Abstracts of papers for the African Respiratory Congress in Durban

■ **Abdellah Ali, Aida Mahmoud**

Sirtuin 1 gene rs2273773 C >T single nucleotide polymorphism and protein oxidation markers in asthmatic patients

Introduction: Sirtuin-1 (SIRT-1), a protein has been found to protect the cells against oxidative stress due to its deacetylase activity. In this investigation, we aimed to study SIRT-1 gene rs2273773 C >T single nucleotide polymorphism and markers of serum protein oxidation (protein carbonyl and sulfhydryl groups) in asthmatic patients.

Methods: 120 asthmatic patients and 120 healthy controls were genotyped for SIRT- 1 gene rs2273773 C > T SNP using poly-merase chain reaction – confronting two pair primer method (PCR-CTPP). Serum protein carbonyl and sulfhydryl groups were measured using colorimetric methods.

Results: SIRT-1 gene rs2273773 C> T SNP genotyping revealed that the TT genotype was significantly higher in the patients compared to the controls (P 0.05). T allele was significantly higher in the patients compared to the controls (P =0.017). The distribution of the genotypes didn't differ among the atopic and the non-atopic asthmatic patients, also no difference was found in the genotype distribution according to the severity of asthma (P >0.05). Serum protein carbonyl group concentration was significantly higher in the patients compared to the con-trols (P 0. 001), while serum protein sulfhydryl group content decreased significantly in the patients compared to the controls (P T genotype were found.

Conclusion: SIRT-1 gene rs2273773 C> T SNP was associated with asthma but not with protein oxidation markers in Egyptian population

■ **Charles Batte, Tasmia Naz, Brooks Morgan, Faith Nassali, Denis Mawanda, Robert Kalyesubula, Bruce Kirenga, Trishul Siddharthan, William Checkley**

Prevalence and associated factors of chronic obstructive pulmonary disease among people living with HIV/AIDs in rural communities of Nakaseke, Uganda

Introduction: Chronic Obstructive Pulmonary Disease (COPD) is highly prevalent in Africa, yet its prevalence and associated factors remain almost unknown especially among people living with HIV/AIDS (PLWHA). In Uganda, there is paucity of evi-dence about COPD among PLWHA, which negatively impacts efforts to develop integrated Non-Communicable Diseases (NCD) care programs among PLWHA. Much remains to be learnt about its risk factors and the mechanisms involved in its pathogenesis. Our aim was to determine the prevalence and risk factors among people living with HIV/AIDS.

Methods: We conducted a cross sectional study and screened 1,000 PLWHA ≥35years attending the ART clinic at Nakaseke Hospital for COPD using the modified BOLD questionnaire and spirometry. Spirometry was performed on the participants before and after bronchodilator therapy (400 mcg of salbutamol using a spacer) following standardised guidelines. COPD was defined as the ratio of post-bronchodilator forced expiratory volume in 1 minute (FEV1), to forced vital capacity (FVC) less than the lower limit of normal.

Results: Of the 719 participants, 424 (59.7%) are female, 433 (60.2%) are aged above 44 years and 641 (90.3%) are on ART. 625 (88.5%) reported exposure to biomass fuel (wood), 599 (84.5%) reported no history of smoking cigarettes. The prevalence of COPD among PLWHA was 7.2% and COPD was significantly associated with being male (OR = 2.5), smoking cigarettes (OR = 3.2), and history of TB diseases. There is also a strong association for COPD with duration of ART treatment, CD4 count, using biomass fuel wood and age.

Conclusion: COPD is prevalent among PLWHA. Given its chro-nicity and impact on the quality of life of a patient it has potential of reversing the achievements of the global community in the fight against HIV/AIDS. It is thus imperative to extensively study the prevalence of COPD in the special population and its associated factors to inform policy formulation and design of interventions intended to address the ongoing double burden of comorbidity with NCDs and HIV/AIDS.

■ **Karlhans Che, Magnus Paulsson, Kristian Riesbeck, Anders Lindén**

Release of Interleukin-26 from Alveolar Type II Cells in Response to Bacterial Extracellular Vesicles from Haemophilus influenzae and Pseudomonas aeruginosa

Introduction: Until date, known cellular sources of the presumed Th17- cytokine interleukin (IL)-26 include T-lymphocytes, bronchial epithelial cells and alveolar macrophages in human airways. This IL-10-related cytokine is involved in the innate immune response to bacterial endotoxins in healthy human airways. However, alveolar type II cells, which also play a role in the innate immune responses to bacteria, have not been investigated in terms of IL-26 release. Moreover, Haemophilus influenzae and Pseudomonas aeruginosa are two common causes of pneumonia that may outmanoeuvre innate immune responses while invading human airways, in part through the actions of extracellular vesicles (EV). The IL-26-stimulating properties of EV from these pathogens have not previously been investigated. We hypothesised that alveolar type II epithelial cells release IL-26 protein in response to EV from H. influenzae and P. aeruginosa.

Methods: The EV from H. influenzae and P. aeruginosa were isolated and separated after overnight culture of bacteria. A model of alveolar type II epithelial cells (A549 cell line) was utilised.

