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Formative research - an essential step in developing and adapting health interventions and policies in low- and lower-middle income countries

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Affidavit

I hereby declare, that the submitted thesis entitled: *Formative research - an essential step in developing and adapting health interventions and policies in low- and lower-middle income countries,* is my own work. I have only used the sources indicated and have not made unauthorised use of services of a third party. Where the work of others has been quoted or reproduced, the source is always given. I further declare that the submitted thesis or parts thereof have not been presented as part of an examination degree to any other university.

Olena Ivanova Munich, 21/10/2021

1. Table of Contents

2. Abbreviations

ATS	American Thoracic Society
ERS	European Respiratory Society
DRC	Democratic Republic of Congo
FGD	Focus Group Discussion
FGM	Female Genital Mutilation
FVC	Forced Vital Capacity
FEV1	Forced Expiratory Volume in 1 second
GLI	Global Lung Function Initiative
HIV	Human Immunodeficiency Virus
INS	Instituto Nacional de Saúde
LMICs	Low- and Lower-Middle Income Countries
SRH	Sexual and Reproductive Health
TB	Tuberculosis

3. Publication list

1. **Ivanova, O**.; Khosa, C.; Bakuli, A.; Bhatt, N.; Massango, I.; Jani, I.; Saathoff, E.; Hoelscher, M.; Rachow, A. Lung function testing and prediction equations in adult population from Maputo, Mozambique. *Int. J. Environ. Res. Public Health* 2020, *17*, 4535.

2. **Ivanova, O.;** Rai, M.; Mlahagwa, W.; Tumuhairwe, J.; Bakuli, A.; Nyakato, V. N.; Kemigisha, E. A cross-sectional mixed-methods study of sexual and reproductive health knowledge, experiences and access to services among refugee adolescent girls in the Nakivale refugee settlement, Uganda. *Reprod Health.* 2019, 16(1), 35.

4. Abstract (English)

Background: Situation analysis is an important component of designing and developing healthcare interventions and allows us to describe health gaps and needs of different population groups in various settings. The overall objective of both studies was to shed light on the health situation and needs of adolescents and adults living in low- and low-middle income countries in Africa, with a focus on sexual and reproductive health (SRH) and respiratory health.

Methods: We employed mixed-methods research. The data collection took place in 2017 and 2018 in Maputo, Mozambique and in the Nakivale refugee settlement in Mbarara, Uganda. Data was collected in healthcare facilities and communities. We used questionnaires, focus group discussions and individual interviews, as well as clinical assessments and lung function testing. Data was analysed using statistical methods: descriptive statistics and logistic regression, and qualitative thematic analysis.

Results: In Study I, a total of 212 male and female participants were recruited, from whom 155 participants provided usable spirometry results. The mean age of participants was 35.20 years (SD 10.99) and 59.35% (93 of 155) were female. Spirometric prediction equations were developed based on the studied population. The predicted values for spirometric parameters: forced vital capacity (FVC), forced expiratory volume in 1 s (FEV1) and the FEV1/FVC ratio using Mozambican equations were lower than the GLI- and the South African-based predictions [1].

In Study II, a total of 260 female participants were recruited, with a median age of 15.9 years. The countries of origin for majority of girls were DR Congo and Burundi. A total of 43% of girls, who had experienced menstruation (93%), had ever missed school due to pain, lack of hygiene products or shame. SRH knowledge was poor: a total of 11.7% of the girls were not aware of how HIV is prevented and 13.8% could not name any methods to prevent pregnancy. Thirty girls were sexually active at the time of interview, 11 of them had experienced forced sexual intercourse, which occurred during conflict, in transit or within the camp. A total of 27 participants had reported female genital mutilation (FGM). The most preferred sources for SRH information were parents or guardians, however, some participants mentioned that they were shy or afraid to discuss other sexuality topics apart from menstruation with their parents. A total of 30% of girls had ever visited an SRH service centre, mostly to seek medical aid for menstrual problems or to test for HIV [2].

Conclusions: These studies contribute to knowledge on the health status of vulnerable populations, i.e. adolescents in a refugee camp in Uganda and adults living in poor urban neighbourhoods in Mozambique, and provide valuable data for the design and implementation of future research projects and programs in these settings, addressing specific health issues (SRH and respiratory health).

5. Abstract (German)

Hintergrund: Die Situationsanalyse ist eine wichtige Komponente bei der Konzeption und Entwicklung von Maßnahmen der Gesundheitsversorgung. Sie ermöglicht die Beschreibung von Lücken in der gesundheitlichen Versorgung und Bedürfnissen verschiedener Bevölkerungsgruppen in unterschiedlichen Umfeldern. Übergeordnetes Ziel beider Studien war, die Gesundheitssituation und die Bedürfnisse von Jugendlichen und Erwachsenen in Ländern mit niedrigem und mittleren Einkommen in Afrika zu beleuchten, mit einem Schwerpunkt auf der sexuellen und reproduktiven Gesundheit (SRG) sowie der Lungengesundheit.

Methoden: Wir haben einen gemischte Forschungsmethodenansatz benutz. Die Datenerhebung fand jeweils im Jahr 2017 und 2018 in Maputo, Mosambik, und in der Flüchtlingssiedlung Nakivale in Mbarara, Uganda, statt. Die Daten wurden in Gesundheitseinrichtungen und in den Gemeinden erhoben. Wir haben dafür Fragebögen, Fokusgruppendiskussionen und Einzelinterviews sowie klinische Untersuchungen und Lungenfunktionstests durchgeführt. Die Daten wurden mit statistischen Methoden analysiert, z.B. deskriptive Statistik und logistische Regression, sowie mit Mitteln der qualitativ-thematischen Analyse.

Ergebnisse: In Studie I wurden insgesamt 212 Männer und Frauen rekrutiert, wobei 155 Teilnehmer brauchbare Spirometrie Ergebnisse aufwiesen. Das Durchschnittsalter der Teilnehmer betrug 35,20 Jahre (SD 10,99), und 59,35% (93 von 155) Teilnehmern waren weiblich. Neue spirometrische Vorhersagegleichungen wurden auf der Datengrundlage der untersuchten Population entwickelt. Die Vorhersagewerte für die forcierte Vitalkapazität (FVC), das forcierte exspiratorische Volumen in 1 s (FEV1) und das FEV1/FVC-Verhältnis auf der Grundlage der neu generierten mosambikanischen Gleichungen waren niedriger als die Volumenvorhersagen, die auf GLI- sowie Südafrikanischen-Daten basierten [1].

