorded, transcribed verbatim and analysed thematically. FGDs were conducted in Kumasi (Ghana), Blantyre (Malawi), Lagos (Nigeria), Durban (South Africa), Kampala (Uganda), and Harare (Zimbabwe) between 01 November 2020 and 30 June 2021. We identified two key themes related to asthma care; barriers to asthma care and suggestions to improve the care of adolescents with asthma. Barriers reported by teachers included a lack of knowledge and skills among themselves, adolescents, and caregivers. In

addition, some traditional beliefs of teachers on asthma exacerbated challenges with asthma care in schools. Regarding suggestions, most teachers identified a need for all-inclusive asthma training programmes for teachers, adolescents and caregivers, focusing on acute episodes and mitigating triggers. Utilising teachers with personal experiences with asthma to advocate and support these initiatives was suggested. Further suggestions included the need for annual screening to enable early identification of adolescents with asthma and clarify restrictions on teachers administering asthma medications. Teachers across African schools identify multiple barriers to asthma care. Structured school education programs and annual asthma screening are key to addressing some barriers to care.

Clinical features, resistance patterns and treatment outcomes of drug-resistant extra-pulmonary tuberculosis: A scoping review

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BACKGROUND: Drug-resistant tuberculosis (DR-TB) is a threat to tuberculosis (TB) control. Extra-pulmonary forms of DR-TB (DR-epTB) are not well characterized. This review summarizes the clinical features, resistance patterns and treatment outcomes of DR-epTB.

METHODS: We searched EMBASE to identify studies that reported drug-resistance among extra-pulmonary TB sites. All age groups were included in this review. Studies which did not describe drug-resistance patterns at extra-pulmonary TB sites were excluded. We summarized the proportion of resistance to individual anti-TB drugs as well as multi-drug resistant (MDR), pre-extensively drug resistant (pre-XDR) and extensively drug-resistant (XDR) TB.

RESULTS: Eighteen studies with a total of 10,222 patients with extra-pulmonary TB of whom 1,236 (12.0%) had DR-epTB, were included in this review. DR-epTB was mostly reported in young people aged 28 to 46 years. While TB meningitis is the most commonly studied form, adenitis is the commonest form of DR-epTB reported in 21% to 47%. Central nervous system TB (3.8% to 51.6%), pleural TB (11.3% to 25.9%), skeletal TB (9.4% to 18.1%), abdominal TB (4.3% to 6.5%), and disseminated TB (3.8%) are also encountered. The HIV co-infection rate is reported to be 5.0% to 81.3% while 2.6% to 25.4 % have diabetes mellitus. Clinical symptoms of DR-epTB are consistent with morbidity in the affected body system. Among patients with DR-epTB, the proportion of MDR TB was 5% to 53% while that for pre-XDR TB and XDR TB was 3% to 40% and 4% to 33%, respectively. Treatment success is achieved in 26% to 83% of patients with DR-epTB while death, treatment loss-to-follow up, and treatment failure occur in 2% to 76%, 7% to 15%, and 0% to 4% respectively. Patients with DR-epTB were reported to have poorer outcomes than those with pulmonary DR-TB and extra-pulmonary drug-susceptible TB.

Conclusion: Clinical features of DR-epTB are similar to those observed among people with drug-susceptible EPTB but patients with DR-epTB post worse treatment outcomes.

LIST OF
PUBLICATIONS
2021/22

The availability, cost, and affordability of essential medicines for asthma and COPD in low-income and middle-income countries: a systematic review

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BACKGROUND: Asthma and [chronic obstructive pulmonary disease](#) (COPD) cause a considerable burden of morbidity and mortality in low-income and middle-income countries (LMICs). Access to safe, effective, quality-assured, and affordable essential medicines is variable. We aimed to review the existing literature relating to the availability, cost, and affordability of WHO's essential medicines for asthma and COPD in LMICs.

METHODS: A [systematic review](#) of the literature was done by searching seven databases to identify research articles published between Jan 1, 2010, and June 30, 2022. Studies on named essential medicines for asthma and COPD in LMICs were included and review articles were excluded. Two authors (MS and HT) screened and extracted data independently, and assessed bias using Joanna Briggs Institute appraisal tools. The main outcome measures were availability (WHO target of 80%), cost (compared with median price ratio [MPR]), and affordability (number of days of work of the lowest paid government worker). The study was registered with PROSPERO, CRD42021281069.

FINDINGS: Of 4742 studies identified, 29 met the inclusion criteria providing data

from 60 LMICs. All studies had a low risk of bias. Six of 58 countries met the 80% availability target for short-acting beta-agonists (SABAs), three of 48 countries for inhaled corticosteroids (ICSs), and zero of four for inhaled corticosteroid–long-acting beta-agonist (ICS–LABA) combination inhalers. Costs were reported by 12 studies: the range of MPRs was 1.1–351 for SABAs, 2.6–340 for ICSs, and 24 for ICS–LABAs in the single study reporting this. Affordability was calculated in ten studies: SABA inhalers typically cost around 1–4 days' wages, ICSs 2–7 days, and ICS–LABAs at least 6 days. The included studies showed heterogeneity.

INTERPRETATION: Essential medicines for treating asthma and COPD were largely unavailable and unaffordable in LMICs. This was particularly true for inhalers containing corticosteroids.

Impact of on-site Xpert on TB diagnosis and mortality trends in Uganda

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SETTING: Since 2012, Uganda expanded the Xpert® MTB/RIF network for diagnosis of TB.

OBJECTIVES: We compared TB care cascades at health facilities with on-site Xpert vs. facilities that accessed the assay through specimen referral.

DESIGN: We analysed secondary aggregate data of the National TB and Leprosy Program (NTLP) from 2016 to 2019. We computed the proportions of notified TB cases and mortality ratios in relation to the estimated TB burden.

RESULTS: TB case notifications per annum increased from 24,287 in 2016 to 30,739 in 2019, and the proportion of cases diagnosed at facilities with on-site Xpert testing increased from 62% (15,070/24,287) to 81% (24,829/30,739) ($P = 0.41$), while it increased at facilities without on-site Xpert from 6.9% (638/9,217) to 8.8% (521/5,910) ($P = 0.23$). Furthermore, mortality among TB-HIV co-infected patients at facilities with on-site Xpert dropped from 5.0% (760/15,070) in 2016 to 4.8% (1,187/24,826) in 2019 ($P = 0.84$) compared to 4.4% (407/9,217) in 2016 to 5.3% (315/5,910) in 2019 ($P = 0.57$).

CONCLUSION: Wider installation and decentralisation of Xpert leads to increased case-finding. However, the impact on reduction in mortality remains limited. Interventions to address TB-related mortality in addition to Xpert roll-out are required.

Facilitators and barriers to the implementation of improved solid fuel cookstoves and clean fuels in low-income and middle-income countries: an umbrella review

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SUMMARY: 2·6 billion people rely on solid fuels for cooking or heating. Accelerating access to cleaner solutions is crucial to reduce the negative effects of solid fuel use. Despite abundant evidence on how to implement these solutions, previous attempts have been disappointing. An overview of the evidence is missing and the translation of the evidence into practice is poor. We conducted an umbrella review using eight databases to: consolidate evidence on the factors that influence the implementation of improved solid fuel cookstoves and clean fuels in low-income and middle-income countries; weigh the level of confidence in existing evidence; and develop two practical implementation strategy tools. We identified 31 relevant reviews (13 systematic reviews and 18 narrative reviews) that covered over 479 primary studies. We found 15 implementation factors supported by the highest level of evidence. Regarding improved solid fuel cookstoves, these factors included: cost; knowledge and beliefs about the innovation; and compatibility. For clean fuels these factors included: cost; knowledge and beliefs about the innovation; and external policy and incentives. The factors were synthesised into the Cleaner Cookstove Implementation Tool and the Clean Fuel Implementation Tool. These tools can be used to optimise the implementation of cleaner cooking solutions, thereby improving health, environmental, climate, and gender equity outcomes.

Systematic Review of Physical Activity, Sedentary Behaviour and Sleep Among Adults Living with Chronic Respiratory Disease in Low- and MiddleIncome Countries

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ABSTRACT: Physical activity (PA), sedentary behaviour (SB) and sleep are important lifestyle behaviours associated with chronic respiratory disease (CRD) morbidity and mortality. These behaviours need to be understood in low- and middle-income countries (LMIC) to develop appropriate interventions.

PURPOSE: Where and how have free-living PA, SB and sleep data been collected for adults living with CRD in LMIC? What are the free-living PA, SB and sleep levels of adults living with CRD?

PATIENTS AND METHODS: The literature on free-living PA, SB and sleep of people living with CRD in LMIC was systematically reviewed in five relevant scientific databases. The review included empirical studies conducted in LMIC, reported in any language. Reviewers screened the articles and extracted data on prevalence, levels and measurement approach of PA, SB and sleep using a standardised form. Quality of reporting was assessed using bespoke criteria.

RESULTS: Of 89 articles, most were conducted in Brazil (n=43). PA was the commonest behaviour measured (n=66). Questionnaires (n=52) were more commonly used to measure physical behaviours than device-based (n=37) methods. International Physical Activity Questionnaire was the commonest for measuring PA/SB (n=11). For sleep, most studies used Pittsburgh Sleep Quality Index (n=18). The most common ways of reporting were steps per day (n=21), energy expenditure (n=21), sedentary time (n=16), standing time (n=13), sitting time (n=11), lying time (n=10) and overall sleep quality (n=32). Studies revealed low PA levels [steps per day (range 2669–7490steps/day)], sedentary lifestyles [sitting time (range 283–418min/day); standing time (range 139–270min/day); lying time (range 76–119min/day)] and poor sleep quality (range 33–100%) among adults with CRD in LMIC.

CONCLUSION: Data support low PA levels, sedentary lifestyles and poor sleep among people in LMIC living with CRDs. More studies are needed in more diverse populations and would benefit from a harmonised approach to data collection for international comparisons.

Molecular characterisation of second-line drug resistance among drug resistant tuberculosis patients tested in Uganda: a two and a half-year's review

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ABSTRACT: Second-line drug resistance (SLD) among tuberculosis (TB) patients is a serious emerging challenge towards global control of the disease. We characterized SLD-resistance conferring-mutations among TB patients with rifampicin and/or isoniazid (RIF and/or INH) drug-resistance tested at the Uganda National TB Reference Laboratory (NTRL) between June 2017 and December 2019. This was a descriptive cross-sectional secondary data analysis of 20,508 M. tuberculosis isolates of new and previously treated patients' resistant to RIF and/or INH. DNA strips with valid results to characterise the SLD resistance using the commercial Line Probe Assay Genotype MTBDRsl Version 2.0 Assay (Hain Life Science, Nehren, Germany) were reviewed. Data were analysed with STATAv15 using cross-tabulation for frequency and proportions of known resistance-conferring mutations to injectable agents (IA) and fluoroquinolones (FQ). Among the eligible participants, 12,993/20,508 (63.4%) were male and median (IQR) age 32 (24–43). A total of 576/20,508 (2.8%) of the M. tuberculosis isolates from participants had resistance to RIF and/or INH. These included; 102/576 (17.7%) single drug-resistant and 474/576 (82.3%) multidrug-resistant (MDR) strains. Only 102 patients had test results for FQ of whom 70/102 (68.6%) and 01/102 (0.98%) had resistance-conferring mutations in the *gyrA* locus and *gyrB* locus respectively.

Among patients with FQ resistance, gyrAD94G 42.6% (30.0–55.9) and gyrA A90V 41.1% (28.6–54.3) mutations were most observed. Only one mutation, E540D was detected in the gyrB locus. A total of 26 patients had resistance-conferring mutations to IA in whom, 20/26 77.0% (56.4–91.0) had A1401G mutation in the rrs gene locus. Our study reveals a high proportion of mutations known to confer high-level fluoroquinolone drug-resistance among patients with rifampicin and/or isoniazid drug resistance. Utilizing routinely generated laboratory data from existing molecular diagnostic methods may aid real-time surveillance of emerging tuberculosis drug-resistance in resource-limited settings.

Asthma care in sub-Saharan Africa: Mind the gap!

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Link: <https://t.ly/40dec>

ABSTRACT: Asthma is the most common chronic disease in children and adolescents globally and one of the most common chronic diseases in adults.[1-3] The World Health Organization (WHO) and others have highlighted asthma as an underappreciated cause of poverty in low-and middle-income countries that hold back economic and social development, erode the health and well-being of those affected, and have a negative impact on families and societies.[4-6] Asthma is a recognized cause of catastrophic health expenditure and a threat to universal health coverage.[7] The WHO succinctly states “that in children with asthma, poverty aggravates asthma and asthma aggravates poverty.”[8] Children miss out on education, adults lose days at work and the costs of medicines, emergency visits, and hospitalization are major financial burdens not only for individuals and their families but also for struggling health systems.[4-8]

Asthma prevalence has been increasing across Africa: In 1990, about 11.7%(74 million including 34.1 million children) of the population had asthma; by 2010, this

had increased to 12.8%(119 million including 49.7 million children).[9] Despite the high prevalence, there are limited data about the burden and determinants of asthma in sub-Saharan Africa.[10, 11] Asthma morbidity in sub-Saharan Africa today is further compounded by myths and stigma; however, a positive lesson of history from high-income counties is that these can be overcome.[12-14].

Hypovitaminosis D among newly diagnosed pulmonary TB patients and their household contacts in Uganda

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ABSTRACT: An estimated one billion people globally live with hypovitaminosis D. Studies have indicated that vitamin D deficiency is a risk factor for active tuberculosis (TB) disease. The aim of this study was to determine the association between vitamin D deficiency and TB status among patients with active TB, latent TB infection (LTBI) and those without TB infection. In a cross-sectional study of active TB patients, LTBI, QuantiFERON GOLD testpositive and (QFN+TST+) household contact and controls QuantiFERON GOLD testnegative (QFN-TST-) samples vitamin D levels were compared. Vitamin D status was determined by measurement of total vitamin D levels with 56 samples of active TB patients, 17 with LTBI, and 22 without TB infection using electrochemiluminescence. The median interquartile range (IQR) age of the study participants was 28 (20–35) years, and the majority (63%) were females. The median (IQR) vitamin D levels were 18 ng/ml (14–24). All groups had vitamin D hypovitaminosis with significantly lower levels among active TB patients (17 ng/ml, 13, 2) than among LTBI individuals (23 ng/ml 16–29) and those without TB infection (22 ng/ml, 17–28).

Factors Associated with Linkage to HIV Care Among Oral Self-Tested HIV Positive Adults in Uganda

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BACKGROUND: HIV oral self-testing (HIVST) was rolled out in Uganda in 2018. However, data reported by public facilities show that less than 60% of oral self-tested HIV positive adults were linked to HIV care. This study set out to determine the factors associated with linkage to HIV care among adults with positive HIV oral self-test results in Uganda.

METHODS: A cross-sectional study was carried out at Nabweru HCIII and Entebbe Hospital in central Uganda. The study reviewed medical records from January 2019 to May 2020 and successfully invited 144 self-tested HIV positive participants for the quantitative interview process. Data on socio-demographics and health-related characteristics were collected. Bivariate and multivariable analysis was used to determine the factors associated with linkage to care.

RESULTS: The proportion of participants linked to HIV care was 69.6% (100/144). The majority of the participants were female (71%), with a mean age of 29 (± 8) years. Participants within age groups of 31–35 years and 41–60 years, who used directly assisted HIVST, disclosed their HIV status to their sexual partners, are ready to start ART, do not consume alcohol and having a supportive sexual partner were more likely to be linked to HIV care. Single participants, separated/divorced, female, fear unfair treatment after HIV status disclosure and those who fear ART side effects were less likely to be linked to HIV care.

CONCLUSION: Our study showed that less than 70% were linked to HIV care. It also shows that HIV status disclosure, readiness to start ART, type of HIVST used, fear of ART side effects, and being divorced/separated negatively associated with linkage to HIV care among self-test HIV positive adults. There is a need for HIV programs to address the above factors to improve linkage to HIV care to realize the national targets towards the UNAIDs 2035 goals.

Safety and efficacy of hydroxychloroquine for treatment of non-severe COVID-19 among adults in Uganda: a randomized open label phase II clinical trial

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BACKGROUND: Several repurposed drugs such as hydroxychloroquine (HCQ) have been investigated for treatment of COVID-19, but none was confirmed to be efficacious. While in vitro studies have demonstrated antiviral properties of HCQ, data from clinical trials were conflicting regarding its benefit for COVID-19 treatment. Drugs that limit viral replication may be beneficial in the earlier course of the disease thus slowing progression to severe and critical illness.

DESIGN: We conducted a randomized open label Phase II clinical trial from October–December 2020.

METHODS: Patients diagnosed with COVID-19 using RT-PCR were included in the study if they were 18 years and above and had a diagnosis of COVID-19 made in the last 3 days. Patients were randomized in blocks, to receive either HCQ 400 mg twice a day for the first day followed by 200 mg twice daily for the next 4 days plus standard of care (SOC) treatment or SOC treatment alone. SARS COV-2 viral load (CT values) from RT-PCR testing of samples collected using nasal/oropharyngeal swabs was performed at baseline, day 2, 4, 6, 8 and 10. The primary outcome was median time from randomization to SARS COV-2 viral clearance by day 6.

RESULTS: Of the 105 participants enrolled, 55 were assigned to the intervention group (HCQ plus SOC) and 50 to the control group (SOC only). Baseline characteristics were similar across treatment arms. Viral clearance did not differ by treatment arm, 20 and 19 participants respectively had SARS COV-2 viral load

clearance by day 6 with no significant difference, median (IQR) number of days to viral load clearance between the two groups was 4(3–4) vs 4(2–4); $p=0.457$. There were no significant differences in secondary outcomes (symptom resolution and adverse events) between the intervention group and the control group. There were no significant differences in specific adverse events such as elevated alkaline phosphatase, prolonged QTc interval on ECG, among patients in the intervention group as compared to the control group.

CONCLUSION: Our results show that HCQ 400 mg twice a day for the first day followed by 200 mg twice daily for the next 4 days was safe but not associated with reduction in viral clearance or symptom resolution among adults with COVID-19 in Uganda.

Trial registration: NCT04860284.

Prevalence of *Aspergillus fumigatus* skin positivity in adults without an apparent/known atopic disease in Uganda

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BACKGROUND: Skin prick testing (SPT) is an important investigation in the evaluation of allergy to fungal pathogens. However, the background sensitivity to fungal allergens among healthy people in Uganda is unknown. Our aim was to assess the background prevalence of *Aspergillus fumigatus* SPT positivity in apparently healthy adults without known atopic disease in Uganda.

METHODS: For this pilot study, we recruited 50 healthy volunteers using convenience sampling, 56% of whom were health workers. We performed the SPT for *A. fumigatus* according to manufacturer's instructions. A wheal diameter of $f \geq 3$ mm was considered positive.

RESULTS: The prevalence of *A. fumigatus* skin positivity was 60% (30/50). Participants with a positive *A. fumigatus* SPT were significantly younger than those with a negative result [median age (years): 28 versus 35; $p=0.005$].

CONCLUSION: There is a high skin positivity against *A. fumigatus* among non-atopic healthy Ugandan adults. There is an urgent need to establish a normal wheal cut-off value for this population. SPT alone may be an unreliable test for the diagnosis of *A. fumigatus* associated allergic syndromes. More studies are needed to define the prevalence of *A. fumigatus* skin positivity among non-atopic healthy population in Africa.