Cells were cultured and stimulated in triplicates with different concentrations (0.1 and 1µg/mL) of the respective EV during several incubation times (1, 3, 6 and 24 h). IL-26 protein concentrations were thereafter measured in the cell-free conditioned media using Enzyme-Linked Immunosorbent Assay (ELISA)
Results: We found that A549 cells release substantial amounts of IL-26 protein in response to the EV from H. influenzae (p=0.03, n=6) as well as from P. aeruginosa (p=0.03, n=6). Notably, we found a concentration-dependent (n=3) as well as time-dependent (n=6) increase in IL-26 concentrations.
Conclusion: Our results suggest that human alveolar type II cells produce IL-26 in response to EV from H. influenzae and P. aeruginosa in vitro. Thus, given the documented involvement of IL-26 in bacterial responses in human airways, and our current finding suggests that IL-26 is involved in the innate immune responses during bacterial infections. This data also argues for the further exploration of the mechanisms through which alveolar type II cells and IL-26 are involved in the pathogenesis of pneumonia as well as other bacterial infections in the airways.

■ **Bilkisu Ilah Garba, Aminu Sakajiki Muhammad, Ibrahim Yusuf, Bello Alhaji Mohammed, Umar Abdullahi**
Treatment outcome of Tuberculosis at a specialist hospital in North-Western Nigeria
Introduction: Tuberculosis (TB) is a chronic infectious disease that is preventable, treatable and curable, yet it is a major cause of morbidity and mortality. Prevalence and mortality of TB are under-estimated in many high burden countries including Nigeria. In order to decrease transmission of the disease, effective identification, diagnosis and treatment of infectious TB patients is required. A proven strategy to ensure patients' adherence to anti-tuberculous medication is the use of Directly Observed Treatment Short course (DOTS) therapy. DOTS lead to improved treatment outcome with overall reduction in morbidity and development of multidrug resistant TB. We aimed to determine the form of TB and treatment outcome of patients managed at our DOTS clinic.
Methods: A retrospective study of patients managed for tuberculosis at the DOTS clinic of Ahmad Sani Yariman Bakura Specialist Hospital (ASYBSH), Gusau, Zamfara State, Nigeria over a 30-month period (Jan 2015 to June 2017). All patients that were treated for TB over the study period were included in the study. Relevant information from the register was reviewed. Tuberculosis treatment outcomes were assessed according to World Health Organisation (WHO) and National TB and Leprosy Control Programme guidelines. 'Cured'' and 'treatment completed outcomes' were referred to as treatment successful.
Results: Of the 415 patients, 76 (18.3%) were children while 339 (81.7%) were adults. Males were 254 (61.2%), with a M:F ratio of 1.6:1. 348 (83.9%) had pulmonary TB while 67 (16.1%) had extra pulmonary TB. More males had pulmonary TB than females, which was not significant (χ^2=0.678, p=0.410). There were more male adults than females or children which was significant (χ^2=18.504, p=0.000). Majority (97.6%) of the patients were new cases, 4 (1.0%) were relapse, while 3 (0.7%) were TB patients with unknown previous TB treatment history. Treatment completed was observed in 184 (44.2%), 161 (38.8%) were cured, 35 (8.4%) were transferred out, 29 (7.0%) died, while 2 (0.5%) were removed from register and 2 (0.5%) were lost to follow up. Treatment success rate was 83.0%.
Conclusion: Treatment outcome of patients treated for TB in our centre was good, with a success rate close to WHO benchmark of 85%. However, it shows that childhood TB is still under diagnosed and under treated as the number of paediatric cases were low.

■ **Leah Githinji, Diane Gray, Sipho Hlengwa, Takwanisa Machemedze, Landon Myer, Heather Zar**
Longitudinal changes in lung function in HIC- infected adolescents on antiretroviral therapy in Cape Town, South Africa
Introduction: Over 90% of HIV-infected children live in Sub-Saharan Africa. Despite increased access to antiretroviral therapy, respiratory illness remains common in HIV-infected youth. There is limited information on progression of lung function in HIV-infected adolescents on antiretroviral therapy.
Objective: The aim of this study was to investigate progression of lung function over 2 years in HIV-infected adolescents on antiretroviral therapy in a prospective cohort, the Cape Town Adolescent Anti-retroviral cohort (CTAAC).
Methods: HIV-infected adolescents aged 9-14 years, with at least 6 months of antiretroviral therapy, enrolled on CTAAC, underwent lung function testing. Spirometry and bronchodilator testing was done at enrolment and annually for two years. Healthy HIV-uninfected, age, sex and ethnically matched controls were also tested. Linear mixed models were used to compute longitudinal changes in lung function outcomes.
Results: 428 HIV-infected and 90 HIV-uninfected adolescents were tested at baseline and at 24 months. Mean (SD) age was 12.0 (1.6) years and 50.4% male. Median (IQR) viral load and CD4 count at baseline were 2.2 (1.6-3.3) log copies and 731 (580-959) cells/mm3 respectively. HIV-infected adolescents had lower lung function compared to the uninfected at all time points, p<0.05FEV1 and FVC z-scores showed similar change over two years in both groups. Obstructive and mixed spirometry patterns were more common in HIV-infected adolescents compared to the uninfected, p<0.05for both time points. Previous pulmonary tuberculosis and previous lower respiratory tract infections were significant associations of lung function, p<0.05 for both.
Conclusion: HIV-infected adolescents had significantly lower lung function and more obstructive and mixed spirometry patterns than HIV-uninfected at all time points. Lung function tracked similarly over 2 years between groups, suggesting no catch-up growth nor lung function deterioration over time. This study informs the importance of lung function surveillance in HIV-infected adolescents.