In Studie II wurden insgesamt 260 Teilnehmer mit einem mittleren Alter von 15,9 Jahren rekrutiert. Die Mehrheit der Mädchen wurde in der DR Kongo und in Burundi geboren. Von den 93% der Mädchen, die bereits menstruieren, hatten 43% mindestens einmal die Schule aufgrund von Schmerzen, mangelnder Verfügbarkeit von Hygieneprodukten oder Scham verpasst. Die SRG-Kenntnisse der befragten Mädchen waren gering: insgesamt 11,7% der Mädchen wussten nicht, wie eine Infektion mit HIV verhindert wird, und 13,8% kannten keine Methode zur Verhütung einer Schwangerschaft. Insgesamt waren zum Zeitpunkt der Befragung 30 Mädchen sexuell aktiv, von denen 11 erzwungenen Geschlechtsverkehr erlebt hatten. Letzteres geschah während des kriegerischen Konflikts, auf Flucht oder innerhalb des Lagers. Insgesamt 27 Teilnehmerinnen sind einer weiblichen Genitalverstümmelung unterzogen worden. Die am meisten bevorzugten Quellen für SRG-Informationen waren Eltern oder Erziehungsberechtigte. Einige Teilnehmerinnen gaben

jedoch an, dass sie Angst oder Scheu hätten, mit den Eltern über andere Sexualitätsthemen als die Menstruation zu sprechen. Insgesamt 30% der weiblichen Jugendlichen hatten jemals ein SRG-Gesundheitszentrum besucht, meist um sich auf HIV testen zu lassen und um medizinische Hilfe bei Menstruationsproblemen zu suchen [2].

Fazit: Beide Studien tragen zum Wissen über den Gesundheitszustand gefährdeter Bevölkerungsgruppen bei, konkret von Jugendlichen in einem Flüchtlingslager in Uganda und Erwachsenen, die in armen Stadtvierteln in Mosambik leben, und liefern wertvolle Daten für die Planung und Durchführung künftiger Forschungsprojekte und Programme in diesen Umfeldern, die sich mit diesen spezifischen Krankheiten und Gesundheitsfragen (SRG und respiratorische Gesundheit) befassen.

4. Introduction

Improving the health of populations living in low- and lower-middle income countries (LMICs) is essential to overcome and prevent adverse health outcomes and mortality, including maternal mortality, gender-based violence and chronic lung diseases. The design and implementation of health interventions, strategies and policies should be preceded by a careful assessment of the local situation and health needs of potential beneficiaries [3,4]. Thus, formative research should be a first step in any health programming effort.

4.1 Formative research: what, how, and why we need it

Formative research, also referred to as *situation analysis, formative assessment, explorative research* or *needs assessments*, generates information and data needed to design health interventions and policies. It allows us to understand contextual factors and identify gaps between an existing health situation and desired outcomes. Formative research also helps to make interventions culturally and geographically more appropriate [4]. Additionally, it can contribute to assessment of clinical practice, planning of quality improvement initiatives and understanding many other aspects of health programming [5].

Formative research is primarily conducted before an intervention or policy is developed and implemented, or alongside these processes. It can be also used to develop a data collection tool or instrument, for example a formative study to develop an adolescent nicotine dependence tool [6]. Situation analysis itself can be seen as an intervention, which initiates public discussions on relevant health issues, raises awareness and opens dialogues between different actors, such as researchers, communities and decision-makers [7]. In this case, beneficiaries are directly engaged in the formative research using Participatory Action Research [8] or other methods.

Depending on the goal, the applied methodologies comprise literature reviews, qualitative data collection (interviews, focus group discussions, observations and social mapping, etc.) and/or primary or secondary quantitative data collection (household surveys, health care facilities data, etc.). There are readily available and validated tools to assess needs and conduct health situation analysis, e.g. the Reproductive Health Assessment Toolkit for Conflict-Affected Women, CDC [9], tools for demographic health surveys [10] or health screening programs including hypertension and sexually transmitted infections (STIs).

To guide formative research, some authors used different theoretical frameworks, which helped to provide directions for the research process [11], such as Social Cognitive Theory in the study on Girls Health Enrichment [12] or Ecological Model in the Child Growth Monitoring Project [13].

Currently, there is a growing body of literature reporting on formative research from clinical to educational interventions in different health domains and contexts; for instance, a complex formative research project used to develop an intervention with the aim to reduce maternal and neonatal mortality in Nepal [14], or formative research activities to inform and improve active case finding strategies for tuberculosis in South Africa [15].
To summarize, formative research plays a critical role in providing health data, needed to understand why certain approaches work and others do not, and for developing culturally appropriate and targeted health interventions and programs.

4.2 Brief overview of the health situation of adolescents and adults living in low-resource settings

According to the classification of the World Bank, almost all countries on the African continent are situated in LMICs groups [16]. Nowadays, they are undergoing a shift from health profiles dominated by communicable diseases, e.g. HIV and tuberculosis (TB), to those with an increased proportion in chronic non-communicable diseases (NCDs), such as chronic respiratory diseases, i.e. asthma, diabetes and hypertension [17]. This new health situation in many African communities poses a significant additional burden on the surveillance systems and healthcare services that were primarily targeting non-NCDs in the past, as well as producing a demand to find suitable, locally-adapted interventions and polices to address this double burden. In order to do so, there is a need to collect and analyse local and contextual data. Below is a brief overview of the situation in two health domains: respiratory health and sexual and reproductive health (SRH) in African countries.