Vitamin D binding protein gene polymorphism and its association with free serum bioavailability among tuberculosis patients and household contacts

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Link: <https://www.researchsquare.com/article/rs-1819336/latest>

BACKGROUND: Genetic variants influence the distribution of vitamin D in circulation leading to vitamin D deficiency. This study aimed to determine the association between the DBP gene polymorphism with vitamin D bioavailability among active tuberculosis patients, latent Tuberculosis and with no Tuberculosis infection individuals.

METHODS: This was a cross-sectional study of 52 active tuberculosis patients, 23 latent tuberculosis individuals, and 27 with no tuberculosis infection. Sanger sequencing was performed and single nucleotide polymorphisms were identified using the BioEdit tool. Logistic regression was used to determine associations. Frequencies of 97% Gc1F, 2% Gc2 and 1% Gc1S genotypes were reported. The median (IQR) vitamin D levels of the predominant genotype, Gc1F were 3.8 (1.1-

10.5) ng/ml, Gc1S individual, 2.2 ng/ml, and Gc2 individuals were 1.9 ng/ml. No significant association was found between vitamin D binding protein gene and free and bioavailable vitamin D levels, p -value 0.05. Spearman's correlation revealed a negative association ($r=0.0404$) between the two.

CONCLUSION: The Gc1F genotype was predominantly found in the study population with the minor alleles associated with active and latent TB states. However, the non-significant association observed between the vitamin D Binding Protein gene and the free and bioavailable vitamin D levels may be a consequence of the homogenous population.

Patient level barriers to accessing TB care services during the COVID-19 pandemic in Uganda, a mixed methods study. (Under review by BMC Health Services Research journal)

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Introduction: Lockdown measure has been utilized widely to mitigate COVID-19 pandemic transmission and recently during the 2022 Sudan Ebola Virus Disease outbreak in Uganda. These have setback effects on the continuity of essential health services such as tuberculosis (TB) care, reversing progress made in the fight against tuberculosis (TB) over the past decade. We set out to understand patient-reported barriers to accessing TB care services during the COVID-19 pandemic in Uganda.

Methods: Mixed methods study involving review of medical records of TB patients who received TB care from January to September 2020. We used quantitative and qualitative methods including phone questionnaires and in-depth interviews.

We carried out descriptive statistics, a chi-square test and conducted a thematic analysis

Results: We carried out phone interviews with 672 participants. The majority (60%) were male and with an average of 35 years (SD:11). A significantly higher proportion of patients reported a barrier to TB care access during the COVID-19 lockdown than pre-lockdown (79.9% vs 68.1% p=0.027). We carried out in-depth interviews with 28 participants (54% (15/28): male). Barriers experienced by these participants included lack of a means of transport to reach the health facility, lack of money to pay the transport fares, long distances to the facility, fear of COVID-19 infection, stigma due to overlap between TB and COVID-19 symptoms, and few health care workers available during the lockdown period.

Conclusion: Lockdown measures instituted to mitigate the transmission of COVID-19 affected access to TB care services in Uganda. Uganda is at risk of future emerging and re-emerging diseases of epidemic potential. Therefore, there should be measures to ensure the continuity of essential services such as tuberculosis care during the implementation of future epidemic response interventions such as a lockdown.

Keywords: Tuberculosis, COVID-19 pandemic, lockdown, Uganda, qualitative, quantitative, mixed methods.

Perceptions of Adolescents and Health Workers Towards Adolescents' TB Diagnosis in Central Uganda: A Cross-Sectional Qualitative Study

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PURPOSE: Prompt diagnosis of TB among adolescents may reduce transmission and improve individual outcomes. However, TB diagnosis in adolescents is challenging. This study sought to understand challenges to adolescent TB diagnosis.

METHODS: We conducted qualitative focus group discussions (FGDs) to explore adolescents' and health workers' perspectives on challenges to TB diagnosis among adolescents seeking care at four secondary health care facilities in Uganda. Eight FGDs were conducted: four with 32 adolescents consulting for medical care and four with 34 health workers involved in TB care.

RESULTS: Adolescents were aware of TB and associated risk factors and believed behaviours like smoking and alcohol use are risk factors for TB. They reported school schedules limit them from seeking TB care and have to miss school or wait for holidays to seek TB diagnosis. They noted school nurses do not take much interest in diagnosing TB and do not refer them to hospitals for further evaluation when they present with TB symptoms. Furthermore, adolescents reported cross-cutting issues like loss of trust in public health systems, encountering unfriendly, judgmental and uncooperative health workers. Health workers mentioned the school environment exposes adolescents to TB as the dormitories they sleep in are overcrowded. They indicated that it was difficult to make a diagnosis of TB in adolescents as the adolescents do not disclose health information. They reported fellow health workers perceive adolescents as being at low risk of TB as they believe most often adolescents are HIV negative and thus have reduced risk of TB.

CONCLUSION: Adolescents present unique challenges that need to be addressed if TB diagnosis is to improve. These challenges could be handled by interventions that lead to minimal disruptions on school schedules, provision of adolescent-friendly services and intervention to build capacity of health care workers in the provision of adolescent-friendly services.

Rifampicin susceptibility discordance between Xpert MTB/RIF G4 and Xpert Ultra before MDRT-TB treatment initiation: A case report from Uganda

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Abstract

Tuberculosis (TB) resistance to rifampicin, the most powerful drug leads to increase in mortality. Globally, half a million new patients develop such resistant TB each year, coupled with both inappropriate diagnosis and treatment initiation.

We report a case of rifampicin resistant Mycobacterium tuberculosis whose rifampicin resistance was missed by Xpert MTB/RIF Assay G4 but detected by the Xpert MTB/RIF Ultra assay at different time points leading to increased delays for MDR-TB treatment initiation at Mulago Hospital, Kampala, Uganda. Our case report compels greater urgency in accelerating the transition to the newer assay, Ultra, to benefit from higher sensitivity of rifampicin resistance detection.

Impact of socio-economic factors on Tuberculosis treatment outcomes in north-eastern Uganda: a mixed methods study

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BACKGROUND: Tuberculosis (TB) is a major public health problem and at 48%, Karamoja in North-Eastern Uganda has the lowest treatment success rate nationally. Addressing the social determinants of TB is crucial to ending TB. This study sought to understand the extent and ways in which socio-economic factors affect TB treatment outcomes in Karamoja.

METHODS: We conducted a convergent parallel mixed methods study in 10 TB Diagnostic and Treatment Units. The study enrolled former TB patients diagnosed with drug-susceptible TB between April 2018 and March 2019. Unit TB and laboratory registers were reviewed to identify pre-treatment losses to follow-up. Four focus group discussions with former TB patients and 18 key informant interviews with healthcare workers were conducted. Principle component analysis was used to generate wealth quintiles that were compared to treatment outcomes using the proportion test. The association between sociodemographic characteristics and TB treatment outcomes was evaluated using the chi-square test and multiple logistic regression.

RESULTS: A total of 313 participants were randomly selected from 1184 former TB patients recorded in the unit TB registers. Of these, 264 were contacted in the community and consented to join the study: 57% were male and 156 (59.1%) participants had unsuccessful treatment outcomes. The wealthiest quintile had a 58% reduction in the risk of having an unsuccessful treatment outcome (adj OR=0.42, 95% CI 0.18–0.99, p=0.047). People who were employed in the informal sector (adj OR=4.71, 95% CI 1.18–18.89, p=0.029) and children under the age of 15 years who were not in school or employed (adj OR=2.71, 95% CI 1.11–6.62, p=0.029) had significantly higher odds of unsuccessful treatment outcome. Analysis of the pre-treatment loss to follow-up showed that 17.2% of patients with pulmonary bacteriologically confirmed TB did not initiate treatment with a higher proportion among females (21.7%) than males (13.5%). Inadequate food, belonging to migratory communities, stigma, lack of social protection, drug

stock-outs and transport challenges affected TB treatment outcomes.

CONCLUSIONS: This study confirmed that low socio-economic status is associated with poor TB treatment outcomes emphasizing the need for multi- and cross-sectoral approaches and socio-economic enablers to optimise TB care.

Feasibility of using a mobile App to monitor and report COVID-19 related symptoms and people's movements in Uganda

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BACKGROUND: Feasibility of mobile Apps to monitor diseases has not been well documented particularly in developing countries. We developed and studied the feasibility of using a mobile App to collect daily data on COVID-19 symptoms and people's movements.

METHODS: We used an open source software “KoBo Toolbox” to develop the App and installed it on low cost smart mobile phones. We named this App “Wetaase” (“protect yourself”). The App was tested on 30 selected households from 3 densely populated areas of Kampala, Uganda, and followed them for 3 months. One trained member per household captured the data in the App for each enrolled member and uploaded it to a virtual server on a daily basis. The App is embedded with an algorithm that flags participants who report fever and any other COVID-19 related symptom.

RESULTS: A total of 101 participants were enrolled; 61% female; median age 23 (interquartile range (IQR): 17–36) years. Usage of the App was 78% (95% confidence interval (CI): 77.0%–78.8%). It increased from 40% on day 1 to a peak of 81% on day 45 and then declined to 59% on day 90. Usage of the App did not significantly vary by site, sex or age. Only 57/6617 (0.86%) records included a report of at least one of the 17 listed COVID-19 related symptoms. The most reported symptom was flu/runny nose (21%) followed by sneezing (15%), with the rest ranging between 2% and 7%. Reports on movements away from home were 45% with 74% going to markets or shops. The participants liked the “Wetaase” App and recommended it for use as an alert system for COVID-19.

CONCLUSION: Usage of the “Wetaase” App was high (78%) and it was similar across the three study sites, sex and age groups. Reporting of symptoms related to COVID-19 was low. Movements were mainly to markets and shops. Users reported that the App was easy to use and recommended its scale up. We recommend that this App be assessed at a large scale for feasibility, usability and acceptability as an additional tool for increasing alerts on COVID-19 in Uganda and similar settings.

The rural Uganda non-communicable disease (RUNCD) study: prevalence and risk factors of self-reported NCDs from a cross sectional survey

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BACKGROUND: Non-communicable diseases (NCDs) are an increasing global concern, with morbidity and mortality largely occurring in low- and middle-income settings. We established the prospective Rural Uganda Non-Communicable Disease (RUNCD) cohort to longitudinally characterize the NCD prevalence, progression, and complications in rural Africa.

METHODS: We conducted a population-based census for NCD research. We systematically enrolled adults in each household among three sub-counties of the larger Nakaseke Health district and collected baseline demographic, health status, and self-reported chronic disease information. We present our data on self-reported chronic disease, as stratified by age, sex, educational attainment, and sub-county.

RESULTS: A total of 16,694 adults were surveyed with 10,563 (63%) respondents enrolled in the self-reported study. Average age was 37.8 years (SD=16.5) and 45% (7481) were male. Among self-reported diseases, hypertension (HTN) was most prevalent (6.3%). 1.1% of participants reported a diagnosis of diabetes, 1.1% asthma, 0.7% COPD, and 0.4% kidney disease. 2.4% of the population described more than one NCD. Self-reported HTN was significantly higher in the peri-urban subcounty than in the other two rural sub-counties ($p < 0.001$); diagnoses for all other diseases did not differ significantly between sub-counties. Odds for self-reported HTN increased significantly with age (OR=1.87 per 10 years of age, 95% CI 1.78–1.96). Male sex was associated with lower odds of reporting asthma (OR=0.53, 95% CI 0.34–0.82) or HTN (OR=0.31, 95% CI 0.26–0.40).

CONCLUSIONS: The RUNCD will establish one of the largest NCD patient cohorts in rural Africa. First analysis highlights the feasibility of systematically enrolling large numbers of adults living in a rural Ugandan district. In addition, our study demonstrates low levels of self-reported NCDs compared to the nation-wide established levels, emphasizing the need to better educate, characterize, and care for the majority of rural communities.

Music and dance in respiratory disease management in Uganda: a qualitative study of patient and healthcare professional perspectives.

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INTRODUCTION: Music and dance are increasingly used as adjunctive arts-in-health interventions in high-income settings, with a growing body of research suggesting biopsychosocial benefits. Such low-cost, low-resource interventions may have application in low-resource settings such as Uganda. However, research on perceptions of patients and healthcare professionals regarding such approaches is lacking.

METHODS: We delivered sample sessions of music and dance for chronic respiratory

disease (CRD) to patients and healthcare professionals. Seven participants took part in one singing and dance sample session. One patient completed only the dance session. We then conducted an exploratory qualitative study using thematic analysis of semistructured interviews with healthcare professionals and patients regarding (1) the role of music and dance in Ugandan life and (2) the perceived acceptability and feasibility of using music and dance in CRD management in Uganda.

RESULTS: We interviewed 19 participants, made up of 11 patients with long-term respiratory conditions and 8 healthcare professionals, who were selected by purposeful convenience sampling. Four key themes were identified from interview analysis: music and dance (1) were central components of daily life; (2) had an established role supporting health and well-being; and (3) had strong therapeutic potential in respiratory disease management. The fourth theme was (4) the importance of modulating demographic considerations of culture, religion and age.

CONCLUSION: Music and dance are central to life in Uganda, with established roles supporting health and well-being. These roles could be built on in the development of music and dance interventions as adjuncts to established components of CRD disease management like pulmonary rehabilitation. Through consideration of key contextual factors and codevelopment and adaptation of interventions, such approaches are likely to be well received.

Adoption of evidence-informed guidelines in prescribing protease inhibitors for HIV-Tuberculosis co-infected patients on rifampicin and effects on HIV treatment outcomes in Uganda

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Link: <https://doi.org/10.1186/s12879-021-06533-6>

BACKGROUND: We aimed to determine how emerging evidence over the past decade informed how Ugandan HIV clinicians prescribed protease inhibitors (PIs) in HIV patients on rifampicin-based tuberculosis (TB) treatment and how this affected HIV treatment outcomes.

METHODS: We reviewed clinical records of HIV patients aged 13 years and above,

treated with rifampicin-based TB treatment while on PIs between 1st—January -2013 and 30th—September—2018 from twelve public HIV clinics in Uganda. Appropriate PI prescription during rifampicin-based TB treatment was defined as; prescribing doubled dose lopinavir/ritonavir- (LPV/r 800/200 mg twice daily) and inappropriate PI prescription as prescribing standard dose LPV/r or atazanavir/ ritonavir (ATV/r).

RESULTS: Of the 602 patients who were on both PIs and rifampicin, 103 patients (17.1% (95% CI: 14.3–20.34)) received an appropriate PI prescription. There were no significant differences in the two-year mortality (4.8 vs. 5.7%, $P=0.318$), loss to follow up (23.8 vs. 18.9%, $P=0.318$) and one-year post TB treatment virologic failure rates (31.6 vs. 30.7%, $P=0.471$) between patients that had an appropriate PI prescription and those that did not. However, more patients on double dose LPV/r had missed anti-retroviral therapy (ART) days (35.9 vs 21%, $P=0.001$).

CONCLUSION: We conclude that despite availability of clinical evidence, double dosing LPV/r in patients receiving rifampicin-based TB treatment is low in Uganda's public HIV clinics but this does not seem to affect patient survival and viral suppression.

Undernutrition and Treatment Success in Drug Resistant Tuberculosis in Uganda

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BACKGROUND: Undernutrition is associated with unfavourable treatment outcomes among people with drug-resistant tuberculosis (DRTB). Factors influencing the treatment outcomes among undernourished people with DRTB are not well characterised. The aim of this study was to determine factors associated with treatment success among undernourished people with DRTB in Uganda.

METHODS: We analysed data from a retrospective cohort of people with DRTB from 16 treatment sites in Uganda. We included participants with a pre-treatment body mass index (BMI) of <18.5 kilograms/meters² (kg/m²). Participants were categorised as having mild (BMI of 18.5–17 kg/m²), moderate (BMI of 16.9–16.0 kg/m²) or severe (BMI of <16.0 kg/m²) undernutrition. We performed logistic regression analysis to determine factors associated with treatment success.

RESULTS: Among 473 people with DRTB, 276 (58.4%) were undernourished (BMI < 18.5 Kg/m²) and were included in the study. Of these, 92 (33.3%) had mild, 69 (25.0%) had moderate and 115 (41.7%) had severe undernutrition. The overall treatment success rate (TSR) for the undernourished was 71.4% (n = 197). Although the TSR was similar among participants with mild (71.7%), moderate (78.3%) and severe (67.0%) undernutrition (p = 0.258), all treatment failure cases (n =6) were among participants with severe undernutrition (p = 0.010). Cigarette smoking (odds ratio (OR) = 0.19, 95% CI 0.07–0.47, p < 0.001), urban residence (OR = 0.31, 95% CI 0.14–0.70, p = 0.005) and moderate (OR = 0.14, 95% CI 0.06–0.35, p < 0.001) and severe anaemia (OR = 0.06, 95% CI 0.01–0.29, p = 0.001) were associated with lower odds of treatment success.

CONCLUSION: Most undernourished people with DRTB have severe undernutrition. Smoking and anaemia are modifiable factors which upon appropriate intervention could improve treatment success. The effect of urban residence on the TSR needs to be evaluated further.

Efficacy of convalescent plasma for treatment of COVID–19 in Uganda

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RATIONALE: Convalescent plasma (CCP) has been studied as a potential therapy for COVID-19, but data on its efficacy in Africa are limited.

OBJECTIVE: In this trial we set out to determine the efficacy of CCP for treatment of COVID-19 in Uganda.

MEASUREMENTS: Patients with a positive SARS-CoV-2 reverse transcriptase (RT)-PCR test irrespective of disease severity were hospitalised and randomised to receive either COVID-19 CCP plus standard of care (SOC) or SOC alone. The primary outcome was time to viral clearance, defined as having two consecutive RT-PCR-negative tests by day 28. Secondary outcomes included time to symptom resolution, clinical status on the modified WHO Ordinal Clinical Scale (≥ 1 -point increase), progression to severe/critical condition (defined as oxygen saturation $< 93\%$ or needing oxygen), mortality and safety.

MAIN RESULTS: A total of 136 patients were randomised, 69 to CCP+SOC and 67 to SOC only. The median age was 50 years (IQR: 38.5–62.0), 71.3% were male and the median duration of symptom was 7 days (IQR=4–8). Time to viral clearance was not different between the CCP+SOC and SOC arms (median of 6 days (IQR=4–11) vs 4 (IQR=4–6), $p=0.196$). There were no statistically significant differences in secondary outcomes in CCP+SOC versus SOC: time to symptom resolution (median=7 (IQR=5–7) vs 7 (IQR=5–10) days, $p=0.450$), disease progression (9 (22.0%) vs 7 (24.0%) patients, $p=0.830$) and mortality (10 (14.5%) vs 8 (11.9%) deaths, $p=0.476$).

CONCLUSION: In this African trial, CCP therapy did not result in beneficial virological or clinical improvements. Further trials are needed to determine subgroups of patients who may benefit from CCP in Africa.