■ **Carvern Jacobs, Aneesa Vanker, Lauren Willemse, Rae MacGinty, Lidija Turkovic**
Exhaled Nitric Oxide in the first two years of life in African infants: impact of maternal smoking and indoor air pollution
Introduction: Environmental pollution and maternal smoking may increase risk of infant respiratory disease. Exhaled nitric oxide (eNo), a marker of airway inflammation, is increased in respiratory disease. The impact of indoor air pollution on eNO in early life is poorly understood.

Objective: To asses changes in eNO in the first two years of life in African infants and the impact of tobacco smoke exposure and environmental pollutants on eNO at birth and two years.
Methods: Infants enrolled in the Drakenstein Child Health Study had lung function tested at 6 weeks and 23-25 months. Lung function testing, completed in unsedated quiet sleep, included eNO and tidal breathing (tbfvl) measures. Antenatal smoke exposure was confirmed on maternal urine cotinine. Postnatal smoke exposure was self-reported by questionnaire. Benzene, particulate matter (PM10) and nitric dioxide (NO2), were measured durring antenatal home visits over a two-week period. The association of exposures and lung function outcomes was investigated using multiple linear regression, with statistical significance p0.05.
Results: At 6 weeks 839 and at 2 years 640 infants had eNO measured. Exhaled NO increased from an average(SD) of 10.4(7.6) ppb at 6 weeks to 17.5(12.6) ppb at 2 years.
At 6 weeks, infants of mothers who smoked during pregnancy, had lower eNO [10.2 (6.7) vs.11.5 (7.9) ppb; p=0.016] and NO output [32.2 (22.1) vs 38.6 (25.4) nL.sec-1, p=0.001]; and lower tidal volume [33,2 (6,1) mL vs. 35,5 (6,5) mL, p0.001] compared to unexposed infants. After adjusting for size, sex and race, male and HIV exposed infants had higher tidal volumes, average 2.1 ml (p=0.000.CI=1.0-3.1) and 1.7 ml higher (p=0.024 CI=0.2-3.2) respectively. Household smoke exposure was not associated with lung function. Adjusted results showed that high benzene levels were associated with reduced eNO (average 1.47 ppb lower, p=0.027, CI=2.77-0.17) and NO output (average 5.5 nl/sec lower, p=0.009, CI=9.6-1.3) at 6 weeks but not at 2 years. Other air pollutants were not associated with eNO levels at 6 weeks or 2 years of age.
Conclusion: Maternal smoking during pregnancy and high benzene levels were associated with lower eNO and NO output at birth in African infants. Effects did not persist to 2 years. Further investigation on the impact of eNO levels on disease risk in early life is needed.

■ **Nkosana Jafta, Lars Barregard, Prakash M Jeena, Rajen N Naidoo**
Exposure to indoor air pollutants and childhood pulmonary tuberculosis
Introduction: There is increasing evidence in studies that have used proxy measures of exposure that indoor air pollution increases the risk for tuberculosis. Our study aim was to determine association between exposure to indoor air pollution (IAP) in the homes and childhood pulmonary tuberculosis (PTB).
Methods: In this age- and sex-matched case control study, cases were children diagnosed with PTB and controls were children without PTB. Questionnaires about children's health; and house characteristics and activities (including household air pollution) and secondhand smoke (SHS) were administered to all the caregivers of the participants. A subset of the participants' homes was sampled for measurements of PM10 over a 24-hour period (n=105), and NO2 and SO2 over a period of 2 to 3 weeks (n=82). IAP concentrations of PM10 and NO2 were estimated in unsampled homes using predictive models. Logistic regression was used to look for association between IAP concentrations, crude measures of IAP and PTB.
Results: Of the 134 participants, 107 were cases and 127 were controls. Pollutants concentrations (µg/m3) for were PM10 GM: 50.50 (47.50-53.70) and NO2 GM: 15.74 (14.99-16.53) and SO2 GM:0.2 (95%CI 0.2-0.3). Day-to-day variability was large. All multivariate models were adjusted for age, sex, socioeconomic status, TB contact and HIV status. No significant association was observed between pollutant concentrations and PTB in children for PM10 and NO2. When using the crude exposure measure of pollution namely fuel type (clean or dirty fuel) and SHS the association was positive but not significant. Presence of dampness in the household was a surprising significant risk factor for childhood TB with aOR ranging from 2.10 to 2.17 for different models. The crude predictors are less influenced by day-to-day variability.
Conclusion: Our study suggests a risk of childhood tuberculosis disease when children are exposed to secondhand smoke (SHS) and dirty cooking fuel but this is not supported by objective measurement of air pollution in the homes. HIV status and TB contact are important factors of childhood PTB in this population.