4.2.1 Respiratory health

Tuberculosis remains one of the leading respiratory infections and causes of death in adults in high-burden countries in Africa [18]. There is accumulating evidence suggesting that active pulmonary TB is also accompanied with residual lung damage after microbiological cure [19]. Together, TB and post-TB lung disease (PTLD) directly contribute to a double burden of disease – communicable diseases and NCDs [20]. Like other chronic respiratory diseases such as asthma and COPD, PTLD is also associated with multiple other risk factors, such as indoor air pollution, early childhood development and chest infections, poverty, (passive) smoking and chronic HIV infection [21–23]. COPD is the third leading cause of death worldwide with 3 million deaths in 2016 [24], however, it remains a “silent epidemic” in Africa with a low number of available prevalence studies due to a lack of standardised epidemiological instruments and expertise [25]. In general, a scarcity of data on

prevalence and associated morbidity and mortality is present for chronic respiratory diseases in LMICS, especially in Sub-Saharan African countries [26,27].

This lack of data directly influences clinical practice and management of patients. For instance, to diagnose respiratory morbidities, a number of clinical methods are used, including spirometry (lung function testing). For example, according to WHO, spirometry is requested to diagnose COPD. In order to interpret the spirometry result of a specific person, it is important to have access to local reference data derived from a healthy population with the same characteristics, e.g. age, ethnic origin or anthropometric characteristics [28]. While the Global Lung Function Initiative (GLI) is aiming to provide spirometric reference values for the majority of populations worldwide [29], they, however, do not include data from sub-Saharan African countries, which may render the provided references unusable for the clinical diagnosis and medical treatment of African individuals with or without pulmonary symptoms [1]. Knowing the respiratory situation and pulmonary risk factors of the normal, asymptomatic population, as well as of people suffering from chronic lung diseases, is a necessary prerequisite to improve clinical services and produce local health strategies for respiratory diseases. This also includes the availability of local spirometric reference values for African populations.

4.2.2 Sexual and reproductive health

Communicable and non-communicable diseases' burden in LMICs is aggravated by high rates of maternal mortality and morbidity among women, which remain a key challenge in African countries in particular [30]. Failure to improve sexual and reproductive health (SRH), and access to SRH services as a human right, leads to adverse outcomes such as maternal mortality, HIV and STIs, unplanned pregnancies and unsafe abortions. Adolescent girls and young women are largely affected.

Despite a fast-growing aged population around the globe, there are also unprecedentedly high numbers of young people (10-24 years old) – 1.8 billion, with the largest concentration in Africa [30]. Young people, girls in particular, in LMICs are facing significant challenges in accessing contraception and SRH information, a high burden of gender-based and sexual violence, health risks related to early childbearing and early marriages, high prevalence of HIV and many other adverse health outcomes [31].

Additionally, young women and girls are an overlooked population within humanitarian settings and conflict-affected regions [32]. Meanwhile, Africa hosts one of the largest populations of refugees and displaced people in the world, three main hosting countries being Uganda, Sudan and Ethiopia [33]. Our recent review (Ivanova et al., 2018) demonstrated that knowledge of young refugee

women and girls regarding STIs, contraceptive methods and HIV/AIDS is limited [34]. This population group often suffers sexual violence, abuse and gender-based violence. They face challenges accessing SRH services due to distances, costs and stigma [34]. However, there is still a lack of literature and information on SRH situations and needs among migrant, refugee and displaced girls and young women in African countries. Thus, it is of the utmost importance to explore these challenges in depth as a basis to develop suitable interventions such as comprehensive sexuality education and youth-friendly SRH services in refugee settlements and disadvantaged communities.

4.3 Objectives

The **overall objective** of the two studies forming the basis for this thesis was to shed light on the health situation and needs of adolescents and adults living in LMICs in Africa, with a focus on respiratory health and SRH. We therefore conducted two formative assessments: one clinical assessment and one situation analysis.

4.3.1 Study I: "Lung function testing and prediction equations in adult population from Maputo, Mozambique"

In this study, we aimed to collect lung function data from non-symptomatic adults living in Maputo, Mozambique, in order to derive spirometric prediction equations for this specific population. They are urgently needed to evaluate lung function of participants in future clinical research studies and in patients with respiratory diseases in this area [1].

4.3.2 Study II: "A cross-sectional mixed-methods study of sexual and reproductive health knowledge, experiences and access to services among refugee adolescent girls in the Nakivale refugee settlement, Uganda"

In this study, we aimed to assess the situation of SRH knowledge, experiences and access to services among adolescent girls living in a refugee settlement in Uganda. It provides the basis for the future development of a locally-adapted sexuality education intervention [2].

4.4 Methods

A mixed-method approach was employed. The data collection for both studies took place in 2017-2018 in two African countries: Mozambique and Uganda.

4.4.1 Study I

We applied a cross-sectional design to this study. Data for this study was collected from April to December 2017.

Setting: This research was conducted at the TB Research Study Clinic in Mavalane (run by the Instituto Nacional de Saúde (INS)) and the HIV counselling and testing clinic at the Mavalane Health Centre. These centres are situated in a poor urban neighbourhood of Maputo.

Quantitative data collection and analysis: Data collection using a validated questionnaire was performed. It included demographic characteristics and respiratory symptoms. Additionally, participants underwent anthropometric data collection (weight and height) and lung function testing. Spirometry tests were performed according to American Thoracic Society and European Respiratory Society (ATS/ERS) guidelines [35]. Recorded spirometry parameters were forced vital capacity (FVC) and forced expiratory volume in 1 s (FEV1). Data were analysed using descriptive statistics and regression models to derive spirometric prediction equations. Further details on different models and lung function of individual participants are provided in Publication I [1].

Contribution of the Dr. med. candidate: I contributed to the study conceptualization including the development of the study (protocol and data collection tools), analysed data jointly with a statistician and the study co-investigator in Mozambique and drafted the manuscript.

4.4.2 Study II

We combined qualitative and quantitative designs for this study, linking common themes, i.e. menstrual health and SRH knowledge, across the survey and semi-structured interviews. Data for this study was collected from March to May 2018.