Trial registration number NCT045429

Association of fluvoxamine with mortality and symptom resolution among inpatients with COVID-19 in Uganda: a prospective interventional open-label cohort study

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Abstract

Prior research suggests that fluvoxamine, a selective serotonin reuptake inhibitor (SSRI) used for the treatment of obsessive-compulsive disorder and major depressive disorder, could be repurposed against COVID-19. We undertook a prospective interventional open-label cohort study to evaluate the efficacy and tolerability of fluvoxamine among inpatients with laboratory-confirmed COVID-19 in Uganda. The main outcome was all-cause mortality. Secondary outcomes were hospital discharge and complete symptom resolution. We included 316 patients, of whom 94 received fluvoxamine in addition to standard care [median age, 60 years (IQR=37.0); women, 52.2%]. Fluvoxamine use was significantly associated with reduced mortality [AHR=0.32; 95% CI=0.19–0.53; $p<0.001$, NNT=4.46] and with increased complete symptom resolution [AOR=2.56; 95% CI=1.53–5.51; $p<0.001$, NNT=4.44]. Sensitivity analyses yielded similar results. These effects did not significantly differ by clinical characteristic, including vaccination status. Among the 161 survivors, fluvoxamine was not significantly associated with time to hospital discharge [AHR 0.81, 95% CI (0.54–1.23), $p=0.32$]. There was a trend toward greater side effects with fluvoxamine (7.45% versus 3.15%; SMD=0.21; $\chi^2=3.46$, $p=0.06$), most of which were light or mild in severity and none of which were serious. One hundred mg of fluvoxamine prescribed twice daily for 10 days was well tolerated and significantly associated with reduced mortality

and with increased complete symptom resolution, without a significant increase in time to hospital discharge, among inpatients with COVID-19. Large-scale randomized trials are urgently needed to confirm these findings, especially for low- and middle-income countries, where access to vaccines and approved treatments against COVID-19 is limited.

Prevalence, risk factors and outcome in Ugandan children infected with *Mycoplasma pneumoniae*: a prospective study

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Link: <https://doi.org/10.1080/20469047.2021.1980698>

BACKGROUND: Atypical bacteria cause 10–40% of all childhood community-acquired pneumonia and severe disease in children under 5 years of age. Data on the burden of atypical pneumonia in sub-Saharan Africa are limited.

AIM: To determine the prevalence, associated factors, and outcome of *Mycoplasma pneumoniae* infection in children presenting with respiratory symptoms at Mulago National Referral Hospital, Kampala.

METHODS: Children aged 2 months to 12 years who presented with cough and/or difficult breathing and fast breathing were recruited. A clinical history and physical examination were undertaken. Blood samples were taken at enrolment (Day 0) and on Day 21 to determine the presence of *Mycoplasma pneumoniae* IgM antibodies, and induced sputum for DNA-PCR. Admitted participants were followed for a maximum of 7 days or until discharge or death, whichever came first.

RESULTS: A total of 385 children were enrolled, and, of these, 368 (95.6%) were < 5 years of age and the other 17 (4.4%) 5–12 years. Overall, 60/385 (15.6%) participants tested positive for *M. pneumoniae* IgM and/or DNA-PCR. Of these, 56/60 (93.3%) were < 5 years of age. Wheezing was present in 21/60 (35.0%) of the children with atypical pneumonia (*Mycoplasma pneumoniae*) and in 128/325 (39.4%) of those with typical pneumonia. The factors associated with *M. pneumoniae* were female sex (AOR 1.94, 95% CI 1.22–3.08, $p < 0.001$), age \geq 12 months (AOR 2.73, 95% CI 1.53–4.87, $p = 0.01$) and a history of prematurity (AOR 2.07, 95% CI 1.23–3.49, $p = 0.01$). The overall mortality was 17/352 (4.8%) and, of these, 4/17 (23.5%) had *M. pneumoniae*.

CONCLUSION: In Uganda, *M. pneumoniae* is common in children < 5 years of age, especially females above 2 years, and in those with a history of prematurity. It

presents with severe symptoms requiring hospitalisation. The results highlight the importance of considering atypical bacteria in under-5s who present with symptoms of pneumonia.

COVID-19 vaccine acceptance among high-risk populations in Uganda

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BACKGROUND: Immunization is an important strategy for controlling the COVID-19 pandemic. COVID-19 vaccination was recently launched in Uganda, with prioritization to healthcare workers and high-risk individuals. In this study, we aimed to determine the acceptability of COVID-19 vaccine among persons at high risk of COVID-19 morbidity and mortality in Uganda.

METHODS: Between 29 March and 14 April 2021, we conducted a cross-sectional survey consecutively recruiting persons at high risk of severe COVID-19 (diabetes mellitus, HIV and cardiovascular disease) attending Kiruddu National Referral Hospital outpatient clinics. A trained research nurse administered a semi-structured questionnaire assessing demographics, COVID-19 vaccine related attitudes and acceptability. Descriptive statistics, bivariate and multivariable analyses were performed using STATA 16.

RESULTS: A total of 317 participants with a mean age 51.5 ± 14.1 years were recruited. Of this, 184 (60.5%) were female. Overall, 216 (70.1%) participants were willing to accept the COVID-19 vaccine. The odds of willingness to accept COVID-19 vaccination were four times greater if a participant was male compared with if a participant was female [adjusted odds ratio (AOR): 4.1, 95% confidence

interval (CI): 1.8–9.4, $p=0.00$]. Participants who agreed (AOR: 0.04, 95% CI: 0.01–0.38, $p=0.003$) or strongly agreed (AOR: 0.04, 95% CI: 0.01–0.59, $p=0.005$) that they have some immunity against COVID-19 were also significantly less likely to accept the vaccine. Participants who had a history of vaccination hesitancy for their children were also significantly less likely to accept the COVID-19 vaccine (AOR: 0.1, 95% CI: 0.01–0.58, $p=0.016$).

CONCLUSION: The willingness to receive a COVID-19 vaccine in this group of high-risk individuals was comparable to the global COVID-19 vaccine acceptance rate. Increased sensitization, myth busting and utilization of opinion leaders to encourage vaccine acceptability is recommended.

Impact of the bacillary load on the accuracy of rifampicin resistance results by Xpert[®] MTB/RIF

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Abstract

The WHO-endorsed Xpertw MTB/RIF (Xpert; Cepheid, Sunnyvale, CA, USA) is

one of the most widely used molecular assays for the simultaneous detection of Mycobacterium tuberculosis complex (MTBC) and antimicrobial susceptibility testing (AST) for rifampicin (RIF), which serves as a surrogate for multidrug-resistant TB (MDR-TB). 1–3 Xpert interrogates the RIF resistance-determining region (RRDR) of rpoB spanning codons 426–452 and the adjacent codon 453. 4 It cannot distinguish between mutations that cause RIF resistance and neutral ones that do not (ie, usually synonymous mutations), resulting in systematic false-resistant results. 5–8 Consequently, the WHO now recommends that ‘resistance inferred’ be reported instead of ‘resistance detected’, as is currently done by the assay software. 6, 7, 9 The Xpert G4 cartridge design is the same globally, but within the United States the Xpert software does not provide a semi-quantitative bacillary load (BL) result that stratifies samples into ‘very low’, ‘low’, ‘medium’ or ‘high’. 10–12 The performance of Xpert for RIF AST has been evaluated repeatedly. 13–20 Nevertheless, in this issue of the Journal, Muriithi et al. highlight one particular limitation linked to ‘very low’ BL samples that has not received necessary attention, even though it is more likely to affect children and HIV-positive patients. 21

In 2016, Ocheretina et al. reported an error caused by probe-binding delays in ‘very low’ BL samples tested as part of routine clinical care in Haiti. 22 Specifically, they observed a false resistance rate (FRR) of 4% (95% confidence interval [CI] 2–7) for Xpert (Table). 22 We define FRR as the number of false-resistant results based on the initial Xpert result (ie, ‘inferred’ RIF resistance without any mutations in the RRDR based on the WHO-endorsed assumption that any mutation, except synonymous ones, in this region confers resistance) divided by the sum of the number of the aforementioned false-resistant results, the number of initial Xpert results with ‘resistance not detected’ (ie, Xpert-susceptible) and false-resistant results caused by synonymous rpoB mutations. 4, 7, 23 Isolates with synonymous mutations were only included in the denominator as the resulting false-resistant errors occur irrespective of the BL. 7, 24 In 2017, Cepheid published the findings of experiments in which sputum was spiked with RIF-susceptible MTBC at concentrations of 200 colony.

Gaps related to screening and diagnosis of tuberculosis in care cascade in selected health facilities in East Africa countries: A retrospective study

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INTRODUCTION: East Africa countries (Tanzania, Kenya, and Uganda) are among tuberculosis high burdened countries globally. As we race to accelerate progress towards a world free of tuberculosis by 2035, gaps related to screening and diagnosis in the cascade care need to be addressed.

METHODS: We conducted a three-year (2015–2017) retrospective study using routine program data in 21 health facilities from East Africa. Data abstraction were done at tuberculosis clinics, outpatient departments (OPD), human immunodeficiency virus (HIV) and diabetic clinics, and then complemented with structured interviews with healthcare providers to identify possible gaps related to integration, screening, and diagnosis of tuberculosis. Data were analyzed using STATA™ Version 14.1.

RESULTS: We extracted information from 49,454 presumptive TB patients who were registered in the 21 facilities between January 2015 and December 2017. A total of 9,565 tuberculosis cases were notified; 46.5% (4,450) were bacteriologically confirmed and 31.5% (3,013) were HIV-infected. Prevalence of tuberculosis among presumptive pulmonary tuberculosis cases was 17.4%. The outcomes observed were as follows: 79.8% (7,646) cured or completed treatment, 6.6% (634) died, 13.3% (1,270) lost to follow-up or undocumented and 0.4% (34) treatment failure. In all countries, tuberculosis screening was largely integrated at OPD and HIV clinics. High patient load, weak laboratory specimen referral system, shortage of trained personnel, and frequent interruption of laboratory supplies were the major cited challenges in screening and diagnosis of tuberculosis.

CONCLUSION: Screening and diagnostic activities were frequently affected by scarcity of human and financial resources. Tuberculosis screening was mainly integrated at OPD and HIV clinics, with less emphasis on the other health facility clinics. Closing gaps related to TB case finding and diagnosis in developing countries requires sustainable investment for both human and financial resources and strengthen the integration of TB activities within the health system.

Efficacy of convalescent plasma for treatment of COVID-19 in Uganda

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Link: <http://dx.doi.org/10.1136/bmjresp-2021-001017>

RATIONALE: Convalescent plasma (CCP) has been studied as a potential therapy for COVID-19, but data on its efficacy in Africa are limited.

OBJECTIVE: In this trial we set out to determine the efficacy of CCP for treatment

of COVID-19 in Uganda.

MEASUREMENTS: Patients with a positive SARS-CoV-2 reverse transcriptase (RT)-PCR test irrespective of disease severity were hospitalised and randomised to receive either COVID-19 CCP plus standard of care (SOC) or SOC alone. The primary outcome was time to viral clearance, defined as having two consecutive RT-PCR-negative tests by day 28. Secondary outcomes included time to symptom resolution, clinical status on the modified WHO Ordinal Clinical Scale (≥ 1 -point increase), progression to severe/critical condition (defined as oxygen saturation $< 93\%$ or needing oxygen), mortality and safety.

MAIN RESULTS: A total of 136 patients were randomised, 69 to CCP+SOC and 67 to SOC only. The median age was 50 years (IQR: 38.5–62.0), 71.3% were male and the median duration of symptom was 7 days (IQR=4–8). Time to viral clearance was not different between the CCP+SOC and SOC arms (median of 6 days (IQR=4–11) vs 4 (IQR=4–6), $p=0.196$). There were no statistically significant differences in secondary outcomes in CCP+SOC versus SOC: time to symptom resolution (median=7 (IQR=5–7) vs 7 (IQR=5–10) days, $p=0.450$), disease progression (9 (22.0%) vs 7 (24.0%) patients, $p=0.830$) and mortality (10 (14.5%) vs 8 (11.9%) deaths, $p=0.476$).

CONCLUSION: In this African trial, CCP therapy did not result in beneficial virological or clinical improvements. Further trials are needed to determine subgroups of patients who may benefit from CCP in Africa.

Adoption of evidence-informed guidelines in prescribing protease inhibitors for HIV-Tuberculosis co-infected patients on rifampicin and effects on HIV treatment outcomes in Uganda.

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BACKGROUND: We aimed to determine how emerging evidence over the past decade informed how Ugandan HIV clinicians prescribed protease inhibitors (PIs) in HIV patients on rifampicin-based tuberculosis (TB) treatment and how this affected HIV treatment outcomes.

METHODS: We reviewed clinical records of HIV patients aged 13 years and above, treated with rifampicin-based TB treatment while on PIs between 1st—January—2013 and 30th—September—2018 from twelve public HIV clinics in Uganda. Appropriate PI prescription during rifampicin-based TB treatment was defined as; prescribing doubled dose lopinavir/ritonavir- (LPV/r 800/200 mg twice daily) and inappropriate PI prescription as prescribing standard dose LPV/r or atazanavir/ritonavir (ATV/r).

RESULTS: Of the 602 patients who were on both PIs and rifampicin, 103 patients (17.1% (95% CI: 14.3–20.34)) received an appropriate PI prescription. There were no significant differences in the two-year mortality (4.8 vs. 5.7%, $P=0.318$), loss to follow up (23.8 vs. 18.9%, $P=0.318$) and one-year post TB treatment virologic failure rates (31.6 vs. 30.7%, $P=0.471$) between patients that had an appropriate PI prescription and those that did not. However, more patients on double dose LPV/r had missed anti-retroviral therapy (ART) days (35.9 vs 21%, $P=0.001$).

CONCLUSION: We conclude that despite availability of clinical evidence, double dosing LPV/r in patients receiving rifampicin-based TB treatment is low in Uganda's public HIV clinics but this does not seem to affect patient survival and viral suppression.

Chronic obstructive pulmonary disease prevalence and associated factors in an urban HIV clinic in a low income country

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INTRODUCTION: In the last decade, survival of people living with HIV (PLHIV) has dramatically increased due wide availability of effective antiretroviral therapy. However, PLHIV remain at a comparatively higher risk of non-communicable comorbidities. We sought to determine the burden of COPD and its associations in an urban tertiary HIV clinic in Uganda.

METHODS AND FINDINGS: HIV-infected adults attending the Makerere University Joint AIDS program; aged ≥ 30 years without acute ailments were screened for COPD using study questionnaires and spirometry (post-bronchodilator FEV1/

FVC<0.7). We determined its prevalence and association with demographic characteristics, body mass index (BMI) and known risk factors.

Of 288 participants enrolled, 177 (61%) were female; 253 (88%) were from urban residences, median age was 45 years (IQR: 39–51), 71(25%) were 'ever' smokers, 284(99%) reported biomass fuel use and 72(25%) had a history of tuberculosis. All except 1 participant were on antiretroviral therapy, median current CD4 (cells/mm³) was 558 (IQR 402–753) and 275(96%) were virologically suppressed. Nearly half (130/288, 45%) had recurrent respiratory symptoms. The prevalence of COPD was 3.1% (9/288) [95% CI: 1.63–5.92]. COPD was associated with: previous tuberculosis, (adjusted odds ratio (AOR): 6.36, [95% CI 1.64–35.84], P = 0.036), self-reported chronic shortness of breath (AOR: 9.06, [95% CI 1.34–61.10], P = 0.024) and a BMI <21 Kg/m² (AOR: 10.42 [95% CI: 1.61–100.00], P = 0.013).

CONCLUSION: In this HIV population, COPD prevalence was low and was associated with previous tuberculosis, self-reported chronic shortness of breath and BMI <21 Kg/m².

Health workers' perspectives of a mobile health tool to improve diagnosis and management of paediatric acute respiratory illnesses in Uganda: a qualitative study

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OBJECTIVES: Mobile health tools have potential to improve the diagnosis and management of acute lower respiratory illnesses (ALRI), a leading cause of paediatric mortality worldwide. The objectives were to evaluate health workers' perceptions of acceptability, usability and feasibility of Acute Lower Respiratory Illness Treatment and Evaluation (ALRITE), a novel mobile health tool to help frontline health workers diagnose, treat and provide education about ALRI in children <5 years.

DESIGN: A qualitative study including semistructured interviews with health facility administrators and focus groups with primary care health workers.

SETTING: Two federally funded Ugandan primary care health facilities, one peri-urban and one rural.

PARTICIPANTS: We enrolled 3 health administrators and 28 health workers (clinical officers and nurses).

INTERVENTION: The ALRITE smartphone application was developed to help frontline health workers adhere to ALRI guidelines and differentiate wheezing illnesses from pneumonia in children under 5 years of age. ALRITE contains a simple decision tree, a partially automated respiratory rate counter, educational videos and an adapted respiratory assessment score to determine bronchodilator responsiveness. We performed a demonstration of ALRITE for participants at the beginning of interviews and focus groups. No participant had used ALRITE prior.

RESULTS: Themes impacting the potential implementation of ALRITE were organised using individual-level, clinic-level and health-system level determinants. Individual-level determinants were acceptability and perceived benefit, usability, provider needs and provider–patient relationship. Clinic-level determinants were limited resources and integration within the health centre. Systems-level determinants included medication shortages and stakeholder engagement.

CONCLUSIONS: Incorporation of these themes will ready ALRITE for field testing. Early engagement of end users provides insights critical to the development of tailored mHealth decision support tools.

Challenges in the Implementation of Chronic Obstructive Pulmonary Disease Guidelines in Low- and Middle-Income Countries

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Abstract

There is a substantial burden of chronic respiratory diseases, including chronic obstructive pulmonary disease (COPD), in low- and middle-income countries (LMICs). LMICs have particular challenges in delivering cost-effective prevention, diagnosis, and management of COPD. Optimal care can be supported by effective implementation of guidelines. This American Thoracic Society workshop considered challenges to implementation of COPD guidelines in LMICs. We make 10 specific recommendations: 1) relevant organizations should provide LMIC-specific COPD management guidance; 2) patient and professional organizations must persuade policy-makers of the importance of lung function testing programs in LMICs; 3) healthcare education and training should emphasize the early-life origins of COPD; 4) urgent action is required by governments to reduce airborne exposures, including exposures to tobacco smoke and indoor and outdoor air pollution; 5) guidance for COPD in LMICs should explicitly link across Essential Medicine Lists and the World Health Organization package of essential noncommunicable disease interventions for primary health care in low-resource settings and should consider availability, affordability, sustainability, and cost-effective use of medicines; 6) the pharmaceutical industry should work to make effective COPD and tobacco-dependence medicines globally accessible and affordable; 7) implementation of locally adapted, cost-effective pulmonary rehabilitation programs should be an international priority; 8) the World Health Organization Global Action Plan for the Prevention and Control of Noncommunicable Diseases should specify how improvements in respiratory health will be achieved; 9) research funders should increase the proportion of funding allocated to COPD in LMICs; and 10) the respiratory community should leverage the skills and enthusiasm of earlier-career clinicians and researchers to improve global respiratory health.

Identifying Appropriate Delivery of and Referral to Pulmonary Rehabilitation in Uganda: A Survey Study of People Living with Chronic Respiratory Disease and Health Care Workers

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INTRODUCTION: Pulmonary rehabilitation (PR) is a low cost, high impact intervention that ameliorates the disability associated with chronic respiratory diseases (CRD). PR is becoming increasingly recognized in low resource settings where the burden of CRD is rapidly increasing. To aid the implementation of PR in Uganda, we conducted a study to assess the attitudes and opinions towards PR among patients with CRD in Uganda and explore barriers faced by health care workers (HCWs) in referring to PR.