■ **Ivan Kimuli, Abdallah Muhofa, Winceslaus Katagira, Levi Mugenyi, Bruce Kirenga**
Impact of a primary care-led asthma clinic model on asthma control in a Resource Limited Setting
Introduction: Recent advances in health care have dedicated efforts to reduce unnecessary health care spending while improving the quality of patient care and outcomes. Despite asthma being a very common disease with immense social impact, data on strategies for its control is very limited especially in resource limited settings. We assessed asthma control and its evolution over time among asthmatics treated using a primary care-led asthma clinic model which included evidence based asthma diagnosis and step-wise management.
Methods: Asthma patients aged ≥ 5years presenting at Mulago Hospital between August 2013 and April 2017 were enrolled and followed up every 6 months for 2 years. A separate clinic manned by a medical officer, a nurse and a counselor was set up within the pulmonary unit. These were trained in evidence-based asthma diagnosis and step-wise asthma management. At each visit, clinical assessments including history, physical exam, asthma control test (a short tool to assess symptoms, use of rescue medications, and activity), and spirometry were performed. In addition to recording clinical assessment, providers recorded modification of treatment as 'stepped down,' 'no change,' or 'stepped up' and classified patients as 'controlled', 'partially controlled', or 'uncontrolled' based on the Asthma Control Test.
Results: A total of 449 patients, with mean age 32 years were enrolled, 149 (33.2%) were classified as controlled, 176 (38.8%) partly controlled, and 124 (28.1%) uncontrolled. At six months of follow up, 306 (69%) patients were seen, 198 (64.7%) were classified as controlled (Prevalence ratio [PR] compared to baseline 1.9, 95% confidence interval [CI] 1.6 – 2.2, p0.001). At 12 months of follow-up, a total of 303 (67%) patients were seen, 230 (75.9%) were classified as controlled (PR 2.9 95% CI 1.9 – 2.6; p 0.001).
Conclusion: A primary care-led asthma clinic model more than doubled the proportion of controlled asthma patients. Capacity development through medical education and training of primary health care providers on evidence-based diagnosis and management of asthma significantly resulted in the control of

asthma among patients. These results suggest that the primary care provider-led model on asthma control could be used to improve asthma outcomes in low-resource settings.

■ **Jithan Jacob Koshy, Akinwumi Ogunromb**

A case series of minimally invasive lobectomy for inflammatory lung disease

Introduction: Minimally invasive lung resection is the standard of care for the management of surgically resectable malignant lung disease. However, its role in inflammatory lung disease with significant adhesions is still debatable. We present a case series of the use of multiport VATS lung resection for patients presenting with various inflammatory lung pathologies including recurrent hemoptysis due to mycetoma, destroyed lobe due to tuberculosis and infected bronchogenic cyst.

Methods: Surgical Approach: Double lumen intubation and right lung isolation, left lateral decubitus position, anterior approach via 3 ports including camera port the right upper lobe is approached through the pleural space. However, initial finger extra pleural dissection for port placement may be required if at the commencement thick adhesions are encountered. Subsequently, the upper lobe is freed by extra-pleural dissection. Once the entire upper lobe is freed, the hilar structures are approached with arterial then venous and lobar bronchial division. The order is altered depending on the anatomical difficulty in isolation or divided and stapled in combination depending on the difficulty in separation. Suturing versus stapling is used depending on the safety of passing the stapling device around the structures without avulsion. Vascular rubber tapes are used for traction and control. The lung is completely freed from diaphragm to allow for adequate re-expansion.

Results: 1. 40yr old female with right upper lobe mycetoma and recurrent massive hemoptysis 2. 20yr old female with right upper lobe mycetoma and recurrent minor hemoptysis 3. 54yr old male with destroyed right upper lobe due to recurrent tuberculosis. 4. 30yr old male with right upper lobe infected bronchogenic cyst.

Conclusion: Well motivated anaesthetic and nursing teams. Allow adequate time on the theatre list. Avoid intra pleural dissection to free thick adhesions. Minimise blood loss with extrapleural dissection and swab application. Patients progressed well postoperatively with minimal pain and early mobilisation. Drains were removed within 48hrs and discharged with good lung expansion and return to their routine physical activities.

■ **Diana Marangu, Ju-Wei Chang, Fatai Akemokwe, Blessings Chisunkha**

Knowledge, attitude and practice of primary care physicians in Kenya, Nigeria and South Africa regarding obstructive sleep apnea in children

Introduction: Obstructive sleep apnea (OSA) significantly impacts the morbidity of children globally, resulting in decreased quality of life and increased health care utilisation costs. Primary care physicians (PCPs) should be familiar and confident in their abilities to diagnose and manage OSA in children, for an effective impact on public health. Our study aims to describe the knowledge, attitude and practice of PCPs in Kenya, Nigeria and South Africa regarding OSA in children.

Methods: Between April 2016 and July 2017, we conducted a multicenter cross-sectional survey in Cape Town, South Af-

rica; Edo State, Nigeria and Nairobi, Kenya. A minimum of 40 participants were randomly selected from a register of PCPs at each site. Following ethical approval, potential participants were contacted telephonically to obtain permission to email them the link to the online/paper-based validated OSA Knowledge and Attitudes in Children (OSAKA-KIDS) questionnaire. PCPs were excluded from the study if they had retired from medical practice, were not currently practising in the study site regions, or declined to provide informed consent.