Setting: The Nakivale refugee camp is located in Isingiro District in Southwestern Uganda. It was established in 1960 for refugees from Burundi and later became a home for many refugees from Rwanda in 1994. Currently, it is hosting refugees from South Sudan, Somalia and Democratic Republic of Congo (DRC) due to ongoing or past conflicts. Women and girls comprise 46.8% of the Nakivale's total population, and half of the population are below 18 years old [36]. Socio-economic conditions in the settlement are very challenging: limited access to water sources, security problems, lack of access to education for children, etc. [37].

Quantitative data collection and analysis: A questionnaire was created to collect data from 260 girls living in the settlement. A convenience sample of girls recruited in different camp communities was employed. The questionnaire consisted of four sections and was designed using validated tools. Data was collected using tablets, extracted as Excel files and analysed using STATA version 14 and R 3.5.1 software. Descriptive analysis and multinomial logistic regression were used for statistical analysis [2].

Qualitative data collection and analysis: Qualitative data was collected using semi-structured interviews with 28 girls. Five interviews were excluded due to a low quality. A guide for semi-structured interviews was developed, based on the topics addressed in the questionnaire. During the interviews, notes were taken. The interviews were recorded with voice recorders, transcribed and translated to English, where necessary. Data was coded manually using deductive coding. A codebook and themes were generated based on the literature, quantitative data and qualitative guide [2]. We employed thematic content analysis for this research [38].
Contribution of the Dr. med. candidate: I designed the study protocol and data collection tools; trained field workers in data collection in Mbarara, Uganda; supervised study activities; analysed quantitative data jointly with a statistician and the study co-investigator in Uganda; analysed qualitative data jointly with a student assistant and the study co-investigator in Uganda; and drafted the manuscript.

4.4.3 Ethical considerations and funding

Both studies received ethical approvals from the relevant ethics committees (see details in Publication I and II) and all participants signed informed consent forms and/or assent forms. Funding sources were acknowledged in the publications.

4.5 Results

The results of two studies are presented and discussed in Publications I and II. The first publication describes lung function results and reference standards in adults in Maputo, Mozambique [1]. The second publication reports on findings related to sexual and reproductive health knowledge, needs and experiences of girls living in the Nakivale refugee settlement in Mbarara, Uganda [2].

4.5.1 Publication I

Ivanova, O.; Khosa, C.; Bakuli, A.; Bhatt, N.; Massango, I.; Jani, I.; Saathoff, E.; Hoelscher, M.; Rachow, A. Lung function testing and prediction equations in adult population from Maputo, Mozambique. *Int. J. Environ. Res. Public Health* 2020, *17*, 4535.

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Article

Lung Function Testing and Prediction Equations in Adult Population from Maputo, Mozambique

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Abstract: Background: Local spirometric prediction equations are of great importance for interpreting lung function results and deciding on the management strategies for respiratory patients, yet available data from African countries are scarce. The aim of this study was to collect lung function data using spirometry in healthy adults living in Maputo, Mozambique and to derive first spirometric prediction equations for this population. **Methods:** We applied a cross-sectional study design. Participants, who met the inclusion criteria, underwent a short interview, anthropometric measurements, and lung function testing. Different modelling approaches were followed for generating new, Mozambican, prediction equations and for comparison with the Global Lung Initiative (GLI) and South African equations. The pulmonary function performance of participants was assessed against the different reference standards. **Results:** A total of 212 males and females were recruited, from whom 155 usable spirometry results were obtained. The mean age of participants was 35.20 years (SD 10.99) and 93 of 155 (59.35%) were females. The predicted values for forced vital capacity (FVC), forced expiratory volume in 1 s (FEV1) and the FEV1/FVC ratio based on the Mozambican equations were lower than the South African—and the GLI-based predictions. **Conclusions:** This study provides first data on pulmonary function in healthy Mozambican adults and describes how they compare to GLI and South African reference values for spirometry.

Keywords: lung function; spirometry; prediction equation; adult; Mozambique; Africa

1. Introduction

Local reference data is important for interpreting spirometry test results and deciding on the management strategies for respiratory patients. According to the American Thoracic Society (ATS) recommendations, reference values should be derived from a healthy population with the same ethnic origin and anthropometric characteristics as the participants and patients being tested in studies or clinical services [1]. The Task Force of the Global Lung Function Initiative (GLI) aimed to establish improved international lung function reference data and to derive continuous prediction equations for spirometric indices, which are applicable globally [2]. This approach included data from various countries around the world yet data from African, South Asian and Latin American countries are lacking [3]. Therefore, the reference standards published by GLI for lung function parameters of

African populations may not be appropriate for use in all African settings. Local prediction equations are also unavailable in many African countries, including Mozambique. Thus, international reference values adjusted by ethnic correction factors are often used for spirometry in African settings [4,5]. This might lead to lower diagnostic standards in specific ethnic groups and, ultimately, incorrect clinical diagnoses in patients with (or without) pulmonary symptoms.

In the present study, we aimed to collect spirometry data from non-symptomatic adults living in urban Maputo, Mozambique, to derive prediction equations for this specific population, which can be used to evaluate lung function in participants of clinical research studies [6,7], and also, in patients with respiratory diseases in this area.

2. Materials and Methods

2.1. Study Design and Participants

A cross-sectional study was conducted between April and December 2017. Household members and neighborhood contacts of participants of a tuberculosis (TB) cohort study [6] conducted at the Instituto Nacional de Saúde (INS) TB Research Study Clinic in Mavalane, Maputo, and residents attending HIV counselling and testing clinic at the Mavalane Health Centre were recruited using a convenience sampling approach. Exclusion criteria were a history of TB, current symptoms of active TB, any acute or chronic respiratory diseases, and contraindications for spirometry [8,9]. Eligible participants were 18 years or older and willing to provide informed consent for study participation.

2.2. Data Collection

Data collection and lung function measurements were performed at the Instituto Nacional de Saúde (INS) TB Research Clinic in Maputo, Mozambique, on the premises of the Mavalane Health Centre. Height and weight measurement were taken using a stadiometer and an electronic weighing scale, respectively. Body mass index (BMI) was calculated as weight (kg) divided by height (m) squared. Demographic characteristics were collected using a short, standardized questionnaire developed for this study. Spirometry was performed using handheld EasyOne spirometers® (ndd Medizintechnik AG, Zurich, Switzerland), which was previously validated and used in a number of studies [4,10]. Key staff were trained in spirometry technics by a pulmonologist. Further on-site training was provided to the technical staff by trained principal investigators. Spirometry tests were performed according to ATS/ERS (European Respiratory Society) guidelines [9]. Recorded spirometry parameters were forced vital capacity (FVC), forced expiratory volume in 1 s (FEV1) and peak expiratory flow (PEF). A rigorous internal and external quality control process was established based on the spirometry guidelines developed for the TB Sequel study to identify usable curves for inclusion in the final analysis [7].