METHODS: A cross-sectional study comprising two survey populations: people living with CRD and HCWs regarded as potential PR referrers and PR deliverers. This exploratory study sought initial opinions and thoughts regarding PR, as well as baseline knowledge and potential barriers faced in the referral process.

RESULTS: Overall, 30 HCWs (53% female, 43% doctors) and 51 adults with CRD (63% female) participated in the survey. Among those with CRD, the majority reported breathlessness as a major problem (86%) and breathlessness affected their ability to do paid and unpaid work (70%). Interest in PR was high amongst adults with CRD (92%) with preference for a hospital-based programme (67%) as opposed to community-based (16%) or home-based (17%). All HCWs considered PR important in lung disease management, but 77% do not refer patients due to a lack of information about PR. HCWs' free-text responses identified the need for training in PR, patient education and streamlining the referral process as key elements to develop successful PR referral services.

CONCLUSION: To successfully set up a PR service for people with CRD in Uganda, there is a great need for appropriately tailored training and education of prospective referrers about CRD and PR programs. Educating patients about the benefits of PR as well as streamlining the referral process is critical in expanding PR services across Uganda to fulfill this unmet need.

Study protocol for a randomised controlled trial assessing the impact of pulmonary rehabilitation on maximal exercise capacity for adults living with post-TB lung disease: Global RECHARGE Uganda

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LINK: <http://dx.doi.org/10.1136/bmjopen-2020-047641>

INTRODUCTION: The burden of post-tuberculosis (TB) lung disease (PTBLD) is steadily increasing in sub-Saharan Africa, causing disability among TB survivors. Without effective medicines, the mainstay of PTBLD treatment evolves around disease prevention and supportive treatment. Pulmonary rehabilitation (PR), a low-cost, non-pharmacological intervention has shown effectiveness in a group of PTBLD individuals but has not been tested in a clinical trial. This study aims to assess the impact of a 6-week PR programme on maximal exercise capacity and other outcomes among adults in Uganda living with PTBLD.

METHODS AND ANALYSIS: This is a randomised waiting-list controlled trial with blinded outcome measures, comparing PR versus usual care for patients with PTBLD. A total of 114 participants will be randomised (1:1) to receive either usual care (on the waiting list) or PR, with follow-up assessments at 6 weeks and 12 weeks postintervention. The primary outcome is change in walking distance measured by the Incremental Shuttle Walk Test from baseline to the end of 6 weeks of PR. All secondary outcomes will be compared between the PR and usual care arms from baseline to 6-week and 12-week follow-ups. Secondary outcomes include self-reported respiratory symptoms, physical activity, psychological well-being, health-related quality of life and cost-benefit analysis. All randomised participants will be included in the intention-to-treat analysis population. The primary efficacy analysis will be based on both per-protocol and modified intention-to-treat populations.

ETHICS AND DISSEMINATION: The trial has received ethical clearance from the Mulago Hospital Research and Ethics Committee (MHREC 1478), Kampala, Uganda as well as the Uganda National Council for Science and Technology (SS 5105). Ethical approval has been obtained from the University of Leicester, UK research ethics committee (Ref No. 22349). Study findings will be published in

appropriate peer-reviewed journals and disseminated at appropriate local, regional and international scientific meetings and conferences.

Latent Tuberculosis Infection Status of Pregnant Women in Uganda Determined Using QuantiFERON TB Gold-Plus

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Link: <https://doi.org/10.1093/ofid/ofab241>

BACKGROUND: The risk of progression of latent tuberculosis infection (LTBI) to active disease increases with pregnancy. This study determined the prevalence and risk factors associated with LTBI among pregnant women in Uganda.

METHODS: We enrolled 261 pregnant women, irrespective of gestational age. Participants who had known or suspected active tuberculosis (TB) on the basis of clinical evaluation or who had recently received treatment for TB were excluded. LTBI was defined as an interferon- γ concentration ≥ 0.35 IU/mL (calculated as either TB1 [eliciting CD4+ T-cell responses] or TB2 [eliciting CD8+ T-cell responses] antigen minus nil) using QuantiFERON TB Gold-Plus (QFT-plus) assay.

RESULTS: LTBI prevalence was 37.9% (n = 99) (95% confidence interval [CI], 32.3–44.0). However, 24 (9.2%) subjects had indeterminate QFT-plus results. Among participants with LTBI, TB1 and TB2 alone were positive in 11 (11.1%) and 18 (18.2%) participants, respectively. In multivariable analysis, human immunodeficiency virus (HIV) infection (adjusted odds ratio [aOR], 4.4 [95% confidence interval {CI}, 1.1–18.0]; P = .04) and age 30–39 years (aOR, 4.0 [95%

CI, 1.2–12.7]; $P = .02$) were independently associated with LTBI. Meanwhile, smoking status, alcohol use, nature of residence, crowding index, and TB contact were not associated with LTBI.

CONCLUSIONS: Our findings are in keeping with the evidence that HIV infection and advancing age are important risk factors for LTBI in pregnancy. In our setting, we recommend routine screening for LTBI and TB preventive therapy among eligible pregnant women.

Excess COVID–19 mortality among critically ill patients in Africa

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Abstract

As of March 25, 2021, a global total of 124 215 843 cases of COVID-19, including 2 734 374 deaths, had been reported to WHO. 1 COVID-19 is now the 12th leading cause of death worldwide, the sixth leading cause of death in high-income countries, and the 41st leading cause of death in sub-Saharan Africa. 2 However, the reasons why there are lower numbers of cases and deaths reported in sub-Saharan Africa are unclear. One possibility is that there are inadequate levels of testing, which could translate to unreported COVID-19 deaths (both in hospital and those that occur outside of hospital). 3 A study³ in Zambia detected COVID-19 in 70 (19· 2%) of 364 deceased individuals, most of these occurring outside of hospital. In their multicentre, prospective, observational cohort study of 3140 critically ill patients (60· 6% male, mean age 55· 6 years [SD 16· 1]) enrolled from 64 hospitals in ten African countries reported in *The Lancet*, the African COVID-19 Critical Care Outcomes Study (ACCCOS) Investigators⁴ show that, despite having low COVID-19 mortality rates, Africa has the highest global mortality rate in patients with COVID-19 who are critically ill: 48· 2%(95% CI 46· 4–50· 0; 1483 of 3077 patients) against a global average of 31· 5%(27· 5–35· 5). In addition to the previously reported drivers of mortality (eg, the patient's disease severity at presentation and having comorbidities such as HIV/AIDS, diabetes, and chronic liver disease), the ACCCOS Investigators found that having HIV/AIDS (odds ratio 1· 91) and delayed access to high-care units and intensive care units (2· 14) were drivers of mortality.

Their study is, to the best of our knowledge, the first multicountry report of outcomes of critically ill patients with COVID-19 in Africa. The question is which factors drive this high mortality in a continent with lower cases of COVID-19 and overall lower

mortality rates? The authors provide some insights into possible causes, such as a shortage of critical care resources and underuse of those that are available. The underuse of resources is an intriguing finding and contrary to popular belief that resources are scarce. It is shocking to see that 68% of hospitals had access to dialysis but only 10% of the patients received it, as well as to see that proning was not optimised. It is important to think beyond the availability of resources and to also consider issues of functionality. It is common in low-income countries to have expensive equipment that is non-functional due to poor maintenance or lack of skilled human resources. It has been estimated that 40% of the medical equipment in many low-income countries is out of service.

COVID-19 vaccine acceptance among high-risk populations in Uganda

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BACKGROUND: Immunization is an important strategy for controlling the COVID-19 pandemic. COVID-19 vaccination was recently launched in Uganda, with prioritization to healthcare workers and high-risk individuals. In this study, we

aimed to determine the acceptability of COVID-19 vaccine among persons at high risk of COVID-19 morbidity and mortality in Uganda.

METHODS: Between 29 March and 14 April 2021, we conducted a cross-sectional survey consecutively recruiting persons at high risk of severe COVID-19 (diabetes mellitus, HIV and cardiovascular disease) attending Kiruddu National Referral Hospital outpatient clinics. A trained research nurse administered a semi-structured questionnaire assessing demographics, COVID-19 vaccine related attitudes and acceptability. Descriptive statistics, bivariate and multivariable analyses were performed using STATA 16.

RESULTS: A total of 317 participants with a mean age 51.5 ± 14.1 years were recruited. Of this, 184 (60.5%) were female. Overall, 216 (70.1%) participants were willing to accept the COVID-19 vaccine. The odds of willingness to accept COVID-19 vaccination were four times greater if a participant was male compared with if a participant was female [adjusted odds ratio (AOR): 4.1, 95% confidence interval (CI): 1.8–9.4, $p=0.00$]. Participants who agreed (AOR: 0.04, 95% CI: 0.01–0.38, $p=0.003$) or strongly agreed (AOR: 0.04, 95% CI: 0.01–0.59, $p=0.005$) that they have some immunity against COVID-19 were also significantly less likely to accept the vaccine. Participants who had a history of vaccination hesitancy for their children were also significantly less likely to accept the COVID-19 vaccine (AOR: 0.1, 95% CI: 0.01–0.58, $p=0.016$).

CONCLUSION: The willingness to receive a COVID-19 vaccine in this group of high-risk individuals was comparable to the global COVID-19 vaccine acceptance rate. Increased sensitization, myth busting and utilization of opinion leaders to encourage vaccine acceptability is recommended.

Rising and falling prevalence of asthma symptoms

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Abstract

Asthma is the leading chronic disease in children, affecting 5· 1 million children in the USA. 1 However, worldwide important variations have been reported in asthma prevalence. In The Lancet, Innes Asher and colleagues report findings from the Global Asthma Network (GAN), assessing global changes in asthma prevalence over the past three decades, with use of similar, standardised methods as the International Study of Asthma and Allergies in Childhood (ISAAC). 2 Using centres that completed GAN Phase I and ISAAC Phase I (1993–95), ISAAC Phase III (2001–03), or both, the authors assessed the global prevalence and the 10-yearly change in prevalence of current wheeze, severe asthma symptoms, asthma ever, exercise wheeze, and night cough (defined by four core questions in a questionnaire). The study included data from questionnaires filled by almost 120 000 adolescents (aged 13–14 years) and school aged children (aged 6–7 years) from 27 centres in 14 countries.

Asher and colleagues examined trends across world regions and income levels using mixed-effects linear regression models. They reported significant differences in prevalence of asthma symptoms between countries, with the prevalence for current wheeze ranging from 0· 9%(New Delhi, India) to 21· 3%(Cape Town, South Africa) in adolescents and from 1· 1%(Lucknow, India) to 23· 2%(Costa Rica).

LIST OF
PUBLICATIONS
2020/21

Assessing a transmission network of *Mycobacterium tuberculosis* in an African city using single nucleotide polymorphism threshold analysis

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Abstract

Tuberculosis (TB) is the leading cause of death in humans by a single infectious agent worldwide with approximately two billion humans latently infected with the bacterium *Mycobacterium tuberculosis*. Currently, the accepted method for controlling the disease is Tuberculosis Directly Observed Treatment Shortcourse (TB-DOTS). This program is not preventative and individuals may transmit disease before diagnosis, thus better understanding of disease transmission is essential. Using whole-genome sequencing and single nucleotide polymorphism analysis, we analyzed genomes of 145 *M. tuberculosis* clinical isolates from active TB cases from the Rubaga Division of Kampala, Uganda. We established that these isolates grouped into *M. tuberculosis* complex (MTBC) lineages 1, 2, 3, and 4, with the most isolates grouping into lineage 4. Possible transmission pairs containing ≤ 12 SNPs were identified in lineages 1, 3, and 4 with the prevailing transmission in lineages 3 and 4. Furthermore, investigating DNA codon changes as a result of specific SNPs in prominent virulence genes including *plcA* and *plcB* could indicate potentially important modifications in protein function. Incorporating this analysis with corresponding epidemiological data may provide a blueprint for the integration of public health interventions to decrease TB transmission in a region.

Discordance of the Repeat GeneXpert MTB/RIF Test for Rifampicin Resistance Detection Among Patients Initiating MDR-TB Treatment in Uganda

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BACKGROUND: The Global Laboratory Initiative (GLI) guidelines recommend repeat for GeneXpertMTB/RIF (XpertMTB/RIF) in patients with a low pretest probability of rifampicin resistance (RR).

METHODS: This was a cross-sectional study using results of sputum specimens collected from participants screened for the STREAM 2 trial. We recruited all patients with XpertMTB/RIF RR-TB detected who were referred for RR/multidrug-resistant (MDR) TB treatment initiation at Mulago National Referral Hospital, Kampala, between September 2017 and October 2019. At baseline, smear microscopy, repeat XpertMTB/RIF, Xpert Ultra, and MTBDRplus assays were done on sputum specimens. Culture-based drug susceptibility testing (DST) was performed on discordant specimens. We analyzed the prevalence and factors associated with discordance between initial and repeat XpertMTB/RIF RR and false XpertMTB/RIF RR. False XpertMTB/RIF RR was defined as no RR detected by any of Xpert Ultra, LPA, or culture DST (reference comparator).

RESULTS: A total of 126/130 patients had repeat XpertMTB/RIF results, of whom 97 (77.0%) had M. tuberculosis detected, 81 (83.5%) had RR detected, and 1 (1.0%) had RR indeterminate. The prevalence of discordant XpertMTB/RIF RR was 15/96 (15.6%), whereas false XpertMTB/RIF RR prevalence was 10/96 (10.4%).

Low-bacillary load sputum specimens were more likely to have discordant XpertMTB/RIF RR and false XpertMTB/RIF RR results (adjusted odds ratio [aOR], 0.04; 95% CI, 0.00–0.37; P = .01; aOR, 0.02; 95% CI, 0.01–0.35; P = .01, respectively).

CONCLUSIONS: Our findings show a high false-positive rifampicin resistance rate in low-TB burden patients, which calls for repeat testing in order to prevent unnecessary prescription of anti-MDR-TB therapy.

Feasibility of collecting and processing of COVID-19 convalescent plasma for treatment of COVID-19 in Uganda

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Link: <https://doi.org/10.1371/journal.pone.0252306>

INTRODUCTION: Evidence that supports the use of COVID-19 convalescent plasma (CCP) for treatment of COVID-19 is increasingly emerging. However, very few African countries have undertaken the collection and processing of CCP. The aim of this study was to assess the feasibility of collecting and processing of CCP, in preparation for a randomized clinical trial of CCP for treatment of COVID-19 in Uganda.

METHODS: In a cross-sectional study, persons with documented evidence of recovery from COVID-19 in Uganda were contacted and screened for blood donation via telephone calls. Those found eligible were asked to come to the blood donation centre for further screening and consent. Whole blood collection was undertaken from which plasma was processed. Plasma was tested for transfusion transmissible infections (TTIs) and anti-SARS CoV-2 antibody titers. SARS-CoV-2 testing was also done on nasopharyngeal swabs from the donors.

RESULTS: 192 participants were contacted of whom 179 (93.2%) were eligible

to donate. Of the 179 eligible, 23 (12.8%) were not willing to donate and reasons given included: having no time 7(30.4%), fear of being retained at the COVID-19 treatment center 10 (43.5%), fear of stigma in the community 1 (4.3%), phobia for donating blood 1 (4.3%), religious issues 1 (4.4%), lack of interest 2 (8.7%) and transport challenges 1 (4.3%). The median age was 30 years and females accounted for 3.7% of the donors. A total of 30 (18.5%) donors tested positive for different TTIs. Antibody titer testing demonstrated titers of more than 1:320 for all the 72 samples tested. Age greater than 46 years and female gender were associated with higher titers though not statistically significant.

CONCLUSION: CCP collection and processing is possible in Uganda. However, concerns about stigma and lack of time, interest or transport need to be addressed in order to maximize donations.

Characteristics and outcomes of admitted patients infected with SARSCoV-2 in Uganda

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Link: <https://doi.org/10.1136/bmjresp-2020-000646>

RATIONALE: Detailed data on the characteristics and outcomes of patients with COVID-19 in sub-Saharan Africa are limited.

OBJECTIVE: We determined the clinical characteristics and treatment outcomes of patients diagnosed with COVID-19 in Uganda.

MEASUREMENTS: As of the 16 May 2020, a total of 203 cases had been confirmed. We report on the first 56 patients; 29 received hydroxychloroquine (HCQ) and 27 did not. Endpoints included admission to intensive care, mechanical ventilation or death during hospitalisation.

MAIN RESULTS: The median age was 34.2 years; 67.9% were male; and 14.6% were <18 years. Up 57.1% of the patients were asymptomatic. The most common symptoms were fever (21.4%), cough (19.6%), rhinorrhea (16.1%), headache (12.5%), muscle ache (7.1%) and fatigue (7.1%). Rates of comorbidities were 10.7% (pre-existing hypertension), 10.7% (diabetes) and 7.1% (HIV), Body Mass Index (BMI) of ≥ 30 36.6%. 37.0% had a blood pressure (BP) of $>130/90$ mm Hg, and 27.8% had BP of $>140/90$ mm Hg. Laboratory derangements were leucopenia (10.6%), lymphopenia (11.1%) and thrombocytopenia (26.3%). Abnormal chest X-ray was observed in 14.3%. No patients reached the primary endpoint. Time to clinical recovery was shorter among patients who received HCQ, but this difference did not reach statistical significance.

CONCLUSION: Most of the patients with COVID-19 presented with mild disease and exhibited a clinical trajectory not similar to other countries. Outcomes did not differ by HCQ treatment status in line with other concluded studies on the benefit of using HCQ in the treatment of COVID-19.

Health Workers' Practices in Assessment and Management of Children with Respiratory Symptoms in Primary Care Facilities in Uganda: A FRESH AIR Descriptive Study

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INTRODUCTION: Globally, acute lower respiratory infections are the leading cause of mortality among children under 5 years. Following World Health Organization primary care guidelines, pneumonia is diagnosed based on cough/difficult breathing and fast breathing. We aimed to describe the practices of healthcare workers in primary care health facilities in Uganda in the management of young children with respiratory symptoms especially regarding asthma as opposed to pneumonia.

METHOD: Health workers were observed during clinical consultations with children 1–59 months of age presenting with cough and/or difficult breathing at recruitment. Afterward, an exit interview with the caregiver was conducted. Health center availability of clinical guidelines, equipment and supplies for management of children with respiratory symptoms was assessed systematically.

RESULTS: A total of 218 consultations with 50 health workers at six health centers were included. Median consultation time was 4 min. Health workers asked history relevant to distinguishing asthma from pneumonia in 16% of consultations. The respiratory rate was counted in 10%. Antibiotics were prescribed to 32% of all the children and to 39% of children diagnosed with pneumonia. Caregivers reported being informed of findings and possible diagnosis in 5% of cases. Medicine and equipment needed for diagnosing and treating asthma were generally unavailable.

CONCLUSION: Clinical practices among Ugandan health workers in primary care are insufficient to distinguish between main causes of respiratory symptoms, especially asthma as opposed to pneumonia, in children under five. Irrational use of antibiotics is widespread. Clear communication with caregivers is lacking. This could be due to lack of relevant competencies, medicines, time and supplies.

Latent Tuberculosis Infection Status of Pregnant Women in Uganda Determined Using QuantiFERON TB Gold-Plus

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BACKGROUND: The risk of progression of latent tuberculosis infection (LTBI) to active disease increases with pregnancy. This study determined the prevalence and risk factors associated with LTBI among pregnant women in Uganda.