Results: The median OSAKA-KIDS knowledge score among 184 participants was 67% (IQR 56-72) -58% (IQR44-67) among 80 Nigerian physicians, 61% (IQR 50-72) among 41 South African physicians and 67% (IQR 56-72) among 63 Kenyan physicians. Importance of pediatric OSA and confidence in diagnosis and management were rated by PCPs as 4.5 (IQR 4-5) and 2.3 (IQR 1.8-3.0) respectively on a 5-point Likert scale. The overall median OSAKA-KIDS attitude score comprising both importance and confidence parameters among PCPs was 3.2 (IQR 2.8-3.8). One hundred and sixty one (88%) PCPs referred children with suspected OSA to a sub-specialist, mainly otolaryngologists (87%). A Residency training (46 of 184 participants) was associated with OSAKA-KIDS confidence scores independent of respondent age, sex, country and time since graduation (OR= 2.39 [95% CI 1.14-5.00] p=0.02).

Conclusion: PCPs in Cape Town, Edo State and Nairobi have good knowledge and attitude regarding OSA in children; however their perceived confidence in the diagnosis and management is low. Increased emphasis on paediatric OSA management during undergraduate medical training, and through continuing professional development programmes, may be beneficial.

■ **Reratilwe Mphahlele, Kris de Boeck, Harry Cuppens, Refiloe Masekela**

Complete CFTR gene mutation analysis in non-white patients with cystic fibrosis.

Introduction: Background: There is currently a lack of data on cystic fibrosis (CF) causing mutations in African non-white populations.

Aim: Identify mutations and characterize phenotypic presentations of non-white patients diagnosed with CF in whom a disease-causing mutation was not found on both CFTR genes using the Elucigene 30 mutation panel screen.

Methods: Methods and Materials: The complete CFTR gene, including introns and flanking intergenic regions (including the promoter region), was sequenced with a highly parallel sequencing assay on blood extracted DNA from 5 non-white patients from KwaZulu-Natal, South Africa.

Results: Results: DNA samples of 5 patients with a mean age of 121 months (range 68 -181) were sequenced. Four were black African and 1 was of Black/Mauritian/Asian (mixed) ancestry. Four CF causing mutations including 1 novel mutation were identified in 2 patients: S1255P / R709X (black African female) and L218X / c.2788G>5, the latter novel, (mixed ancestry male). The 3 remaining patients were found to have variants of unknown significance (VUS). Age at clinical diagnosis was lower in the subjects with CF causing mutations; 54 months (range 48 - 60) when compared to those with VUS; 128 months (range 84 -156); (p =0.08). The subjects with CF causing mutations had

better nutritional status and higher mean sweat test concentration than those with VUS; weight-for-age z-score -1.71 (range -1.49; -1.93) vs. -4.8 (range - 4.2; -5.8) (p0.05) and 127mmol/L (range 104 -151) vs. 75mmol/L (range 65 - 83); (p=0.07). All the subjects had severe lung disease with a mean FEV1%p of 41 (range 16 - 56). Commonly cultured organisms from sputum, were Staphylococcus aureus and Haemophilus influenza.

Conclusion: A gene sequencing approach can inform phenotypically supported CF molecular data assisting in compilation of an African population specific registry and mutational panel.

■ S Muttoo, R Naidoo, P Jeena, K Ramcharan, A Mitku

Infant Lung Function and Exposure to Oxides of Nitrogen in a South African birth cohort

Introduction: The relationship between air pollution exposure and infant lung function is poorly understood. Exposure to oxides of nitrogen (NOx) has been considered as an important determinant of lung growth in utero and childhood. The aim of this study was to determine the relationship between antenatal and early postnatal exposure to NOx and infant lung function (ILF).

Methods: Newborns, of mothers, in the 'Mother and Child in the Environment' birth cohort, had ILF tests performed at 6 weeks, 6 months, 12 months and 24 months of age. Women in their first trimester of pregnancy were selected from public sector antenatal clinics in both the industrialised south and less polluted north, Durban, South Africa, and were followed to delivery. NOx exposure was determined by land use regression (LUR) for the individual regional areas. ILF was conducted in unsedated asleep infants, according to the ERS standards of ILF testing, with an ultrasonic flowmeter and 5% SF6 tracer gas. Multiple breath washout techniques were used to measure functional residual capacity (FRC) and lung clearance index (LCI).

Results: Mean predicted antenatal exposures for NOx, determined by LUR, was 35.3ug/m3 (17.74-40.86ug/m3). One hundred and eight infants were tested (with n=74, (68%) valid ILF tests), with a mean gestational age of 38.95 weeks and birth weight of 3.2kg. A mean FRC of 178.45 ml (range: 57.65-435.93ml) and LCI of 7.28 (range: 5.71-9.73) was obtained. Tidal breathing and LCI were not associated with exposure. FRC showed a 2 unit (95% CI: -4.10; -0.04) decline with each unit increase in NOx, after adjusting for birthweight, gestational age, current child age and weight.

Conclusion: The dose response, in FRC decline with NOx is promising to understand the determination of lung growth but needs to be viewed cautiously given the limited sample size and percentage of acceptable tests.

■ Motto Malea Nganda, Ajong Brian, Mbatchou Ngahane Bertrand Hugo

Agricultural burning practice and acute respiratory symptoms among rural farmers in Cameroon: a three point cohort study.