2.3. Data Analysis

Tabulations were done to summarize participants' characteristics. Different modelling strategies were followed to generate new Mozambican prediction equations based on the measured spirometry outcomes. FEV1 and FVC were modelled individually using regression models as reported in most studies, including sex, height and age as covariates [11,12]. As evolution with age follows a nonlinear trend, complex models like generalized additive models for location scale and shape (GAMLSS) were used by the GLI in previous studies with large sample size [13,14]. However, due to limited samples size with our data, generalized additive models (GAM) models with the increased complexity for smoothing the effect of age on the outcomes did not perform significantly better than multiple linear regression models. Thus, we finally used regression models including age, height and sex as covariates to predict values for FVC and FEV1. We performed a sensitivity analysis using multiple cross-validation methods: (1) random sample of 2/3rd of the data as training data set, followed by the remaining 1/3rd as the testing data set; (2) leave one out cross validation (LOOCV) or the Jack Knife estimator; (3) k = 10 fold cross-validation; and (4) k = 10 fold cross-validation with 5 repetitions,

to examine the predictive accuracy of our model. The newly generated prediction models were evaluated for predictive efficacy using the measures of root mean square errors (RMSE), mean absolute error (MAE) and R2 (describing the squared correlation between observed and predicted in the test data set) [15]. Further, the stability of regression equations was evaluated by comparing the regression estimates to the non-parametric bootstrap estimates and the corresponding 95% confidence intervals based on 10,000 resamples from our observed data [16–18]. Finally, we assessed the performance of the newly derived Mozambican prediction equation as well as the differences in outcomes using the South African Black and GLI—Others based equations on a spirometry data set from a recently described (post-) TB cohort [6].

The newly generated Mozambican prediction equations were also used to analyze the lung function of individual participants in this study. We calculated a z-score (otherwise known as standardized residual score, or SRS) for the measured FVC, FEV1 and FEV1/FVC ratio in each participant to define how many standard deviations the measured value was away from the predicted value. In line with most recent guidelines, the lower limit of normality (LLN) for each spirometric parameter is represented by a z-score of −1.64, which is equal to the lower 5th percentile of the standard population. That means, participants with a z-score of −1.64 and lower for FVC, FEV1 or FEV1/FVC have lung function parameters of below the 5th percentile of predicted (=LLN) and, thus, are diagnosed with restrictive or obstructive lung function impairment, respectively [19–21]. Severity grading was done as follows: (1) mild impairment: FVC or FEV1/FVC > 85% LLN; (2) moderate: FVC or FEV1/FVC 55–85% of LLN; (3) severe: FVC or FEV1/FVC < 55% of LLN [21]. Resulting differences in ventilation patterns and severity gradings based on the use of the different prediction equations (new Mozambican, GLI—using category "Others", and South African references for the black population) were also assessed [2,22]. In the absence of a South African prediction equation for the FEV1/FVC ratio, we used the GLI equation [2].

2.4. Ethics Approval and Consent to Participate

The study was approved by the Comité Nacional de Bioética para Saúde (CNBS, reference 449/CNBS/16). Written informed consent was obtained from all study participants.

3. Results

3.1. Characteristics of the Study Participants

A total of 212 subjects were recruited in the study, of whom 155 had usable spirometry results and were included in the final analysis. Table 1 shows the characteristics of the participants. The mean age was 35.20 years (SD 10.99) and almost 60% of participants were female (93 of 155; 59.35%). The majority of participants (136 of 155; 87.74%) have never smoked and a relatively high proportion (37.96%) reported as HIV-positive.

3.2. Mozambican Spirometric Reference Equations

We modelled regression equations for each spirometric parameter (FVC, FEV1 and FEV1/FVC ratio) based on the spirometry values obtained from our Mozambican study population, as shown in Table 2. Age, height and sex were covariates for the prediction of FVC, and additionally, the influence of height differed by sex for FEV1, but not for FVC (Table 2 and Figure 1). We could further show that FVC and FEV1 were highly correlated (Figure S1 in Supplementary Materials). The ratio for FEV1/FVC was dependent on the age when we observed a decreasing trend in the ratio with an increase in age (Table 2 and Figure S2). Here, no difference was observed among males and females. A comparison of the final model (most parsimonious) with others—more complex (more parameter) and simpler (less parameter) models, arranged hierarchically, and their corresponding likelihood ratio test results are described in Table S1.

Table 1. Anthropometric, demographic and spirometric characteristics of the participants.