METHODS: We enrolled 261 pregnant women, irrespective of gestational age. Participants who had known or suspected active tuberculosis (TB) on the basis of clinical evaluation or who had recently received treatment for TB were excluded. LTBI was defined as an interferon- γ concentration ≥ 0.35 IU/mL (calculated as either TB1 [eliciting CD4+ T-cell responses] or TB2 [eliciting CD8+ T-cell responses] antigen minus nil) using QuantiFERON TB Gold-Plus (QFT-plus) assay.

RESULTS: LTBI prevalence was 37.9% (n = 99) (95% confidence interval [CI], 32.3–44.0). However, 24 (9.2%) subjects had indeterminate QFT-plus results. Among participants with LTBI, TB1 and TB2 alone were positive in 11 (11.1%) and 18 (18.2%) participants, respectively. In multivariable analysis, human immunodeficiency virus (HIV) infection (adjusted odds ratio [aOR], 4.4 [95% confidence interval {CI}, 1.1–18.0]; P = .04) and age 30–39 years (aOR, 4.0 [95% CI, 1.2–12.7]; P = .02) were independently associated with LTBI. Meanwhile, smoking status, alcohol use, nature of residence, crowding index, and TB contact

were not associated with LTBI.

CONCLUSIONS: Our findings are in keeping with the evidence that HIV infection and advancing age are important risk factors for LTBI in pregnancy. In our setting, we recommend routine screening for LTBI and TB preventive therapy among eligible pregnant women.

Baseline Xpert MTB/RIF ct values predict sputum conversion during the intensive phase of anti-TB treatment in HIV infected patients in Kampala, Uganda: a retrospective study.

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In resource-limited settings, sputum smear conversion is used to document treatment response. Many People living with HIV (PLHIV) are smear-negative at baseline. The Xpert MTB/RIF test can indirectly measure bacterial load through cycle threshold (ct) values. This study aimed to determine if baseline Xpert MTB/RIF could predict time to culture negativity in PLHIV with newly diagnosed TB. A subset of 138 PLHIV from the 'SOUTH' study on outcomes related to TB and antiretroviral drug concentrations were included. Bacterial load was estimated by Mycobacterium Growth Indicator Tubes (MGIT) culture time-to-positivity (TTP) and Lowenstein Jensen (LJ) colony counts. Changes in TTP and colony counts were analyzed with Poisson Generalised Estimating Equations (GEE) and multilevel ordered logistic regression models, respectively, while time to culture negativity analysed with Cox proportional hazard models. ROC curves were used to explore the accuracy of the ct value in predicting culture negativity. A total of 81 patients

(58.7%) were males, median age 34 (IQR 29 –40) years, median CD4 cell count of 180 (IQR 68 –345) cells/ μ L and 77.5% were ART naive. The median baseline ct value was 25.1 (IQR 21.0 –30.1). A unit Increase in the ct value was associated with a 5% (IRR= 1.05 95% CI 1.04 –1.06) and 3% (IRR= 1.03 95% CI 1.03 –1.04) increase in TTP at week 2 and 4 respectively. With LJ culture, a patient's colony grade was reduced by 0.86 times (OR=0.86 95% CI 0.74 –0.97) at week 2 and 0.84 times (OR=0.84 95% CI 0.79 –0.95 P=0.002) at week 4 for every unit increase in the baseline ct value. There was a 3% higher likelihood of earlier conversion to negativity for every unit increase in the ct value. A ct cut point \geq 28 best predicted culture negativity at week 4 with a sensitivity of 91. 7% & specificity 53.7% while a cut point \geq 23 best predicted culture negativity at week 8. Baseline Xpert MTB/RIF ct values predict sputum conversion in PLHIV on anti-TB treatment. Surrogate biomarkers for sputum conversion in PLHIV are still a research priority.

Africa's respiratory “Big Five”

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Abstract

The British Thoracic Society (BTS) launched a Global Health Group in the winter of 2019 in partnership with the Pan African Thoracic Society. This key meeting generated a lot of interest and areas of mutual benefit. Due to the overwhelming interest at the 2019 meeting, a virtual offering of the BTS Winter meeting February 2021, included a symposium by the Global Health Group on Africa's Respiratory “Big Five.” The Winter meeting was free for PATS members and symposium had

an excellent attendance, covering the following areas: Pneumonia in the under 5, impact of air pollution on lung health, post-TB lung disease, and non-communicable respiratory disease across the life course. This paper is a summary of the symposium and seeks to address research priority areas for lung health research on the African continent.

Fungal asthma among Ugandan adult asthmatics.

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Abstract

Fungal sensitization is associated with poor asthma control. We aimed to determine the prevalence and factors associated with fungal asthma among Ugandan adults. Individuals aged ≥ 18 years with a new diagnosis of asthma in the last 12 months participating in the African Severe Asthma Program constituted the study population. Skin prick test results, clinical and demographic data were retrieved from the database, and serum *Aspergillus fumigatus* specific antibodies and total IgE were measured in stored blood. We enrolled 374 patients, median (IQR) age 34 (25–45) years, 286 (76.5%) females and 286 (76.5%) with severe asthma. Prevalence of *Aspergillus fumigatus* sensitization was 42.0% (95% CI: 37.1–47.0%), allergic bronchopulmonary aspergillosis (ABPA) 3.2% (1.8–5.5%), severe asthma with fungal sensitization (SAFS) 16% (12.7–20.1%) and allergic bronchopulmonary mycosis (ABPM) 2.9% (1.7–5.2%). Older age (55–64 years) (crude odds ratio (cOR) = 2.6), sensitization to at least one allergen (cOR = 9.38) and hypertension (cOR = 1.99) were significantly associated with *Aspergillus* sensitization,

whereas tertiary education level (cOR = 0.29), severe depression (cOR = 0.15) and strong emotions (cOR = 0.47) were not. High occupational exposure to *Aspergillus* (cOR = 4.26) and contact with moulds (cOR = 14.28) were significantly associated with ABPA. Palpitations (cOR = 5.54), uncontrolled asthma (cOR = 3.54), eczema/dermatitis (cOR = 3.07), poor lung function (cOR = 2.11) and frequent exacerbations (cOR = 1.01) were significantly associated with SAFS. Eczema/dermatitis (cOR = 1.55) was significantly associated with ABPM, but cold weather trigger (cOR = 0.24) was not. Fungal asthma is a significant problem among Ugandans with asthma and should be particularly considered in individuals who remain uncontrolled despite optimal standard of care for asthma, as it is responsive to available and affordable oral antifungal therapy.

LAY SUMMARY: This study showed that fungal asthma is a significant problem among Ugandans with asthma with a high prevalence. Fungal asthma should be considered in patients with uncontrolled asthma despite receiving optimal standard of care. This is the first modern attempt to define these endotypes of asthma in Africa.

Effectiveness of thermal screening in detection of COVID-19 among truck drivers at Mutukula Land Point of Entry, Uganda

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INTRODUCTION: Despite the limited evidence for its effectiveness, thermal screening at points of entry has increasingly become a standard protocol in numerous parts of the globe in response to the COVID-19 pandemic. We sought to determine the effectiveness of thermal screening as a key step in diagnosing COVID-19 in a resource-limited setting.

MATERIALS AND METHOD: This was a retrospective cross-sectional study based on a review of body temperature and Xpert Xpress SARS CoV-2 test results records for truck drivers entering Uganda through Mutukula between 15th May and 30th July 2020. All records missing information for body temperature, age, gender, and Xpert Xpress SARS CoV-2 status were excluded from the data set. A data set of 7,181 entries was used to compare thermal screening and Xpert Xpress SARS CoV-2 assay test results using the diagnostic statistical test in STATAv15 software. The prevalence of COVID-19 amongst the truck drivers based on Xpert Xpress SARS CoV-2 assay results was determined. The sensitivity, specificity, positive predictive value, negative predictive value, positive and negative Likelihood ratios were obtained using Xpert Xpress SARS CoV-2 assay as the gold standard.

RESULTS: Based on our gold standard test, the proportion of persons that tested positive for COVID-19 was 6.7% (95% CI: 6.1–7.3). Of the 7,181 persons that were thermally screened, 6,844 (95.3%) were male. The sample median age was 38 years (interquartile range, IQR: 31–45 years). The median body temperature was 36.5°C (IQR: 36.3–36.7) and only n (1.2%) had a body temperature above 37.5°C. The sensitivity and specificity of thermal screening were 9.9% (95% CI: 7.4–13.0) and 99.5% (95% CI: 99.3–99.6) respectively. The positive and negative predictive values were 57.8 (95% CI: 46.5–68.6) and 93.9 (95% CI: 93.3–94.4) respectively. The positive and negative Likelihood Ratios (LRs) were 19 (95% CI: 12.4–29.1) and 0.9 (95% CI: 0.88–0.93) respectively.

CONCLUSION: In this study population, the use of Thermal screening alone is ineffective in the detection of potential COVID-19 cases at point of entry. We recommend a combination of screening tests or additional testing using highly sensitive molecular diagnostics such as Polymerase Chain Reaction.

Skin prick reactivity among asthmatics in East Africa

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BACKGROUND: The burden of asthma in Africa is high, and yet the disease is not universally prioritised. Data on allergic asthma and its impact on asthma morbidity are limited in Africa. Our aim was to describe the distribution of skin prick positivity among asthmatics in Eastern Africa.

METHODS: From August 2016 to May 2018, 1671 asthmatic patients were enrolled from Uganda, Kenya, and Ethiopia as part of the African Severe Asthma Program clinical study. Skin prick testing was performed at baseline using a panel of 12 allergens, and factors associated with skin prick reactivity determined.

RESULTS: Of the 1,671 patients recruited, 71% were female with a median age of 40 years, 93.6% were aged >15 years and the patterns of asthma symptom frequency was intermittent in 2.9%, mild persistent in 19.9%, moderate persistent in 42.6% and severe persistent in 34.6% at baseline. Self-reported triggers, were dust (92%), cold weather (89%), upper respiratory infections (84%), strong smells (79%) and exposure to tobacco (78%). The majority (90%) of the participants had at least 1 positive allergen reaction, with 0.9% participants reacting to all the 12 allergens. Participants commonly reacted to house dust mites (66%), *Blomia tropicalis* (62%), and the German cockroach (52%). Patients sensitized to more allergens (>2) had significantly reduced lung function ($FEV_1 \leq 80\%$; $p = 0.001$) and were more likely to visit the emergency department due to asthma ($p = 0.012$). There was no significant relationship between number of allergens and measures of asthma control, quality of life, and other clinical outcomes. Only the country of origin was independently

associated with atopy among African asthmatics.

CONCLUSION: There is a high prevalence of skin prick positivity among East African patients with asthma, with the commonest allergen being house dust mite. Skin reactivity did not correlate well with asthma severity and poor asthma control. The relation between atopy, measured through skin prick testing, and measures of asthma control among asthma patients in Eastern Africa is unclear and needs further study.

Variations in Trim5 α and Cyclophilin A genes among HIV-1 elite controllers and non controllers in Uganda: a laboratory-based cross-sectional study

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BACKGROUND: Tripartite Motif Containing 5 alpha (TRIM5 α), a restriction factor produced ubiquitously in cells and tissues of the body plays an important role in the immune response against HIV. TRIM5 α targets the HIV capsid for proteosomal destruction. Cyclophilin A, an intracellular protein has also been reported to influence HIV infectivity in a cell-specific manner. Accordingly, variations in TRIM5 α and Cyclophilin A genes have been documented to influence HIV-1 disease progression. However, these variations have not been documented among Elite controllers in Uganda and whether they play a role in viral suppression remains largely undocumented. Our study focused on identifying the variations in TRIM5 α and Cyclophilin A genes among HIV-1 Elite controllers and non-controllers in Uganda.

RESULTS: From the sequence analysis, the rs10838525 G>A mutation in exon 2 of TRIM5 α was only found among elite controllers (30%) while the rs3824949 in the 5'UTR was seen among 25% of the non-controllers. In the Cyclophilin A promoter, rs6850 was seen among 62.5% of the non-controllers and only among

10% elite controllers. Furthermore, rs17860048 in the Cyclophilin A promoter was predominantly seen among elite controllers (30%) and 12.5% noncontrollers. From gene expression analysis, we noted that the respective genes were generally elevated among elite controllers, however, this difference was not statistically significant (TRIM5 α p=0.6095; Cyclophilin A p=0.6389).

CONCLUSION: Variations in TRIM5 α and Cyclophilin A promoter may influence HIV viral suppression. The rs10838525 SNP in TRIM5 α may contribute to viral suppression among HIV-1 elite controllers. The rs6850 in the cyclophilin A gene may be responsible for HIV-1 rapid progression among HIV-1 non-controllers. These SNPs should be investigated mechanistically to determine their precise role in HIV-1 viral suppression.

Characteristics and outcomes of admitted patients infected with SARSCoV-2 in Uganda

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RATIONALE: Detailed data on the characteristics and outcomes of patients with COVID-19 in sub-Saharan Africa are limited.

OBJECTIVE: We determined the clinical characteristics and treatment outcomes of patients diagnosed with COVID-19 in Uganda.

MEASUREMENTS: As of the 16 May 2020, a total of 203 cases had been confirmed. We report on the first 56 patients; 29 received hydroxychloroquine (HCQ) and 27 did not. Endpoints included admission to intensive care, mechanical ventilation or death during hospitalisation.

MAIN RESULTS: The median age was 34.2 years; 67.9% were male; and 14.6% were <18 years. Up 57.1% of the patients were asymptomatic. The most common symptoms were fever (21.4%), cough (19.6%), rhinorrhea (16.1%), headache (12.5%), muscle ache (7.1%) and fatigue (7.1%). Rates of comorbidities were 10.7% (pre-existing hypertension), 10.7% (diabetes) and 7.1% (HIV), Body Mass Index (BMI) of ≥ 30 36.6%. 37.0% had a blood pressure (BP) of $>130/90$ mm Hg, and 27.8% had BP of $>140/90$ mm Hg. Laboratory derangements were leucopenia (10.6%), lymphopenia (11.1%) and thrombocytopenia (26.3%). Abnormal chest X-ray was observed in 14.3%. No patients reached the primary endpoint. Time to clinical recovery was shorter among patients who received HCQ, but this difference did not reach statistical significance.

CONCLUSION: Most of the patients with COVID-19 presented with mild disease and exhibited a clinical trajectory not similar to other countries. Outcomes did not differ by HCQ treatment status in line with other concluded studies on the benefit of using HCQ in the treatment of COVID-19.

Dance for Respiratory Patients in Low-Resource Settings

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Abstract

Chronic respiratory disease is a leading cause of morbidity and mortality globally and disproportionately affects people in low-income settings.¹ Pulmonary rehabilitation programs are an effective intervention available for people with chronic respiratory disease, and exercise training is a core component of these

programs.² Recent years have seen growing interest in integrating alternative forms of exercise training, such as yoga, Tai Chi, and dance³ into pulmonary rehabilitation programs to make them more engaging and enjoyable. Dance, in particular, is an effective form of exercise training demonstrated to improve motor function (balance, strength, exercise capacity), metabolic parameters, and quality of life in older patients and persons with movement disorders.⁴⁻⁶ As an intervention for respiratory patients, dance has been shown, in small studies, to improve 6-minute walk distance, balance (measured using the Brief Balance Evaluation Systems Test [BESTest]), balance confidence (measured using the Activities-Specific Balance Confidence Scale [ABC scale]), and Chronic Respiratory Disease Questionnaire-measured symptoms.⁷

Illness representations of chronic obstructive pulmonary disease (COPD) to inform health education strategies and research design—learning from rural Uganda

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Abstract

More than 90% of chronic obstructive pulmonary disease (COPD)-related deaths occur in low- and middle-income countries; however, few studies have examined the illness experiences of individuals living with and providing treatment for COPD in these settings. This study characterizes illness representations for COPD in Nakaseke, Uganda from the perspectives of health care providers, village health teams and community members (CMs) with COPD. We conducted 40 in-depth, semi-structured interviews (16 health care providers, 12 village health teams and

12 CMs, aged 25–80 years). Interviews were analyzed using inductive coding, and the Illness Representations Model guided our analysis. Stakeholder groups showed concordance in identifying causal mechanisms of COPD, but showed disagreement in reasons for care seeking behaviors and treatment preferences. CMs did not use a distinct label to differentiate COPD from other respiratory illnesses, and described both the physical and social consequences of COPD. Local representations can inform development of adapted educational and self-management tools for COPD.

Prevalence and Predictors of CD4+ T-Lymphocytopenia Among HIV-Negative Tuberculosis Patients in Uganda

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PURPOSE: CD4+ T-lymphocytopenia is a risk for tuberculosis (TB) infection, reactivation and severe disease. We sought to determine the prevalence and predictors of CD4 T-lymphocytopenia among HIV-negative patients with bacteriologically confirmed TB in Uganda.

PATIENTS AND METHODS: Eligible participants were adult HIV-negative patients with bacteriologically confirmed TB at the National TB Treatment Centre in Uganda. CD4+ and CD8+ T-lymphocyte counts were determined by flow cytometry. We defined CD4+ T-lymphocytopenia as a CD4+ T-lymphocyte count of <418 cells/mm³ as per the population estimate for Ugandans. We performed logistic regression analysis to determine predictors of CD4+ T-lymphocytopenia.

RESULTS: We enrolled 216 participants whose mean age (standard deviation (\pm SD)) was 32.5 (\pm 12.1) years, of whom 146 (67.6%) were males. The prevalence of CD4+ T-lymphocytopenia was 25% (54/216) (95% confidence interval (CI): 19.6–31.2%). Patients with anaemia (adjusted odds ratio (aOR): 3.83, 95% CI: 1.59–9.23, $p = 0.003$), weight loss (aOR: 3.61, 95% CI: 1.07–12.23, $p = 0.039$) and a low CD8+ T-cell count (aOR: 6.10, 95% CI: 2.68–13.89, $p < 0.001$) were more likely to have CD4+ T-lymphocytopenia while those with monocytosis (aOR: 0.35, 95% CI: 0.14–0.89, $p = 0.028$) were less likely to have CD4+ T-lymphocytopenia.

CONCLUSION: There was a high prevalence of CD4+ T-lymphocytopenia among HIV-negative TB patients. Patients with weight loss, anaemia and a low CD8+ count were more likely to have CD4+ T-lymphocytopenia while those with monocytosis were less likely to have CD4+ lymphocytopenia. The findings suggest that CD4+ lymphocytopenia is indicative of severe disease and globally impaired cell-mediated immune responses against TB.

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Households experiencing catastrophic costs due to tuberculosis in Uganda: magnitude and cost drivers

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BACKGROUND: Tuberculosis (TB) patients in Uganda incur large costs related to the illness, and while seeking and receiving health care. Such costs create access and adherence barriers which affect health outcomes and increase transmission of disease. The study ascertained the proportion of Ugandan TB affected households incurring catastrophic costs and the main cost drivers.

METHODS: A cross-sectional survey with retrospective data collection and projections was conducted in 2017. A total of 1178 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 1178 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 costs of USD 396 for a DS-TB episode and USD 3722 for a Multi drug resistant tuberculosis (MDR TB) episode. Up to 48.5% of households borrowed, used savings or sold assets to defray 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 drivers being non-medical expenditure such as travel, nutritional supplements and food.

CONCLUSION: 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 multi-sectoral action plans with central NTP involvement would palliate these costs.