Introduction: Rural farmers in Cameroon practise controlled burning of agricultural fields and household gardens during the dry pre-planting season, exposing themselves to increased immediate ambient air pollution. This study aimed at measuring ambient PM2.5 exposure and assessing the change in acute respiratory symptoms in these farmers during the pre-burning, burning and post-burning periods.

Methods: We conducted a three points cohort study in January (pre-burning), March (burning) and May (post-burning) 2016 among adult rural farmers in Central Yabassi, Cameroon. A one-stage random cluster sampling of 4 on 15 communities and consecutive sampling of all farmers in clusters literate to French and English was applied. Questionnaires regarding demography, burning practice, and acute respiratory symptoms were investigated on same participants all three periods. Two 24 hours ambient PM2.5 measurements were taken in burning areas with a Dylos DC1700 Air Quality Monitor, and a mean gotten per study period. The prevalence of symptoms over time was compared using the McNemar test.

Results: We studied 251 farmers with mean age 47.79±16.52years. 64.5% (n=162) were exclusive farmers while 70.1% (n=176) were permanent residents. The average number of burning days was 14.41±5.29 with a mean burning time of 7.51±2.41 hours per day. With an mean ambient PM2.5 exposure of 10.7µm, 205.2µm, and 7.0µm for the pre-burning, burning and post-burning periods respectively, the McNemar test revealed a significant increase (P0.001) in all symptoms investigated during burning compared with pre-burning period: sneezing (CI16.76–27.86), runny nose (CI05.7–14.98), dry cough (CI13.86–25.18), phlegm (CI10.17–20.11), nasal congestion (CI08.18–18.14), scratchy throat (CI15.67– 6.56), wheezing (CI09.69–19.79), chest tightness (CI14.94 – 25.70), shortness of breath (CI11.71 – 23.35), and eye irritations (CI24.57 – 36.78). Post-burning was characterised, with the exception of runny nose, nasal congestion and chest tightness, by a significant decrease (P0.001) in symptoms.

Conclusion: Rural farmers in Cameroon actively engaged in agricultural burning suffer from acute respiratory symptoms and are exposed to high levels of PM2.5. A general population survey involving lung functions will better evaluate health effects.

■ Gabriel Okello, Sean Semple

Women and girls in resource poor countries experience much greater exposure to household air pollutants than men: results from Uganda and Ethiopia

Introduction: Household Air Pollution (HAP) generated from burning biomass fuels is a major cause of mortality and morbidity in low-income settings worldwide. Little is known about differences in exposure to HAP by age and gender in homes using biomass fuels. This study examined personal exposure to HAP across six population groups defined by age and gender (infants, young males, young females, adult males, adult females, and elderly) in rural households in Uganda and Ethiopia.

Methods: Personal exposure to HAP in each group was assessed by measuring carbon monoxide (CO) and/or fine particulate matter (PM2.5) concentrations in households using biomass fuels. Measurements were made for approximately 24 hours for each individual with some participants wearing more than one instrument to provide data on comparability. Demographics including household, kitchen characteristics, biomass fuel use assessment and socioeconomic status were recorded. PM2.5 concentrations were measured using; TSI Sidepak AM510 Aerosol Monitor, Particle and Temperature Sensor (PATS+), Dylos and RTI MicroPersonal Exposure Monitors. CO concentrations were measured using EL USB CO Lascar loggers.

Results: Data were collected from 215 participants from 85

households. There was a difference in exposure to HAP between males and females (p0.001). 24h PM2.5 exposures were highest among adult females with Geometric Mean (GM) and Geometric Standard Deviation (GSD) 24h concentrations of 194 μg/m3 (1.6) in Ethiopia; and 156 μg /m3 (1.6 GSD) in Uganda. Lowest PM2.5 exposures were recorded among the 'young male' grouping with GM (GSD) of 25.2 μg /m3 (1.49) in Uganda and 26.4 μg /m3 (2.30) in Ethiopia. 'Young female' group had exposures about two-thirds the value of adult female group. Adult males and the elderly group experienced more moderate exposures. *Conclusion:* There are substantial differences in personal exposure to air pollutants depending on age and gender in the rural households. Adult and young females were exposed to highest concentrations in both countries. We found an approximate five-fold difference in PM2.5 exposure between adult males and adult females. Future work ought to consider differences in exposure to HAP across the life-course and characterise age and gender differences when implementing exposure-reduction interventions.