Characteristics	Male (n = 63)	Female (n = 92)	Total (n = 155)
Age (years)	33.83 (SD 10.74)	36.13 (SD 11.12)	35.20 (SD 10.99)
Height (meters)	1.67 (SD 0.08)	1.60 (SD 0.06)	1.63 (SD 0.08)
Weight (kg s)	65.52 (SD 9.80)	69.24 (SD 15.68)	67.73 (SD 13.69)
BMI (kg/sq. meters)	23.43 (SD 3.70)	26.95 (SD 5.60)	25.52 (SD 5.20)
Age group			
<30 years	27 (42.86%)	30 (32.61%)	57 (36.77%)
30–40 years	20 (31.75%)	28 (30.43%)	48 (30.97%)
≥40 years	16 (25.39%)	34 (39.96%)	50 (32.26%)
BMI Class *			
Underweight	2 (3.17%)	2 (2.17%)	4 (2.58%)
Normal	45 (71.43%)	38 (41.30%)	83 (53.55%)
Overweight	11 (17.46%)	28 (30.43%)	39 (25.16%)
Obese	5 (7.94%)	24 (26.09%)	29 (18.71%)
Smoking			
Never Smoked	49 (77.78%)	87 (94.57%)	136 (87.74%)
Past Smoker	8 (12.70%)	5 (5.43%)	13 (8.39%)
Current Smoker	6 (9.52%)	0 (0%)	6 (3.87%)
Marital Status			
Single	25 (39.68%)	39 (42.39%)	64 (41.29%)
Married	11 (17.46%)	11 (11.96%)	22 (14.19%)
Living with spouse/partner	25 (39.68%)	37 (40.22%)	62 (40.00%)
Widowed	2 (3.17%)	5 (5.43%)	7 (4.52%)
Education			
No formal education	0 (0%)	2 (2.17%)	2 (1.29%)
Grades 1–5	5 (7.94%)	24 (26.09%)	29 (18.71%)
Grades 6–10	27 (42.86%)	43 (46.74%)	70 (45.16%)
Grades 11–12	17 (26.98%)	20 (21.74%)	37 (23.87%)
Vocational	8 (12.70%)	2 (2.17%)	10 (6.45%)
University	6 (9.52%)	1 (1.09%)	7 (4.52%)
HIV status (self-reported) (n = 108, 47 missing observations)			
Negative	27 (72.97%)	40 (56.34%)	67 (62.04%)
Positive	10 (27.03%)	31 (43.66%)	41 (37.96%)
Worked in Mines			
No	61 (96.83%)	92 (100%)	153 (98.71%)
Yes	2 (3.17%)	0 (0%)	2 (1.29%)
Spirometric Parameters **			
FVC (L)	3.77 (SD 0.69)	2.94 (SD 0.46)	3.28 (SD 0.70)
FVC (% of predicted)	90.82 (SD 11.43)	88.62 (SD 11.76)	89.51 (SD 11.65)
FEV1 (L)	3.12 (SD 0.67)	2.43 (SD 0.42)	2.71 (SD 0.63)
FEV1 (% of predicted)	91.28 (SD 13.69)	95.53 (SD 13.02)	93.80 (SD 13.41)
FEV1/FVC ratio	0.83 (SD 0.06)	0.83 (SD 0.06)	0.83 (SD 0.06)

Legend: * BMI according to World Health Organization (WHO) classification; ** predicted FVC and FEV1 based on South African reference standards [22].

Table 2. New spirometric prediction equations obtained from the study sample in comparison to the South African equations.

Outcome (Sex Specific)	South African (Black) Population	Mozambique (Local) Population
FVC (Males)	−3.08 − 0.024 × Age + 4.8 × Height; RSS = 0.54	−2.271 − 0.019 × Age + 3.989 × Height; RSS = 0.43; adj Rsquare = 0.61
FVC (Females)	−3.04 − 0.023 × Age + 4.5 × Height; RSS = 0.41	−2.761 − 0.019 × Age + 3.989 × Height; RSS = 0.43; adj Rsquare = 0.61
FEV1 (Males)	−0.54 − 0.027 × Age + 2.9 × Height; RSS = 0.46	−3.504 − 0.023 × Age + 4.426 × Height; RSS = 0.37; adj Rsquare = 0.65
FEV1 (Females)	−1.87 − 0.028 × Age + 3.4 × Height; RSS = 0.39	−0.170 − 0.023 × Age + 2.150 × Height; RSS = 0.37; adj Rsquare = 0.65
Ratio FEV1/FVC (Not sex specific)	-	0.921 − 0.0027 × Age; RSS = 0.06; adj Rsquare = 0.22

Legend: The regression estimates are smaller in magnitude for Mozambican compared to South African equations, however, the direction of association is the same. We modelled the ratio of forced expiratory volume in 1 s/forced vital capacity (FEV1/FVC). The adjusted, comparably low value for R square (=0.22) indicates that age is only explaining 22% of the observed variability in the ratio of FEV1 and FVC. For the individual outcomes for FEV1 and FVC, both values for R square were higher than 0.6 and hence more than 60% of the variation observed in FEV1 and FVC are explained by the covariates in the regression equation. The Global Lung Initiative (GLI) equations used in this article are based on generalized additive models for location scale and shape (GAMLSS) models and, hence, the regression estimates are not directly comparable and therefore not included in Table 2.

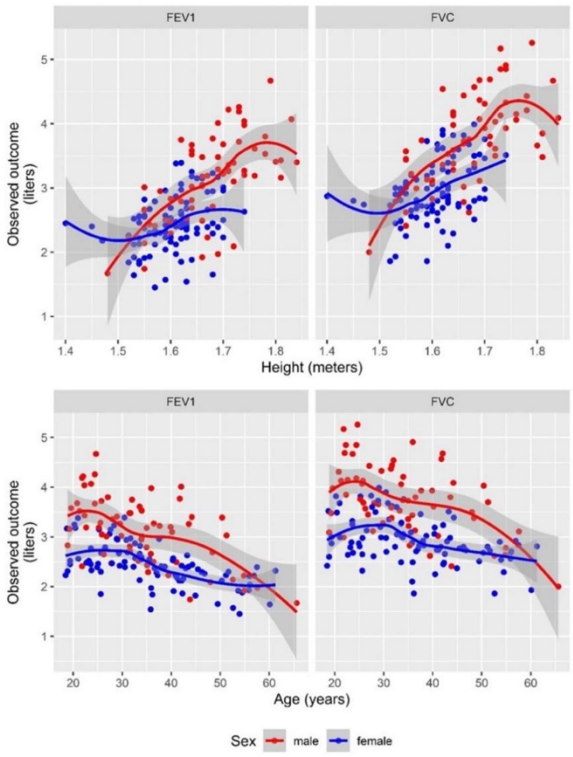

Figure 1. Association of FVC and FEV1 values with height and age and according to sex.

Legend: Lines (LOESS (locally estimated scatterplot smoothing) fit) for FEV1 and FVC, stratified by sex, show predicted values and scatter plots show the spread of the actual data. Fitted lines show the same development over age, with different intercepts for males vs. females. However, for the association with height a difference in slopes for males vs. females is visible. The relationship for the ratio of FEV1/FVC with age, sex and height is shown in the Supplementary Materials Figure S1.