Accuracy and Incremental Yield of the Chest X-Ray in Screening for Tuberculosis in Uganda: A Cross-Sectional Study

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Abstract

The WHO END TB strategy requires $\geq 90\%$ case detection to combat tuberculosis (TB). Increased TB case detection requires a more sensitive and specific screening tool. Currently, the symptoms recommended for screening TB have been found to be suboptimal since up to 44% of individuals with TB are asymptomatic. The chest X-ray (CXR) as a screening tool for pulmonary TB was evaluated in this study, as well as its incremental yield in TB diagnosis using a cross-sectional study involving secondary analysis of data of 4512 consented/assented participants ≥ 15 years who participated in the Uganda National TB prevalence survey between 2014 and 2015. Participants with a cough ≥ 2 weeks, fever, weight loss, and night sweats screened positive for TB using the symptoms screening method, while participants with a TB defining abnormality on CXR screened positive for TB by the CXR screening method. The Löwenstein-Jensen (LJ) culture was used as a gold standard for TB diagnosis. The CXR had 93% sensitivity and 65% specificity compared to LJ culture results, while symptoms had 76% sensitivity and 31% specificity. The screening algorithm involving the CXR in addition to symptoms led to a 38% increment in the yield of diagnosed tuberculosis. The number needed to screen using the CXR and symptoms screening algorithm was 32 compared to 45 when the symptoms are used alone. Therefore, the CXR in combination with symptoms is a good TB screening tool and increases the yield of diagnosed TB.

Association between Blood Pressure and HIV Status in Rural Uganda: Results of Cross-Sectional Analysis

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METHODS: We conducted a cross-sectional analysis in two concurrent cohorts of 600 HIV negative and 721 HIV seropositive individuals aged ≥ 35 years.

RESULTS: Of the 721 HIV positive participants, 59.8% were women and the median age was 44.3 years, while for HIV negative individuals, 55% were women and the median age was 47.8 years. Over 90% of HIV positive individuals were on antiretroviral treatment. The prevalence of hypertension ($\geq 140/\geq 90$ mmHg) was 33.5% in HIV negative individuals and 23.9% in HIV positive individuals. Age (adjusted OR= 1.05, 95% CI 1.03 to 1.06) and BMI (adjusted OR= 1.08, 95% CI 1.05 to 1.12) were associated with higher odds of hypertension. Having HIV was associated with lower odds of hypertension (adjusted OR= 0.66, 95% CI 0.50 to 0.88), lower systolic blood pressure (-5.1 mmHg, 95% CI: -7.4 to -2.4) and lower diastolic blood pressure (-4.0 mmHg, 95% CI: -5.6 to -2.5). We did not observe differences in the odds of hypertension by CD4 count, viral load or ART among HIV positive individuals in this sample.

CONCLUSIONS: Hypertension was prevalent in one third of HIV negative individuals and in one fourth of HIV positive patients. While access to health information among individuals attending HIV clinics may explain observed differences, more research is needed to understand plausible biological and social mechanisms that could explain lower blood pressure among people living with HIV in Uganda.

Incidence and predictors of COPD mortality in Uganda: A 2-year prospective cohort study

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BACKGROUND: Data is lacking on outcomes among COPD patients in sub-Saharan Africa. The objective of the study was to assess the incidence and predictors of mortality among COPD patients enrolled in the Uganda Registry for Asthma and COPD.

RESEARCH QUESTION: What is the Incidence and predictors of mortality among COPD patients in Uganda?

STUDY DESIGN AND METHODS: Individuals with a diagnosis of COPD at six hospitals in Uganda were enrolled into the registry, and followed every six months. Mortality was ascertained through post-mortem reports and verbal autopsies. Mortality rates (MR), mortality rate ratios (MRR), and hazard ratios (HR) were computed to assess associations between socio-demographic, behavioural, and clinical characteristics at enrolment into the registry and mortality up to two years after.

RESULTS: We enrolled 296 COPD patients. Median age was 60 years, and 51.3% were male. The overall mortality rate was 95.90 deaths/1000 person-years. COPD severity by post-bronchodilator FEV1 was the strongest risk factor for mortality. Compared to stage 1, adjusted hazard ratios were as follows for stage 4: 9.86 (95%CI: 1.70–57.14, $p = 0.011$), stage 3: 6.16 (95%CI: 1.25–30.32, $p = 0.025$), and stage 2: 1.76 (95%CI: 0.33–9.48, $p = 0.51$). Underweight patients had a higher incidence of mortality compared to normal weight patients (MRR: 3.47 (95%CI: 1.45–8.31, $p = 0.0026$).

CONCLUSION: Among COPD patients in Uganda, two-year mortality is high, and disease severity at baseline was the strongest risk factor for mortality. Our findings suggest the need for early, accurate, diagnosis and management of COPD, to potentially improve survival.

Back to Basics in Paediatric Pneumonia— Defining a Breath and Setting Reference Standards to Innovate Respiratory Rate Counting

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Abstract

Every November 12th, the global health community hosts World Pneumonia Day, and in 2020, on the 11th iteration, we find ourselves once more facing the fact that pneumonia is the leading global cause of infectious mortality amongst children under-5 years old. Many regions are not within sight of the Sustainable Development Goal 3.2 target. And yet, this situation may be less surprising given we are—11years later—still discussing the basic question of how we define (and count) a child’s single breath. The cornerstone of paediatric pneumonia diagnosis in most low-and middle-income country (LMIC) settings, and particularly in primary care, is the evaluation of respiratory rate (RR), as part of the clinical algorithms that constitute the Integrated Management of Childhood Illness (IMCI). The introduction of this standardized syndromic approach through the WHO case management guidelines has resulted in significant pneumonia mortality reductions [1]. The current standard of determining RR is visually counting the number of breaths a child takes over an uninterrupted 60-second period, using a stopwatch or RR counting timer. However, this can be unreliable (especially amongst younger and/or uncooperative children), challenging in timelimited high-volume settings and often not routinely done by healthcare workers. Additionally, timers are often unavailable [2–4]. Therefore, the lack of lowcost, accurate and easy-to-use RR tools limits diagnostic quality of care, in turn affecting treatment decision-making and health

outcomes. Alternative RR counting tools for LMIC settings have been proposed (eg counting beads) and new technologies are coming to market harnessing mHealth, accelerometers and photoplethysmography. Major barriers to adoption include determining real-world performance, lack of consensus on suitable reference standards and benchmarking against current standard of care [5, 6]. In fact, there is no clear description of a 'breath' within WHO training tools or guidelines. While a 'breath' may seem so intuitive to not warrant defining, this is not necessarily true when comparing novel technologies. A breath could be defined a number of ways, including the observation of one full inhalation and exhalation, a measurable chest movement, blood volume fluctuations, a measurement of ventilation or gas exchange (capnography)[5]. It is unsurprising that these could lead to different RR counts and be the difference between a pneumonia diagnosis or not. To move forward, expert consensus on defining a breath is fundamental. It is important that such a definition retains pragmatism and generalizability across healthcare settings, realistically meaning manual breath counts through non-invasive observation in a consistent way. While this is inherently subjective, we can take lessons from other diagnostics which also suffer from observer variability. For these, expert.

Factors critical to implementation success of cleaner cooking interventions in low-income and middle-income countries: protocol for an umbrella review

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ABSTRACT: Over a third of the world's population relies on solid fuels as their primary energy source. These fuels have damaging effects on health, air quality and forest resources. Interventions to promote access to cleaner solid fuel cookstoves and clean fuels have existed for decades. However, the adoption by local communities has largely failed, which led to a waste of resources and suboptimal outcomes. Therefore, the objective of this umbrella review is to identify factors that determine implementation success for cleaner cooking interventions in low-resource settings and weigh their level of confidence in the evidence.

METHODS AND ANALYSIS: We identified systematic and narrative reviews

examining factors that influence the acquisition, initial adoption or sustained use of cleaner solid fuel cookstoves and clean fuels at any scale by a literature search in PubMed, Embase, Global Health Database, Cochrane, PsycINFO, Emcare, Web of Science and CINAHL, without date or language restrictions. The search was conducted on 23 October 2017 and updated on 10 July 2019. Reviews based on qualitative, quantitative or mixed-methods studies were included and will be appraised using the Meta Quality Appraisal Tool combined with the Assessment of Multiple Systematic Reviews. Data will be extracted and factors affecting implementation will be coded using the Consolidated Framework for Implementation Research. The Grading of Recommendations Assessment, Development and Evaluation-Confidence in the Evidence from Reviews of Qualitative Research tool will be used to determine the level of confidence in the coded factors. Two researchers will independently conduct these steps.

ETHICS AND DISSEMINATION: This umbrella review does not require the approval of an ethical review board. Study results will be published in an international peer-reviewed journal. The outcomes will be converted into two practical tools: one for cleaner solid fuel cookstoves and one for clean fuels. These tools can guide the development of evidence-based implementation strategies for cleaner cooking interventions in low-income and middle-income countries to improve implementation success. These tools should be pilot-tested and promoted among regional and global initiatives.

Global RECHARGE: Establishing a standard international data set for pulmonary rehabilitation in low- and middle-income countries

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Abstract

Chronic respiratory diseases (CRD) are highly prevalent in low- and middle-income countries (LMICs). People living with CRD are often disabled by breathlessness which can result in reduced health-related quality of life, including reduced exercise tolerance, significant psychological morbidity and reduced ability to work. Implementing clinically and cost-effective interventions to tackle these problems can be challenging in low-resource settings. Pulmonary rehabilitation is a low cost, high impact intervention that reverses CRD-related disability and is supported by the highest level of research. Pulmonary rehabilitation is delivered by a multidisciplinary team and has exercise training and education at its core to support effective disease management and improve people's quality of life. There is an unmet need for pulmonary rehabilitation that is profound in LMICs where the demand greatly outweighs the capacity. The sparse existence of pulmonary rehabilitation in LMICs offers an important opportunity to support the expansion of high quality, benchmarked services as it becomes increasingly recognised and available. Quality assurance procedures for pulmonary rehabilitation in the developed world are now in place; helping to ensure a high standard of patient care. In this paper we discuss a common data set that has been developed by the NIHR Global Health Research Group on Respiratory Rehabilitation (Global RECHARGE). Standardising data collection with a pre-determined set of measurements is proposed whereby collaborators will use common data collection tools and procedures. Benchmarking and quality improvement with continuous audit offer a potential to maximise benefits, reduce waste and improve patient outcomes. We welcome expressions of interest from health care professionals and researchers from LMICs, including groups looking to strengthen their local research capacity and from those looking to set up pulmonary rehabilitation through to those already running a service. We believe the wide adoption of this core data set will facilitate quality assurance of pulmonary rehabilitation programmes, provide opportunities to expand services over time, de novo research opportunities offered by trans-national data and enhanced research capacity in partner organisations.

A Novel Case-Finding Instrument for Chronic Obstructive Pulmonary Disease in Low- and Middle-Income Country Settings

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BACKGROUND: Low- and middle-income countries (LMICs) account for >90% of deaths and illness episodes related to COPD; however, this condition is commonly underdiagnosed in these settings. Case-finding instruments for COPD may improve diagnosis and identify individuals that need treatment, but few have been validated in resource-limited settings.

METHODS: We conducted a population-based cross-sectional study in Uganda to assess the diagnostic accuracy of a respiratory symptom, exposure and functional questionnaire in combination with peak expiratory flow for COPD diagnosis using post-bronchodilator FEV₁/FVC z-score below the 5th percentile as the gold standard. We included locally relevant exposure questions and statistical learning techniques to identify the most important risk factors for COPD. We used 80% of the data to develop the case-finding instrument and validated it in the remaining 20%. We evaluated for calibration and discrimination using standard approaches. The final score, COLA (COPD in LMICs Assessment), included seven questions, age and pre-bronchodilator peak expiratory flow.

RESULTS: We analyzed data from 1,173 participants (average age 47 years, 46.9% male, 4.5% with COPD) with acceptable and reproducible spirometry. The seven questions yielded a cross-validated area-under-the-curve [AUC] of 0.68 (95% CI 0.61–0.75) with higher scores conferring greater odds of COPD. The inclusion of peak expiratory flow and age improved prediction in a validation sample (AUC=0.83, 95% CI 0.78–0.88) with a positive predictive value of 50% and a negative predictive value of 96%. The final instrument (COLA) included seven questions, age and pre-bronchodilator peak expiratory flow.

CONCLUSION: COLA predicted COPD in urban and rural settings in Uganda has high calibration and discrimination, and could serve as a simple, low-cost screening tool in resource-limited settings.

Gaps in COPD Guidelines of Low- and Middle-Income Countries: A Systematic Scoping Review

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BACKGROUND: Guidelines are critical for facilitating cost-effective COPD care. Development and implementation in low-and middle-income countries (LMICs)

is challenging. To guide future strategy, an overview of current global COPD guidelines is required.

Research Question: We systematically reviewed national COPD guidelines, focusing on worldwide availability and identification of potential development, content, context, and quality gaps that may hamper effective implementation.

STUDY DESIGN AND METHODS: Scoping review of national COPD management guidelines. We assessed: (1) global guideline coverage; (2) guideline information (authors, target audience, dissemination plans); (3) content (prevention, diagnosis, treatments); (4) ethical, legal, and socio-economic aspects; and (5) compliance with the eight Institute of Medicine (IOM) guideline standards. LMICs guidelines were compared with those from high-income countries (HICs).

RESULTS: Of the 61 national COPD guidelines identified, 30 were from LMICs. Guidelines did not cover 1.93 billion (30.2%) people living in LMICs, whereas only 0.02 billion (1.9%) in HICs were without national guidelines. Compared with HICs, LMIC guidelines targeted fewer health-care professional groups and less often addressed case finding and co-morbidities. More than 90% of all guidelines included smoking cessation advice. Air pollution reduction strategies were less frequently mentioned in both LMICs (47%) and HICs (42%). LMIC guidelines fulfilled on average 3.37 (42%) of IOM standards, compared with 5.29 (66%) in HICs ($P < .05$). LMICs scored significantly lower compared with HICs regarding conflicts of interest management, updates, articulation of recommendations, and funding transparency (all, $P < .05$).

National tuberculosis prevalence surveys in Africa, 2008–2016: an overview of results and lessons learned

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Link: <https://doi.org/10.1111/tmi.13485>

OBJECTIVE AND METHODS: Worldwide, tuberculosis (TB) is the leading cause of death from a single infectious agent. In many countries, national TB prevalence surveys are the only way to reliably measure the burden of TB disease and can also provide other evidence to inform national efforts to improve TB detection and treatment. Our objective was to synthesise the results and lessons learned from national surveys completed in Africa between 2008 and 2016, to complement a previous review for Asia.

RESULTS: Twelve surveys completed in Africa were identified: Ethiopia (2010–

2011), Gambia (2011–2013), Ghana (2013), Kenya (2015–2016), Malawi (2013–2014), Nigeria (2012), Rwanda (2012), Sudan (2013–2014), Tanzania (2011–2012), Uganda (2014–2015), Zambia (2013–2014) and Zimbabwe (2014). The eligible population in all surveys was people aged ≥ 15 years who met residency criteria. In total 588 105 individuals participated, equivalent to 82% (range 57–96%) of those eligible. The prevalence of bacteriologically confirmed pulmonary TB disease in those ≥ 15 years varied from 119 (95% CI 79–160) per 100 000 population in Rwanda and 638 (95% CI 502–774) per 100 000 population in Zambia. The male:female ratio was 2.0 overall, ranging from 1.2 (Ethiopia) to 4.1 (Uganda). Prevalence per 100 000 population generally increased with age, but the absolute number of cases was usually highest among those aged 35–44 years. Of identified TB cases, 44% (95% CI 40–49) did not report TB symptoms during screening and were only identified as eligible for diagnostic testing due to an abnormal chest X-ray. The overall ratio of prevalence to case notifications was 2.5 (95% CI 1.8–3.2) and was consistently higher for men than women. Many participants who did report TB symptoms had not sought care; those that had were more likely to seek care in a public health facility. HIV prevalence was systematically lower among prevalent cases than officially notified TB patients with an overall ratio of 0.5 (95% CI 0.3–0.7). The two main study limitations were that none of the surveys included people < 15 years, and 5 of 12 surveys did not have data on HIV status.

CONCLUSIONS: National TB prevalence surveys implemented in Africa between 2010 and 2016 have contributed substantial new evidence about the burden of TB disease, its distribution by age and sex, and gaps in TB detection and treatment. Policies and practices to improve access to health services and reduce under-reporting of detected TB cases are needed, especially among men. All surveys provide a valuable baseline for future assessment of trends in TB disease burden.

LIST OF
PUBLICATIONS
2019/20

Delays in diagnosis and treatment of pulmonary tuberculosis in patients seeking care at a regional referral hospital, Uganda: a cross sectional study

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OBJECTIVE: A cross-sectional survey involving 134 pulmonary TB patients started on TB treatment at the TB Treatment Unit of the regional referral hospital was conducted to ascertain the prevalence of individual and health facility delays and associated factors. Prolonged health facility delay was taken as delay of more than 1 week and prolonged patient delay as delay of more than 3 weeks. A logistic regression model was done using STATA version 12 to determine the delays.

RESULTS: There was a median total delay of 13 weeks and 110 (82.1%) of the respondents had delay of more than 4 weeks. Patient delay was the most frequent and greatest contributor of total delay and exceeded 3 weeks in 95 (71.6%) respondents. At multivariate analysis, factors that influenced delay included poor patient knowledge on TB (adjOR 6.904, 95% CI 1.648–28.921; $p=0.04$) and being unemployed (adjOR 3.947, 95% CI 1.382–11.274; $p=0.010$) while being female was found protective of delay; adjOR 0.231, 95% CI 0.08–0.67; $p=0.007$). Patient delay was the most significant, frequent and greatest contributor to total delay, and factors associated with delay included being unemployed, low knowledge on TB while being female was found protective of delay

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

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Abstract

Biomass smoke exposure is a threat to child and maternal health in many resource-limited countries and is associated with poor pregnancy outcomes and serious lung diseases in the offspring. We aimed to assess the feasibility, acceptability and impact of a midwife-led education programme on biomass risks and prevention for women attending maternity clinics in Uganda. Education materials were co-developed through an iterative process by midwives and other stakeholders. The materials were serially tested and approved by the Ministry of Health and used by midwives and village health teams (VHTs). The district health team, 12 midwives and 40 VHTs were sensitised on biomass smoke. Two hundred and forty-four women were educated about biomass smoke by midwives; pre- and post-session questionnaires showed major improvements in knowledge of biomass smoke risks. Qualitative interviews with women three months after the sessions showed that they made behavioural changes such as avoiding smoke while cooking, using dry wood, solar power for lighting and improved ventilation. The major barrier to behavioural changes was poverty, but some improvements cost no money. The programme delivered by midwives was feasible and acceptable; implementing this programme has the potential to reduce exposure to smoke with major benefits to mother, foetus, and children throughout their lives.

Health seeking behaviour among individuals presenting with chronic cough at referral hospitals in Uganda; Missed opportunity for early tuberculosis diagnosis

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BACKGROUND: Tuberculosis (TB) is the 9th leading cause of death from a single infectious agent. Patients live in a complex health care system with both formal and informal providers, and it is important that a TB diagnosis is not missed at the first interaction with the health care system. In this study, we highlight the health seeking behavior of patients and missed opportunities for early TB diagnosis 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 referral hospitals in Uganda. We documented the symptom profile of presumptive TB patients and assessed the health seeking behavior of those with chronic cough by calculating proportion 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.