■ **Olatunde Olayanju, Jason Limberis, Aliasgar Esmail, Suzette Oelofse, Phindile Gina, Elize Pietersen, Rob Warren, Keertan Dheda**
Treatment outcomes in patients with extensively drug resistant Tuberculosis from South Africa who received Bedaquiline
Introduction: Optimal treatment regimens for patients with extensively drug-resistant TB (XDR-TB) remain unclear. Long-term prospective data comparing XDR-TB regimens, with and without bedaquiline (Bdq), from an endemic setting are lacking. Our aim was to compare treatment outcomes between XDR-TB patients who received Bdq-based regimen and those who did not. *Methods:* We prospectively followed up 272 patients with laboratory-confirmed XDR-TB (49.3% HIV-infected; median CD4 169 cells/μl) in a 24-month programmatic setting. All patients were admitted to Brooklyn Chest Hospital, Cape Town, which is the designated XDR-TB treatment centre in the Western Cape province of South Africa. 204 patients received a non-Bdq based anti-TB regimen while 68 received a Bdq based regimen. The background treatment regimen was prescribed following the results of individual patient's drug susceptibility testing. XDR-TB patients in the non-Bdq group were treated with a backbone of clofazimine and para-aminosalicylic acid (PAS), while those in the Bdq group also received clofazimine, linezolid and levofloxacin as major components. Demographic and clinical information was obtained from the patients' records. Ethical approval was obtained from University of Cape Town human research ethics committee. *Results:* The overall favourable outcome rates were substantially better in the Bdq versus non-Bdq group [66.2% (45/68) versus 12.8% (26/204); p<0.001]. Those in the Bdq group also had overall reduced rates of treatment failure [5.9% (4/68) versus 25.6% (52/204); p=0.001], default [1.5% (1/68) versus 15.7% (32/204); p= 0.003] and mortality [14.7% (10/68) versus 33.8% (69/204); p=0.004]. Admission weight >50kg, an increasing number of anti-TB drugs, and Bdq were independent predictors of survival (Bdq remained significant in HIV-infected persons, irrespective of CD4 count). A negative sputum culture at 6-months of treatment had a sensitivity of 97.2% and 81.0% to predict survival in the BDQ and non-BDQ groups respectively.

Conclusion: XDR-TB patients receiving a backbone of Bdq and linezolid had a substantial improvement in favourable outcome rate compared to those not using these drugs. These data inform the selection of XDR-TB treatment regimens and roll-out of newer drugs in TB-endemic countries.

■ **Jillian Pooler, Andy McEwen, Rupert Jones**
Very brief advice on smoking saves lives, but does it work in low and middle-income countries?
Introduction: The FRESH AIR project aims to improve the prevention, diagnosis and treatment of chronic lung diseases in LMICs. Smoking is the single most preventable cause of death, resulting in an estimated 6 million premature deaths globally per year. Stopping smoking can reduce risk of premature death and improve current and future health. Very Brief Advice on smoking (VBA) is a proven clinical intervention, which identifies smokers, advises them on the best method of quitting and supports subsequent quit attempts. VBA comprises three elements: ASK, ADVISE, ACT and is designed to be used opportunistically with patients by healthcare workers in almost any situation with a smoker.
Aim: i) To determine whether the VBA intervention can be adapted to low and middle income countries ii) to investigate whether training healthcare workers in delivering VBA results in a change to their clinical or professional practice.
Methods: Mixed methods implementation science study. Stakeholders in Crete, Vietnam and Kyrgyzstan reviewed and adapted the standard UK model for the delivery of VBA to ensure suitability to the local context. Training was provided for healthcare workers in the knowledge and skills needed to deliver VBA. Trainees self-efficacy and self-reported practice behaviours related to VBA was assessed through questionnaires before, immediately after and one month following the training. Interviews conducted.
Results: The original model for the delivery of VBA required minor local adaptation before implementation. Concern about effective delivery of VBA training by English speakers to healthcare workers via a translator and long term sustainability, were addressed by adopting the train-the-trainer model whereby local healthcare workers were trained to deliver VBA training to other healthcare workers in the local language. 126 healthcare workers were trained in VBA (Crete 29; Vietnam 60; Kyrgyzstan 37). Initial findings suggest for the majority VBA training improved their skills and they would recommend the training to others. Significant increases in self-efficacy in advising patients on the best methods of quitting and providing support to smokers were reported between the pre and post assessment.
Conclusion: VBA training is a low resource training which is acceptable, practicable and feasible in LMICs.

■ **Mohammed Aejazur Rahman, Pratistadevi K. Ramdial, Rajhmun Madansein, Gerard Alexander**
A Proteomic Atlas of the Human Pulmonary Tuberculosis
Introduction: Tuberculosis (TB) is a severe global health threat caused by Mycobacterium tuberculosis (Mtb) that forms granulomatous lesions in the lung. Host cells in these lesions vary in abundance, identity, activation status and the presence of detectable bacilli. The physiological and biochemical features

of these lesions are poorly defined. Although animal models infected with Mtb have greatly expanded our understanding of TB, the paucity of TB human tissues for study has made it impossible to validate animal models. As a result, there is a scarcity of studies on fundamental mechanisms of human pulmonary TB. We tested the hypothesis that TB restructures the normal pulmonary architecture, forming heterogeneous granulomatous lesions that vary in cellular composition and arrangement, which is reflected in their proteomic composition.

Methods: We appraised the immunohistochemistry of TB granulomas and used proteomics to examine resected pulmonary tissue from 12 TB and 6 healthy (non-TB) patients. The cellular composition of the lung was characterized using flow cytometry. Global proteomic analyses of the lung tissue were examined using a Surveyor HPLC in-line with a Thermo-Orbitrap Velos Pro-hybrid mass spectrometer.