3.3. Lung Impairment in Mozambican Sample: Type and Severity Grading

The newly generated equations were used to calculate the LLN and a z-score for the measured values for FVC, and FEV1 and calculated FEV1/FVC ratio in each study participant.

Table 3 and Table S2 show the lung function of our participants with regards to impairment type and severity grade. Out of the 155 included participants, 16 (10.3%, 95% CI: 6.02% to 16.22%) had abnormal lung function, with nine having an FEV1/FVC ratio below the LLN (obstruction) and seven having FVC values below the LLN (restriction). With regard to severity grading, apart from one subject with moderate obstruction, all other 15 participants with abnormal lung function had only mild impairment (Table 3 and Table S2). None of the risk factors listed in Table 1 was significantly associated with any spirometric parameter.

Table 3. Comparison of outcome categories using Mozambican prediction equations versus South African and GLI equations.

Impairment Type and Severity Grading, N = 155	Mozambique—Local % (n/N)	GLI—Others % (n/N)	South Africa—Black % (n/N)
Normal	89.7 (139/155)	72.9 (113/155)	74.8 (116/155)
Obstruction—Mild	5.2 (8/155)	2.6 (4/155)	5.8 (9/155)
Obstruction—Moderate	0.6 (1/155)	1.9 (3/155)	0.6 (1/155)
Obstruction—Severe	0.0 (0/155)	1.3 (2/155)	0.0 (0/155)
Restriction—Mild	4.5 (7/155)	15.5 (24/155)	12.9 (20/155)
Restriction—Moderate	0.0 (0/155)	3.2 (5/155)	3.9 (6/155)
Restriction—Severe	0.0 (0/155)	0.0 (0/155)	0.0 (0/155)
Mixed—Mild	0.0 (0/155)	0.0 (0/155)	0.0 (0/155)
Mixed—Moderate	0.0 (0/155)	0.6 (1/155)	1.3 (2/155)
Mixed—Severe	0.0 (0/155)	1.9 (3/155)	0.6 (1/155)

Legend: While only 16 (10.3%) subjects had abnormal lung function according to the Mozambican reference standard, 42 (27.1%) and 39 (25.2%) subjects had lung impairment if GLI and South African standards, respectively, had been applied. The greatest discrepancies among the three reference standards are present in the restriction- and mixed-categories as well as in severity categories moderate and severe.

3.4. Comparison of Spirometry Results Based on Different Reference Standards

We assessed the lung function of our study participants by using different reference standards (Mozambican—Local, South African—Black and GLI—Others), and then compared the outcomes. Figure 2 shows the density distribution of the z-scores for FEV1 and FVC for each of the three different reference standards when applied to our study population. Compared to the newly created Mozambican reference standard, a clear shift to lower z-scores for FEV1 and FVC can be observed when the South African and GLI standards are applied to the study sample, resulting in a higher proportion of subjects with abnormal lung function. Complementary to the density distribution of z-scores, we also see a much better fit for the observed data of FVC and FEV1 (in liters) with the Mozambican predictions, while there is a clear shift to and higher predicted values for FEV1 and FVC on average when using the South African and GLI reference standards (Figure S3). No difference was observed for the FEV1/FVC ratio across the different standards. In line with that, the difference in z-scores for FVC between Mozambican prediction equations and the other two predictions was on average one standard deviation (z-score difference = 0.9). For FEV1 z-scores, the overall difference compared to GLI prediction was 1.2 standard deviations but only 0.4 standard deviations compared to South African prediction (Figure S4).

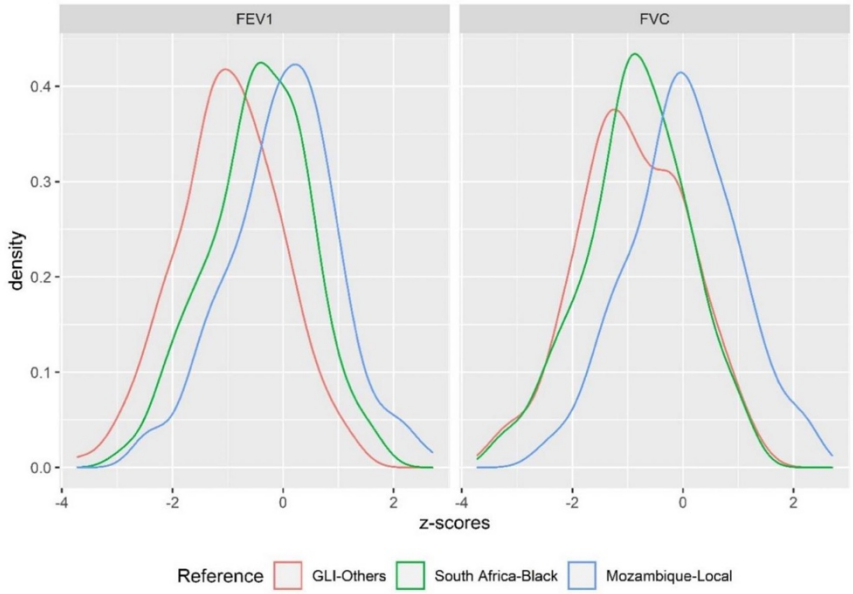

Figure 2. The density distribution of z-scores from the Mozambican sample based on three different reference standards (prediction equations).

Legend: Compared to the newly created Mozambican equations, a clear shift to lower z-scores for FEV1 and FVC can be observed if the South African and GLI equations are applied to the study sample, resulting in a higher proportion of subjects with abnormal lung function.