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. A total of 1352 (75.4%) had previously sought care for chronic cough, with 805 (59.6%) seeking care from a public health facility followed by private health facility (289; 21.4%). Up to 182 (13.5%) patients visited a drug store for chronic cough. Patients whose first contact was a private health facility were more likely to have a positive GeneXpert test (adjOR 1.4, 95% CI: 1.0–1.9; p = 0.047).

CONCLUSIONS: Chronic cough is a main symptom for many of the presumptive TB patients presenting at referral hospitals, with several patients having to visit the health system more than once before a TB diagnosis is made. This suggests the need for patients to be thoroughly evaluated at first interface with the health care system to ensure prompt diagnosis and treatment initiation. 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.

Comparison of GeneXpert cycle threshold values with smear microscopy and culture as a measure of mycobacterial burden in five regional referral hospitals of Uganda– A cross-sectional study

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BACKGROUND: Determining mycobacterial burden is important in assessing severity of disease, evaluating infectiousness and predicting patient treatment outcomes. Mycobacterial burden assessed by smear microscopy grade and time to culture positivity is clearly interpretable by most physicians. GeneXpert (Xpert) has been recommended by WHO as a first line tuberculosis (TB) diagnostic test as an alternative to smear microscopy. Xpert gives cycle threshold (Ct) values as a potential measure for mycobacterial burden. For physicians to clearly interpret Ct values as measures of mycobacterial burden, this study compared the Xpert quantification capabilities with those of smear microscopy and culture. The study also determined a linear relationship between Xpert Ct values and MGIT culture time to positivity (MGIT-TTP) and associated factors. A cut off Ct value which best predicts smear positivity was also determined using the Receiver Operator Curve analysis method.

RESULTS: Excluding missing results and rifampicin resistant TB cases, a moderately strong correlation of 0.55 between Xpert Ct value and smear grade was obtained. A weak correlation of 0.37 was obtained between Xpert Ct values and MGIT time to positivity while that between Xpert Ct values and LJ culture was 0.34. The Xpert Ct values were found to increase by 2.57 for every unit increase in days to positive and HIV status was significantly associated with this relationship. A cut off Ct value of 23.62 was found to best predict smear positivity regardless of HIV status.

CONCLUSION: Our study findings show that GeneXpert Ct values are comparable to smear microscopy as a measure of M. tuberculosis burden and can be used to replace smear microscopy. However, given the low correlation between Xpert Ct value and culture positivity, Xpert Ct values cannot replace culture as a measure of M. tuberculosis burden among TB patients.

Burden of fungal asthma in Africa: A systematic review and meta-analysis

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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.

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 Allergic bronchopulmonary aspergillosis was estimated at 1.6–21.2%. Diagnosis of fungal allergy was mostly made by skin prick tests. 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. 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.

Prevalence of chronic respiratory disease in urban and rural Uganda

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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.

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

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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.

Singing for Breathing Uganda: Group singing for people with chronic lung disease in Kampala

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Abstract

Group singing for people with chronic lung diseases has become increasingly popular in Europe, North America and Australia, with a growing body of research suggesting biopsychosocial benefits for participants. This article presents notes from the field and includes information about the programme sessions and programme evaluation, on Singing for Breathing (SFB) Uganda, a group singing programme for people with chronic lung diseases in Kampala, Uganda. Sessions were delivered by Ugandan singing leaders who were supported by a British Lung Foundation Singing for Lung Health trained leader. Sessions included physical, vocal and breathing warm-ups, rhythm and pitch games, repertoire and relaxation. Programme evaluation indicates that sessions were greatly enjoyed by participants and facilitators. Lessons learnt will inform the development of resources to support other groups in Uganda and other countries in sub-Saharan Africa.

Phenotypic characteristics and asthma severity in an East African cohort of adults and adolescents with asthma: findings from the African severe asthma project

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RATIONALE: The relationship between clinical and biomarker characteristics of asthma and its severity in Africa is not well known.

METHODS: Using the Expert Panel Report 3, we assessed for asthma severity and its relationship with key phenotypic characteristics in Uganda, Kenya and Ethiopia. The characteristics included adult onset asthma, family history of asthma, exposures (smoking and biomass), comorbidities (HIV, hypertension, obesity, tuberculosis (TB), rhinosinusitis, gastro-oesophageal disease (GERD) and biomarkers (fractional exhaled nitric oxide (FeNO), skin prick test (SPT) and blood eosinophils). We compared these characteristics on the basis of severity and fitted a multivariable logistic regression model to assess the independent association of these characteristics with asthma severity.

RESULTS: A total of 1671 patients were enrolled, 70.7% women, with median age of 40 years. The prevalence of intermittent, mild persistent, moderate persistent and severe persistent asthma was 2.9%, 19.9%, 42.6% and 34.6%, respectively. Only 14% were on inhaled corticosteroids (ICS). Patients with severe persistent

asthma had a higher rate of adult onset asthma, smoking, HIV, history of TB, FeNO and absolute eosinophil count but lower rates of GERD, rhinosinusitis and SPT positivity. In the multivariate model, Ethiopian site and a history of GERD remained associated with asthma severity.

DISCUSSION: The majority of patients in this cohort presented with moderate to severe persistent asthma and the use of ICS was very low. Improving access to ICS and other inhaled therapies could greatly reduce asthma morbidity in Africa.

Diagnosis and treatment of acute respiratory illness in children under five in primary care in low-, middle-, and high-income countries: A descriptive FRESH AIR study

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BACKGROUND: Respiratory disease and, specifically, pneumonia, is the major cause of mortality and morbidity in young children. Diagnosis of both pneumonia and asthma in primary care rests principally on clinical signs, history taking, and bronchodilator responsiveness. This study aimed to describe clinical practices in diverse global primary care settings concerning differential diagnosis of respiratory disease in young children, especially between pneumonia and asthma.

METHODS: Health professionals in Greece, Kyrgyzstan, Vietnam, and Uganda were observed during consultations with children aged 2–59 months, presenting

with cough and/or difficult breathing. Data were analyzed descriptively and included consultation duration, practices, diagnoses and availability/use of medications and equipment. The study is part of the European Horizon 2020 FRESH AIR project.

RESULTS: In total, 771 consultations by 127 health professionals at 74 facilities in the four countries were observed. Consultations were shorter in Vietnam and Uganda (3 to 4 minutes) pared to Greece and Kyrgyzstan (15 to 20 minutes). History taking was most comprehensive in Greece. Clinical examination was more comprehensive in Vietnam and Kyrgyzstan and less in Uganda. Viral upper respiratory tract infections were the most common diagnoses (41.7% to 67%). Pneumonia was diagnosed frequently in Uganda (16.3% of children), and rarely in other countries (0.8% to 2.9%). Asthma diagnosis was rare (0% to 2.8%). Antibiotics were prescribed frequently in all countries (32% to 69%). Short acting β agonist trials were seldom available and used during consultations in Kyrgyzstan (0%) and Uganda (1.8%), and often in Greece (38.9%) and Vietnam (12.6%).

CONCLUSIONS: Duration and comprehensiveness of clinical consultations observed in this study seemed insufficient to guide respiratory diagnosis in young children. Appropriate treatment options may further not be available in certain studied settings. Actions aiming at educating and raising professional awareness, along with developing easy-to-use tools to support diagnosis and a general strengthening of health systems are important goals.

The socioeconomic burden of chronic lung disease in low-resource settings across the globe – an observational FRESH AIR study

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Link: <https://doi.org/10.1186/s12931-019-1255-z>

BACKGROUND: Low-resource settings are disproportionately burdened by chronic lung disease due to early childhood disadvantages and indoor/outdoor air pollution. However, data on the socioeconomic impact of respiratory diseases in these settings are largely lacking. Therefore, we aimed to estimate the chronic lung disease-related socioeconomic burden in diverse low-resource settings across the globe. To inform governmental and health policy, we focused on work productivity and activity impairment and its modifiable clinical and environmental risk factors.

METHODS: We performed a cross-sectional, observational FRESH AIR study in Uganda, Vietnam, Kyrgyzstan, and Greece. We assessed the chronic lung disease-related socioeconomic burden using validated questionnaires among spirometry-diagnosed COPD and/or asthma patients (total N=1040). Predictors for a higher burden were studied using multivariable linear regression models including demographics (e.g. age, gender), health parameters (breathlessness, comorbidities), and risk factors for chronic lung disease (smoking, solid fuel use). We applied identical models per country, which we subsequently meta-analyzed.

RESULTS: Employed patients reported a median [IQR] overall work impairment due to chronic lung disease of 30% [1.8–51.7] and decreased productivity (presenteeism) of 20.0% [0.0–40.0]. Remarkably, work time missed (absenteeism) was 0.0% [0.0–16.7]. The total population reported 40.0% [20.0–60.0] impairment in daily activities. Breathlessness severity (MRC-scale) (B=8.92, 95%CI=7.47–10.36), smoking (B=5.97, 95%CI=1.73–10.22), and solid fuel use (B=3.94, 95%CI=0.56–7.31) were potentially modifiable risk factors for impairment.

CONCLUSIONS: In low-resource settings, chronic lung disease-related absenteeism is relatively low compared to the substantial presenteeism and activity impairment. Possibly, given the lack of social security systems, relatively few people take days off work at the expense of decreased productivity. Breathlessness (MRC-score), smoking, and solid fuel use are potentially modifiable predictors for higher impairment. Results warrant increased awareness, preventive actions and clinical management of lung diseases in low-resource settings from health policymakers and healthcare workers.

The role of epigenetics in respiratory health in urban populations in low and middle-income countries

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Link: <https://doi.org/10.1017/gheg.2019.7>

Abstract

As urbanization increases in low- and middle-income countries (LMICs), urban populations will be increasingly exposed to a range of environmental risk factors for non-communicable diseases. Inadequate living conditions in urban settings may influence mechanisms that regulate gene expression, leading to the development of non-communicable respiratory diseases. We conducted a systematic review of the literature to assess the relationship between respiratory health and epigenetic factors to urban environmental exposures observed in LMICs using MEDLINE, PubMed, EMBASE, and Google Scholar searching a combination of the terms: epigenetics, chronic respiratory diseases (CRDs), lung development, chronic obstructive airway disease, and asthma. A total of 2835 articles were obtained, and 48 articles were included in this review. We found that environmental factors during early development are related to epigenetic effects that may be associated with a higher risk of CRDs. Epigenetic dysregulation of gene expression of the histone deacetylase (HDAC) and histone acetyltransferase gene families was likely involved in lung health of slum dwellers. Respiratory-related environmental exposures influence HDAC function and deoxyribonucleic acid methylation and are important risk factors in the development of CRD. Additional epigenetic research is needed to improve our understanding of associations between environmental exposures and non-communicable respiratory diseases.

Algorithm-aided diagnosis of chronic pulmonary aspergillosis in low- and middle-income countries by use of a lateral flow device.

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Abstract

Chronic pulmonary aspergillosis (CPA) is a slowly progressive parenchymal lung disease typically caused by *Aspergillus fumigatus* [1]. CPA affects immunocompetent or subtly immunocompromised patients with underlying structural lung diseases [2] and is estimated to affect approximately three million people per year worldwide [3]. It can co-exist with pulmonary tuberculosis (PTB), has both pulmonary and systemic symptoms that are clinically indistinguishable from that of PTB, and is often misdiagnosed and managed as smear-negative PTB [4]. According to the Infectious Diseases Society of America (IDSA), the European Society for Clinical Microbiology and Infectious Diseases (ESCMID), the European Confederation of Medical Mycology (ECMM), and the European Respiratory Society (ERS) Guidelines, the diagnosis of CPA should be based on characteristic symptoms and radiologic features present or presumed to have been present for at least 3 months in a patient with no or minimal immunosuppression and a prior or current lung condition with microbiological or immunological evidence of *Aspergillus* spp. infection [5]. This definition is consistent with the original definition of CPA proposed by Denning and colleagues [1]. Still, CPA is under- and mis-diagnosed in resource-constrained settings where adequate diagnostics are unavailable [6]. Previously treated PTB is the most common risk factor for the development of CPA even in the developed world [1]. The global burden of CPA attributed to healed TB lesions alone has been estimated to over 1.2 million cases annually globally [7]. On the other hand, active PTB is the number one differential diagnosis for CPA and CPA is the number one differential diagnosis for patients previously treated for microbiologically confirmed PTB who are currently sputum smear-negative [6]. Recent evidence has shown that the annual rate of new CPA development following completion

of PTB treatment is about 6.5% in those with chest radiography cavitation and 0.2% in those without [8](Fig. 1). The diagnosis of CPA is based on a combination of clinical symptoms, compatible chest imaging findings, evidence of *Aspergillus* infection (including *Aspergillus*-specific IgG, precipitins, and mycological cultures of respiratory samples) or histology, and the exclusion of alternative diagnosis [1]. Detection of *Aspergillus*-specific IgG is the most reliable evidence of CPA and has been its diagnostic cornerstone [9, 10]. *Aspergillus*-IgG serology using ELISA has been the mainstay of immunological evidence of *Aspergillus* spp. infection in CPA [11]. ELISA instruments are expensive and labor and resource intensive; diagnostic cutoffs vary by ethnicity and technologies used which renders this tool not suitable for resource-limited laboratory settings. Obviously, this has been a major challenge in making a definitive diagnosis of CPA in resource-constrained settings.

A recent lateral flow device (LDBIO Diagnostics, Lyon, France), which has a run time of less than 30 min, is simple to use, and requires minimal laboratory equipment, has consistently been shown to have a good sensitivity (~ 85–92%) and specificity (~ 94–98%) in multisite validation studies, making it a suitable diagnostic tool for the serological.

Achieving Control of Asthma in Children in Africa (ACACIA): protocol of an observational study of children's lung health in six sub-Saharan African countries.

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INTRODUCTION: Little is known about asthma control in the rising number of African children who suffer from this condition. The Achieving Control of Asthma in Children in Africa (ACACIA) study is an observational study collecting evidence

about paediatric asthma in urban areas of Ghana, Malawi, Nigeria, South Africa, Uganda and Zimbabwe. The primary objectives are: (1) to identify 3000 children aged between 12 years and 14 years with asthma symptoms; and (2) to assess their asthma control, current treatment, knowledge of and attitudes to asthma and barriers to achieving good control. Secondary objective is to develop interventions addressing identified barriers to good symptom control.

METHODS AND ANALYSIS: Each centre will undertake screening to identify 500 school children with asthma symptoms using questions from the Global Asthma Network's questionnaire. Children identified to have asthma symptoms will fill in a digital survey, including: Asthma Control Test, questions on medication usage and adherence, medical care, the Brief-Illness Perception questionnaire and environmental factors. Exhaled nitric oxide testing and prebronchodilator and postbronchodilator spirometry will be performed. A subgroup of children will participate in focus group discussions. Results will be analysed using descriptive statistics and comparative analysis. Informed by these results, we will assess the feasibility of potential interventions, including the adaption of a UK-based theatre performance about asthma attitudes and digital solutions to improve asthma management.

ETHICS AND DISSEMINATION: The ACACIA study has been reviewed by the Queen Mary University of London Ethics of Research Committee in the UK. All African centres have received local ethical approval for this study. Study results will be published in academic journals and at conferences. Study outputs will be communicated to the public via newsfeeds on the ACACIA website and Twitter, and through news media outlets and other local dissemination.

Symptom-based screening tool for asthma syndrome among young children in Uganda

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Abstract

Under-diagnosis of asthma in 'under-fives' may be alleviated by improved

inquiry into disease history. We assessed a questionnaire-based screening tool for asthma among 614 'under-fives' with severe respiratory illness in Uganda. The questionnaire responses were compared to post hoc consensus diagnoses by three pediatricians who were guided by study definitions that were based on medical history, physical examination findings, laboratory and radiological tests, and response to bronchodilators. Children with asthma or bronchiolitis were categorized as "asthma syndrome". Using this approach, 253 (41.2%) had asthma syndrome. History of and present breathing difficulties and present cough and wheezing was the best performing combination of four questionnaire items [sensitivity 80.8% (95% CI 77.6–84.0); specificity 84.7% (95% CI 81.8–87.6)]. The screening tool for asthma syndrome in 'under-fives' may provide a simple, cheap and quick method of identifying children with possible asthma. The validity and reliability of this tool in primary care settings should be tested.

Training needs for Ugandan primary care health workers in management of respiratory diseases: a cross sectional survey

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BACKGROUND: Respiratory diseases are among the leading causes of morbidity and mortality in Uganda, but there is little attention and capacity for management of chronic respiratory diseases in the health programmes. This survey assessed gaps in knowledge and skills among healthcare workers in managing respiratory illnesses.

METHODS: A cross sectional study was conducted among primary care health workers, specialist physicians and healthcare planners to assess gaps in knowledge and skills and, training needs in managing respiratory illnesses. The perspectives of patients with respiratory diseases were also sought. Data were collected using questionnaires, patient panel discussions and review of pre-service training curricula for clinicians and nurses. Survey Monkey was used to collect data and descriptive statistical analysis was undertaken for quantitative data, while thematic

content analysis techniques were utilized to analyze qualitative data.

RESULTS: A total of 104 respondents participated in the survey and of these, 76.9% (80/104) were primary care health workers, 16.3% (17/104) specialist clinicians and 6.7% (7/104) healthcare planners. Over 90% of the respondents indicated that more than half of the patients in their clinics presented with respiratory symptoms. More than half (52%) of the primary care health workers were not comfortable in managing chronic respiratory diseases like asthma and COPD. Only 4% of them were comfortable performing procedures like pulse oximetry, nebulization, and interpreting x-rays. Majority (75%) of the primary care health workers had received in-service training but only 4% of the sessions focused on respiratory diseases. The pre-service training curricula included a wide scope of respiratory diseases, but the actual training had not sufficiently prepared health workers to manage respiratory diseases. The patients were unsatisfied with the care in primary care and reported that they were often treated for the wrong illnesses.

CONCLUSIONS: Respiratory illnesses contribute significantly to the burden of diseases in primary care facilities in Uganda. Management of patients with respiratory diseases remains a challenge partially because of inadequate knowledge and skills of the primary care health workers. A training programme to improve the competences of health workers in respiratory medicine is highly recommended.

Chronic Obstructive Pulmonary Disease Prevalence and Associated Factors in a Setting of Well-Controlled HIV, A Cross-Sectional Study

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Abstract

In Sub-Saharan Africa, COPD remains prevalent but its association with HIV is not well characterized especially in rural settings. We assessed for COPD prevalence, associated factors and lung function profile among HIV-infected individuals attending ART clinics in rural Nakaseke district of Uganda. We enrolled HIV-

positive participants from four HIV treatment centers in rural Uganda. Participants underwent spirometry testing following standard guidelines. We defined COPD as a post-bronchodilator FEV₁/FVC ratio less than the fifth percentile of the NHANES III African-American reference. We assessed for factors associated with COPD and lung function profiles using multivariable logistic and linear regression analyses. We analyzed data from 722 HIV-positive participants (mean age 48.0 years, 59.7% women). Over 90% of participants were on ART for a median duration of 4 years (IQR 2-7 years), with a median viral load of 0 copies/mL (IQR 0-0 copies/mL), current and baseline CD4 + T cell count of 478 cells/mm³ (IQR 346-663 cells/mm³) and 335 cells/mm³ (IQR 187-523 cells/mm³) respectively. The prevalence of COPD was 6.22%. COPD was associated with worse respiratory symptoms and health status. History of pulmonary tuberculosis was strongly associated with COPD (adjusted OR = 4.92, 95% CI 1.71 to 14.15, p = 0.003) and reduced lung function. Use of ART, CD₄+T cell count and viral load were not associated with COPD or reduced lung function. In conclusion, we report a COPD prevalence of 6.22% in HIV-infected individuals in rural Uganda. Pulmonary tuberculosis remains the strongest predictor of COPD risk and reduced lung function in well-controlled HIV.