Results: MetaCoreTM pathway analyses allowed us to identify statistically significant pathways, inclduing: Regulation of Biological and Developmental Process (4.6e-303); Extracellular Component Biogenesis (8.1e-281); Cytoskeleton and Cell Junction Organization (9.1e-267); Phosphatidylinositol and Fibroblast Growth-Factor Signaling (1.9e-246); Response to TGF-β and System Development (3.5e-195); Apoptotic Signaling via Death Receptors (8.4e-79); Regulation of Fatty-Acid Metabolic Process (3.3e-65); Morphogenesis of Epithelium Tissue Development (5.1e-61); Response to Wounding and Stress Signal Transduction (1.8e-40); and Fc-receptor signaling in phagocytosis (2.6e-13). IngenuityTM Pathway Analysis showed upregulation of pathways involved in (i) Mitochondrial Dysfunction, (ii) Production of Reactive Nitrogen and Oxygen Species, and (iii) Glycolysis in the TB diseased lungs compared to healthy samples. Moreover, our histology results demonstrate discrete zonation of metabolic markers and cell types within the granuloma, which may play a role in restricting Mtb growth and/or dissemination.

Conclusion: These pathology and proteomic data provide new insights into the mechanism of human pulmonary TB, which may lead to new paradigms of disease progression; especially how essential host bioenergetic pathways may be subverted by Mtb.

■ Sara-Jane Smith, Lindsay Zurba, Graham Hall, Sanja Stanojevic, Diane Gray, Refiloe Masekela

How well do the 2012 GLI multi-ethnic spirometry reference equations fit healthy South African school children?

Introduction: Spirometry is the most widely used lung function test for the diagnosis and management of patients with chronic lung disease. Interpretation requires accurate, ethnically appropriate reference equations. The Global Lung Function Initiative reference equations published in 2012 (GLI2012) provide reference data for: Caucasian, Black, Southeast Asian, Northeast Asian, and other. However the 'Black' equation was derived from African-American population data and we hypothesise that this may not predict lung function well in black South Africans. We analysed spirometry results from healthy black South African children using the GLI2012 'Black', 'Caucasian' and 'other' reference equations.

Methods: We collected data from school-going children aged 5-16 years in KwaZulu-Natal, South Africa. A minimum of three spirometry measurements were performed to obtain values for FVC, FEV1 and FEV1/FVC. The GLI2012 online calculator was used to generate Z-scores for each prediction equation.

Results: From 443 children screened for the study, 99 were excluded and 344 included, of which 327 (95%) were black African ethnicity and included in this analysis. Of the children included, 208 (63.1%) were female and 236 (72.2%) lived in a rural area. The mean (SD) height-for-age Z-score was -0.46 (SD±1.06) and weight-for-age Z-score was 0.15 (SD±1.63).

Black South African children did not match the GLI2012 'Black' equations, with mean (SD) Z score of 1.04 (SD±1.05) for FVC and 1.06 (SD±1.10) for FEV1. The GLI2012 'other' and 'Caucasian' equations showed a closer fit, with a mean FVC Z-score of 0.45 (SD±1.12) and -0.27(SD±0.99) and mean FEV1 Z score of 0.41 (SD±1.10) and -0.20 (SD±1.03) respectively. All reference equations were more accurate for FEV1/FVC, with a maximum mean Z-score of 0.11 seen in the Caucasian equation analysis (SD±0.86).

Conclusion: Our initial data suggest that GLI2012 'black' reference equations are not valid for estimating FEV1 and FVC in black South African children. A new reference equation for black African populations is needed to aid the interpretation of pulmonary function testing in this setting.

■ Charl Verwey, Azra Ghoor; Lesego Ramocha, Diane Gray, Ziyaad Dangor, Shabir Madhi

Impact of admission for RSV infection on lung function at one year of age: a case control study

Introduction: Respiratory Syncytial Virus (RSV) infection is the commonest cause of acute lower respiratory tract infection (aLRTI) in children less than five years of age. While RSV aLRTI mortality is relatively low, the global impact of RSV hospitalisation has shifted towards the long-term sequelae associated with RSV aLRTI in early life.

Methods: We performed tidal breathing flow-volume loops and SF6 multiple breath wash-out at one year of age in children previously hosptalised for RSV aLRTI (cases; n=83) and compared them with healthy non-hospitalised controls (n=92) during natural sleep as per ERS/ATS guidelines.

Results: There were no differences in reported history of parental or sibling diagnosed asthma; smoke exposure; method of infant feeding; overcrowding and creche attendance between cases and controls. Cases had more exposure to household pets (p=0.046). A larger proportion of cases reported any wheeze (p=0.001), nocturnal cough when well (p=0.003), hospitalisation for subsequent wheezing episodes (p0.001) or recurrent aLRTI (p=0.001). Similarly, a larger proportion of cases had an increased respiratory rate (p=0.004), lower oxygen saturations (p=0.03) and lower tidal volumes (p=0.002). The lung clearance index was significantly increased in cases [7.7 (IQR 6.0-11.0)] compared to controls [7.1 (IQR 5.3-12.8)] (p=0.007).

Conclusion: Children hospitalised with a RSV aLRTI in infancy had more respiratory sequelae at one year of age compared to controls. In addition, these infants had more ventilation inhomogeneity and an increased work of breathing. Longer follow-up of these cases is required to evaluate the impact of RSV aLRTI on respiratory trajectories.

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Learning Objectives

- Increase knowledge and awareness of spirometry
- Develop practical skills to perform high quality spirometry
- Understand interpretation of spirometry results
- Knowledge & awareness spirometry quality assurance and its implementation
- Learn strategies to incorporate spirometry testing systematically into routine clinical practice
- Increase confidence in performing, understanding & implementing spirometry

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