High prevalence of phenotypic pyrazinamide resistance and its association with pncA gene mutations in *Mycobacterium tuberculosis* isolates from Uganda

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INTRODUCTION: Susceptibility testing for pyrazinamide (PZA), a cornerstone anti-TB drug is not commonly done in Uganda because it is expensive and characterized with technical difficulties thus resistance to this drug is less studied. Resistance is commonly associated with mutations in the pncA gene and its promoter region. However, these mutations vary geographically and those conferring phenotypic resistance are unknown in Uganda. This study determined the prevalence of PZA resistance and its association with pncA mutations.

MATERIALS AND METHODS: Using a cross-sectional design, archived isolates collected during the Uganda national drug resistance survey between 2008–2011 were sub-cultured. PZA resistance was tested by BACTEC Mycobacterial Growth Indicator Tube (MGIT) 960 system. Sequence reads were downloaded from the NCBI Library and bioinformatics pipelines were used to screen for PZA resistance–conferring mutations.

RESULTS: The prevalence of phenotypic PZA resistance was found to be 21%. The sensitivity and specificity of *pncA* sequencing were 24% (95% CI, 9.36–45.13%) and 100% (73.54% - 100.0%) respectively. We identified four mutations associated with PZA phenotypic resistance in Uganda; K96R, T142R, R154G and V180F.

CONCLUSION: There is a high prevalence of phenotypic PZA resistance among TB patients in Uganda. The low sensitivity of *pncA* gene sequencing confirms the already documented discordances suggesting other mechanisms of PZA resistance in *Mycobacterium tuberculosis*.

Investigating the Association between Wood and Charcoal Domestic Cooking, Respiratory Symptoms and Acute Respiratory Infections among Children Aged Under 5 Years in Uganda: A Cross–Sectional Analysis of the 2016 Demographic and Health Survey

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BACKGROUND: Household air pollution associated with biomass (wood, dung, charcoal, and crop residue) burning for cooking is estimated to contribute to

approximately 4 million deaths each year worldwide, with the greatest burden seen in low and middle-income countries. We investigated the relationship between solid fuel type and respiratory symptoms in Uganda, where 96% of households use biomass as the primary domestic fuel.

MATERIALS AND METHODS: Cross-sectional study of 15,405 pre-school aged children living in charcoal or wood-burning households in Uganda, using data from the 2016 Demographic and Health Survey. Multivariable logistic regression analysis was used to identify the associations between occurrence of a cough, shortness of breath, fever, acute respiratory infection (ARI) and severe ARI with cooking fuel type (wood, charcoal); with additional sub-analyses by contextual status (urban, rural).

RESULTS: After adjustment for household and individual level confounding factors, wood fuel use was associated with increased risk of shortness of breath (AOR: 1.33 [1.10–1.60]), fever (AOR: 1.26 [1.08–1.48]), cough (AOR: 1.15 [1.00–1.33]), ARI (AOR: 1.36 [1.11–1.66]) and severe ARI (AOR: 1.41 [1.09–1.85]), compared to charcoal fuel. In urban areas, Shortness of breath (AOR: 1.84 [1.20–2.83]), ARI (AOR: 1.77 [1.10–2.79]) and in rural areas ARI (AOR: 1.23 [1.03–1.47]) and risk of fever (AOR: 1.23 [1.03–1.47]) were associated with wood fuel usage.

CONCLUSIONS: Risk of respiratory symptoms was higher among children living in wood compared to charcoal fuel-burning households, with policy implications for mitigation of associated harmful health impacts.

Accuracy of Xpert Ultra in Diagnosis of Pulmonary Tuberculosis among Children in Uganda: a Substudy from the SHINE Trial

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Link: <https://doi.org/10.1128/JCM.00410-20>.

Abstract: Childhood tuberculosis (TB) presents significant diagnostic challenges associated with paucibacillary disease and requires a more sensitive test. We evaluated the diagnostic accuracy of Xpert MTB/RIF Ultra (Ultra) compared to other microbiological tests using respiratory samples from Ugandan children in the SHINE trial. SHINE is a randomized trial evaluating shorter treatment in 1,204 children with minimal TB disease in Africa and India. Among 352 samples and one cervical lymph node fine needle aspirate, one sample was randomly selected per patient and tested with the Xpert MTB/RIF assay (Xpert) and with Lowenstein-Jensen medium (LJ) and liquid mycobacterial growth indicator tube (MGIT) cultures. We selected only uncontaminated stored sample pellets for Ultra testing. We estimated the sensitivity of Xpert and Ultra against culture and a composite microbiological reference standard (any positive result). Of 398 children, 353 (89%) had culture, Xpert, and Ultra results. The median age was 2.8 years (interquartile range [IQR], 1.3 to 5.3); 8.5% (30/353) were HIV infected, and 54.4% (192/353) were male. Of the 353, 31 (9%) were positive by LJ and/or MGIT culture, 36 (10%) by Ultra, and 16 (5%) by Xpert. Sensitivities (95% confidence intervals [CI]) were 58% (39 to 65% [18/31]) for Ultra and 45% (27 to 64% [14/31]) for Xpert against any culture-positive result, with false positives of <1% and 5.5% for Xpert and Ultra. Against a composite microbiological reference, sensitivities were 72% (58 to 84% [36/50]) for Ultra and 32% (20 to 47% [16/50]) for Xpert. However, there were 17 samples that were positive only with Ultra (majority trace). Among children screened for minimal TB in Uganda, Ultra has higher sensitivity than Xpert. This represents an important advance for a condition which has posed a diagnostic challenge for decades.

SYMPOSIUM
ABSTRACTS

Research to support disease outbreak response: Experience from the Ebola Vaccine trial (Tokomeza Ebola trial) in Uganda

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INTRODUCTION: On 20th September 2022, Uganda declared an outbreak of ebolavirus disease (EVD), caused by the Sudan ebolavirus (SUDV) species. Despite vaccines being key in outbreak response, none with proven efficacy and safety against the SUDV species was available. A vaccine trial; the ring vaccination trial (Solidarity against Ebola/Tokomeza trial) to evaluate the efficacy and safety of candidate SUDV species targeted vaccines was sanctioned by the World Health Organisation (WHO) and Uganda Ministry of Health (MoH).

METHODS: We document experiences with Tokomeza Ebola trial set up and highlight factors that facilitated readiness for trial start.

RESULTS: By week 11 of the outbreak, the trial was ready to enrol the first participant. Exemplars of success included: 1) Stewardship from sponsors (WHO and MOH) who assigned and assembled an Investigation team of scientists and an implementing organisation (Makerere University Lung Institute (MLI) within the first week of the outbreak, 2) Internal and external collaborations including a South-South collaboration created by WHO that included experts from the West African Zaire ebolavirus Ebola Virus Vaccine trial (Ebola ca Suffit). Working with the Ebola ca suffit trial experts, the generic protocol and tools were finalised and adapted, 3) The Joint scientific and ethical review mechanism for clinical trials optimized the turnaround time and ensured all ethics and regulatory approvals were obtained within 9 weeks of the outbreak, 4) Close collaboration with national drug authority (NDA) ensured faster regulatory approval process for import of vaccines 5) MLI's prior experience in conducting clinical trials during disease outbreaks provided additional advantage with logistics, study team recruitment and training. The COVID-19 research experience and structures to support the trial processes were leveraged.

CONCLUSION: Planning, regulatory approvals and trial site set up were achieved within 11 weeks of EVD outbreak, which is a first. We commend the strong stewardship of the sponsors, the commitment and resilience of all stakeholders such as the ethics and regulatory bodies.

Building robust laboratory systems for disease outbreak response: Lessons learnt from Uganda's laboratory response to COVID-19

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BACKGROUND: The COVID-19 pandemic highlighted the need for countries to put in place systems to foster rapid response. With COVID-19 no longer a public health emergency, there is need to revisit national level responses and identify lessons for future epidemic response. A health systems analysis has potential to inform interventions to improve future response.

METHODS: A desk review was conducted using USAID's Health System Assessment Approach (HSAA) to identify key features of Uganda's Laboratory systems in response to COVID-19, and lessons to inform pandemic preparedness.

RESULTS: Uganda's laboratory system is organised in a hierarchical structure to mirror healthcare system landscape. This landscape was leveraged to decentralise COVID-19 testing including use of the rapid diagnostic kits. The existing specimen referral system and mobile laboratory testing supplemented by internet connectivity solutions (GX Alert, LabXpert) allowed increased access to COVID-19 testing and reduced turnaround time. The private facilities were found better staffed and delivered testing faster than public healthcare. Existing and widely distributed multi-disease testing platforms for other diseases (e.g., GeneXpert) were used for testing. The analysis revealed that laboratory services face several challenges including: overreliance on donor support, chronic underfunding, vertical disease programming, lack of equipment/reagents, machine breakdown, inadequate and disparities in regional distribution of laboratory workers, reactive instead of proactive hiring during the outbreak, fragmented and isolated digital health systems unable to give individual patient level data. The failure to fully transition from paper to electronic laboratory data systems increases the workload for staff.

CONCLUSION: The assessment revealed Uganda's laboratory systems had been primed to respond to the pandemic based on previous experience with other epidemics. However, highlighted challenges may have influenced limited scale of the response, and if resolved could make the laboratory systems mount a more robust and faster response to future pandemics.

Computed Tomography and histopathological correlative Imaging of lung cancer in Uganda

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BACKGROUND: Lung cancer is one of the leading causes of cancer-related morbidity and mortality in Uganda. The incidence and mortality rates of lung cancer in Uganda are projected to rise due to factors such as population growth, aging, and increased tobacco use. In this study, we aimed to determine the histopathological subtypes of lung cancer in Uganda and describe their corresponding appearance on Chest Computed Tomography.

METHODS: This was a one-year cross sectional study nested within an ongoing cancer cohort study at the Makerere Lung Institute. Patients with histologically confirmed lung cancer with available Chest CT scan images and clinical information were enrolled. Socio-demographic data and histopathology was abstracted and entered into our data collection tool. CT scan images were interpreted by a thoracic radiologist. Staging of the tumors was done following the eighth edition TNM stage classification for lung cancer

RESULTS: A total of 85 lung cancer patients were enrolled, mean age was 60 years, 57.7% patients were female and majority (10.6%) were HIV seropositive. Among these, 70 (82.4%) had never smokers, and only 7 (8.2%) were current smokers. Fifty-nine patients (77%) were histologically confirmed as adenocarcinoma, 16 (21%) squamous cell carcinoma, 6 (%) small cell cancer, 2 (2%) as large cell cancer, 1(%) small round blue cell tumor, and 1 (%) primary pulmonary malignant melanoma. The average tumor size was 62.4mm. The majority (82, 95.3%) were solid tumors and 70.6% were situated centrally. Among the central masses, 61.7% were adenocarcinomas, while 23.3% were squamous cell carcinomas. In terms of configuration, 47 (55.3%) were ovoid, 21 (24.7%) irregular /polyhedral, 12(14.1%) lobulated and 7 (5.9%) were round.

CONCLUSION: The most common lung cancer subtypes in Uganda are adenocarcinoma and squamous cell carcinoma. Both subtypes tend to be large centrally located masses.

Is HIV-1 infection a risk factor for Lung Cancer initiation and progression in Uganda and Tanzania?

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BACKGROUND: Due to immunosuppression, the risk of developing malignancies in individuals with Human Immunodeficiency Virus (HIV) increases compared to non-HIV-infected individuals. In 2022, HIV prevalence was 5.8% in Uganda, with higher rates among women (7.2%) than men (4.3%). A lower prevalence (4.8%) was reported in Tanzania. In Uganda, approximately, 1.5 million new HIV infections occurred in 2022, which was more than the global target of 1 million new cases. As the number living with HIV infection increases, non-communicable diseases, including cancer are expected to rise accordingly. We aimed to assess the epidemiology of lung cancer in Uganda and Tanzania and clarify the role of HIV-1 infection as a risk factor for lung cancer initiation and progression.

METHODS: Individuals ≥ 18 years with biopsy-proven lung cancer were enrolled in the study. Disease free and AIDS-defining malignancies controls matched for age, gender, smoking status and residence were identified for each lung Cancer patient enrolled. Chi-square test was used to assess differences in mortality by HIV status.

RESULTS: Within two years, we have screened 268 potential lung cancer cases; 114 (42.5%) have been biopsy-confirmed. The median age (Inter quartile range) was 60 (51 to 67). The majority were females, 69 (60.5%), 21 (28.6%) smokers, and only 8 (7%) were HIV positive. The majority were adenocarcinoma 64 (67.4%) and presented with stage III and stage IV disease in 78 (86.7%). For disease progression, 53 patients were assessed; for those who were HIV-negative, 15 (41.7%) were responding to treatment, 3 (8.4%) were not responding to treatment, and 18 (50%) died. While those who were HIV positive, 1 (14.3%) responded to treatment, and 6 (85.7%) died. The difference in mortality stratified by HIV status was statistically significant ($P < 0.001$).

IN CONCLUSION: We observed a significant difference in mortality stratified by HIV status. There is need for more research on lung cancer mortality by HIV status to better understand the relationship by assessing potential risk factors like increased level of immunosuppression, anti-retroviral therapy effect and genetic factors.

“Screening and Diagnostic Pathways for Lung Cancer Patients in two East African Countries: Experience from the Lung Cancer in East Africa in Relation To HIV–1 Infection project”

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BACKGROUND AND AIMS: Preliminary studies in Africa point to i) excess risk of lung cancer in HIV-1 positive individuals and ii) very low tobacco-associated incidence of lung cancer. World Health Organization registries show low rates of lung cancer in Africa mainly due to under-reporting which is linked to limited diagnostic capacity. We set out to determine the clinical epidemiology of lung cancer in relation to HIV-1 infection in Uganda and Tanzania.

METHODS: Individuals ≥ 18 years suspected to have lung cancer clinically and abnormal chest X-rays or Chest CT scans demonstrating nodules/masses were screened for lung cancer. Patients with biopsy proven lung cancer were enrolled into the study. Patients were followed up in a longitudinal cohort study to assess for outcomes, disease-free disease and assessment of potential risk factors for lung cancer including air quality assessment. Patients with HIV infection were identified to evaluate the effects of HIV on lung cancer risk and progression of disease.

RESULTS: Within one year, we have screened a total of 143 potential lung cancer cases and 50 (35%) have been biopsy-confirmed to have lung cancer. Most of the cases (64%) are females, 80% non-smokers and 90% HIV negative. The majority are adenocarcinoma (61.2%) and more than 50% present with stage 4 disease. About 30% of the lung cancer patients were misdiagnosed to have TB leading to delay in seeking health care in the cancer clinics.

SUMMARY: High diagnostic costs remain a major challenge where only 60% of the patients can afford to pay for the biopsy and histopathology procedures. The other challenge is poor storage and documentation which makes retrieving patients' CT scan images difficult.

Lung cancer screening should be integrated in standard of care to increase awareness, so as to shorten the diagnostic period, improve case finding and hence improve patient outcomes.

Prevalence Of Pulmonary Tuberculosis Among Casual Labourers Working In Road Construction Sites In Central Uganda

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Link: <http://hdl.handle.net/10570/11586>

INTRODUCTION: Workers with occupational exposure to respirable silica dust, such as casual labourers at road construction sites (RCSs), are known to be at a high risk of developing pulmonary tuberculosis (TB). There is limited literature about the burden of PTB among this subpopulation with high occupational exposure to silica dust at road construction sites. We aimed to determine the prevalence of PTB among casual labourers working at road construction sites in Central Uganda.

METHODS: We enrolled 297 participants by consecutive sampling into a cross-sectional study between 1st and 30th September 2022 at four road construction sites in four districts in central Uganda. A structured questionnaire was administered, and the PTB cases were identified using Gene Xpert and/or Computer Aided Detection for TB (CAD4TB). Data were analysed in STATA version 17.0. Descriptive statistics adjusted for clustering were used to summarize the data, and the relationship between PTB and independent variables was assessed using a mixed effect modified Poisson regression model to estimate the adjusted prevalence ratios.

RESULTS: Most participants were males (95.6% (284/297)), and the median age was 29 years [interquartile range (IQR); 25, 33]. The prevalence of PTB among casual labourers was 2.4% (95% CI: 1.9, 2.8). Being vaccinated with BCG (3.45, 95% CI (1.02, 11.61)), alcohol use (2.70, 95% CI (1.52, 4.80)) and staying in overcrowded houses (8.13, 95% CI (4.37, 15.12)) were positively associated with having PTB.

CONCLUSION: There is a high prevalence of PTB among casual labourers working at road construction sites in Central Uganda. Individuals who had never been vaccinated with BCG, alcohol users and those staying in overcrowded houses were at an increased risk of having PTB. We recommend routine screening of casual labourers at road construction sites to optimize active TB case finding.

Using a multi component Quality Improvement interventions to reduce TB/HIV mortality among admitted patients at a large tertiary care hospital.

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INTRODUCTION: Tuberculosis (TB) is a leading cause of mortality among hospitalized persons living with HIV (PLHIV). At Kiruddu National Referral Hospital (KNRH), the TB/HIV inpatient mortality was high at 29% between July 2022 and September 2022. We present the role of quality improvement interventions to reduce TB associated mortality among hospitalized PLHIV at a large tertiary care hospital.

METHODS: We conducted key informant interviews among 12 purposively selected healthcare providers (3 medical officers, 2 intern doctors, 1 pharmacist and 6 nurses) based on their responsibility for TB care and management. Open-ended structural questionnaires were used to get their perspectives on the root causes for inpatient TB/HIV mortality. A prioritization matrix was used to identify areas of focus on root causes. A quality improvement (QI) team developed key interventions, which were implemented over quarterly periods while monitored monthly.

RESULTS: The root causes identified were; lack of standard operating procedures (SOPs) on TB management, delayed TB diagnosis, patients presenting with poor function status (Eastern Co-operative Oncology Group (ECOG) score (3-4)), and long turnaround time of laboratory test results as predominant contributors of TB/HIV inpatient mortality. Implementation of the package (use of SOPs on TB management, conducting CMEs and use of MEWs triaging system) resulted to a reduction in TB/HIV mortality from 45% in October 2022 to 21% in December 2022. With other tested changes (intensified screening of opportunistic infections (OIs) using CD4 cell testing, malnutrition screening and one-on-one mentorship), a 13% additional reduction in TB/HIV mortality was observed in July 2023.

CONCLUSION: Dissemination of SOPs on management of TB, conducting CMEs, use of MEWs triaging system, intensified CD4 testing, malnutrition screening and one-on-one mentorship led to a significant reduction of TB/HIV inpatient mortality. We recommend adoption of the above strategies to reduce inpatient TB/HIV mortality.

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