These findings are supported by the observed numbers of participants with abnormal lung function and the corresponding severity grading, depending on the different reference standard used for the studied population (Table 3 and Table S2). Using GLI and South African standards results in a relevantly higher number of subjects with pulmonary restriction (= FVC values below LLN: 21.3% for GLI; 18.7% for South African) compared to applying Mozambican prediction equations (4.5% of FVC values with a z-score of below −1.64). On average, z-scores for FEV1 retrieved from GLI and South African standards equations were also lower compared to z-scores based on Mozambican predictions, there were also higher proportions of subjects with obstruction, which corresponds to an abnormal FEV1/FVC ratio (8.4% for GLI and South African; 5.8% for Mozambique) (Table 3 and Table S2). The number of subjects classified as having abnormal lung function would increase alongside the number of subjects diagnosed with moderate and even severe impairment if non-Mozambican prediction equations were used (Table 3 and Table S2). The fact that the GLI derived z-scores for FEV1 were lower on average than those for FVC (Figure S4) resulted in five (5/155 = 3.2%) subjects, who would be diagnosed with severe obstructive impairment (three of them with mixed impairment) compared to none if the Mozambican equations would be used as a reference.

3.5. Validation of Models

To validate our modelled prediction equations, we performed several sensitivity analyses (Table S3). In most scenarios, the assessed parameters (RMSE, MAE and R2) performed better for the models built on the Mozambique data than South African or GLI prediction equation models. Additionally, in terms of stability of estimates, the bootstrapped confidence intervals from the Mozambican data

were in alignment with the estimated regression coefficients estimated by multiple linear regression methods (Table S4).

As another test for our prediction model, we applied the new equations as well as GLI and South African standards to the spirometry data of a (post-) TB cohort [6]. As expected, for all reference standards, we observed the improvement of lung function under treatment, with best lung function results at 52 weeks after TB diagnosis and treatment start. However, the comparison of z-scores of the different standards shows that less impairment is described by the local Mozambican standard compared to South African and GLI equations, suggesting overall better fits for the Mozambican standard (Figure S5 and Table S5).

4. Discussion

Ethnicity has been recognized to play a significant role in the variability of lung function, thus it is important to establish reference values relevant to the ethnic characteristics of the local population [23–25]. In this study, we have generated prediction equations for FVC and FEV1 as well as for the ratio of FVC/FEV1 based on lung function data from 155 healthy adults living in Maputo, Mozambique. Compared to the prediction equations from the neighboring country, South Africa, the estimated coefficients associated with age and height of the Mozambican formulas were mostly smaller, except height in FEV1 for males. The South African model regression parameters were not statistically significantly different from the local Mozambican population-based regression model; however, the implications on predictions were different. This resulted in lower predicted values for FEV1, FVC and the FEV1/FVC ratio and, thus, higher (more normal) z-scores for measured values of study participants. Even larger differences were observed in a comparison of predicted values and z-scores based on the new Mozambican prediction equations versus GLI equations. This means, in the absence of the newly generated Mozambican standard, a relevant proportion of our asymptomatic study participants might have been misclassified and placed in abnormal lung function categories, including shifts into higher severity grades, which would be considered clinically relevant. Thus, these patients should be considerably limited in lung function and be symptomatic during routine activities. However, this was denied by all participants at the recruitment. The same trend was observed when we applied our newly derived Mozambican equation, GLI and South African equations to our dataset derived from the (post-) TB cohort in Maputo, Mozambique. As the differences were substantial in some subjects, our findings are relevant for clinical practice. They suggest that individuals from certain ethnic groups might be incorrectly diagnosed and treated for pulmonary conditions due to the application of an inappropriate reference standard to their spirometry results [25]. However, we cannot exclude that lung damage is prevalent in a certain proportion of our clinically asymptomatic study participants. In fact, about 10% of our study population was diagnosed with mild spirometric abnormalities based on the newly generated Mozambican standard. Similar to other spirometric studies with healthy adults included in GLI prediction equations calculations, data on exclusion criteria such as acute or chronic respiratory symptoms and medical history of lung conditions were collected with a standardized and validated questionnaire in our study. Thus, "healthy" volunteers are often equivalent to non-symptomatic (asymptomatic) adults or children, which, however, does not necessarily exclude abnormal results for physiological lung function testing. Further, our study population was recruited in a poor urban area of Maputo with a high prevalence of risk factors for lung health, such as indoor and environmental air pollution, smoking habits or recurrent respiratory infections in childhood, which might explain the mild pathology found in the participants of this study. Interestingly, findings on lung impairment are rarely reported from other spirometric surveys with asymptomatic adults, as they are mostly limited to the description of the newly derived equations and associated methodology. However, regardless from what asymptomatic (healthy) cohort spirometric values were taken, due to the underlying basic statistical assumptions (normally distributed), the resulting modelled prediction equations will always lead to the diagnosis of abnormally low values in some of the survey participants, usually in the 5% with the lowest and

highest values. For analysis of spirometry data, the lowest 5% are considered as abnormal, according to internationally accepted conventions [20]. In order to establish a spirometric reference standard, which is generalizable to a broader Mozambican population, the lung function of more volunteers with a greater age span and from different socio-economic backgrounds would need to be analyzed.

There are a number of limitations of our study that may also render the newly generated prediction equations not generalizable to the broader population of Maputo or Mozambique. Firstly, our study has a small sample size. As we employed a convenient sampling strategy to generate a local spirometric reference from the general population from which we recruited a TB-cohort [6], we were able to recruit only 212 volunteers in the temporal context of the main study. Recently, Quanjer et al. 2012 suggested that in order to validate reference equations for spirometry data, a sample of 300 healthy subjects would be more favorable [14]. Simulation studies in the publication by Austin and Steyerberg, 2015 [26] suggested, that only two subjects per variable are needed for an adequate estimation of coefficients in linear regression models. However, testing for the predictive accuracy of the regression model would require an effectively larger sample size to have separate training and testing data, which we lacked by design. Nevertheless, we still tried to evaluate the predictive accuracy of our model using sensitivity analysis by fitting the regression models on subsamples of the observed data and testing on the remaining data. Finally, there is a huge variety in sample sizes of spirometric data sets, which were included in GLI multi-ethnic reference values calculations: from 108 participants in Ben Saad et al., 2008—Tunis [27] to 5315 in Pérez-Padilla et al., 2006—five Latin American countries [28], indicating that also smaller data sets, which were collected according to ATS/ERS and GLI recommendations, are valuable and could provide important evidence for the generation of prediction equations, that are more representative for specific populations, e.g., in Sub-Saharan Africa. Secondly, our study could only include participants older than 18 years, despite the current trend of including people of all ages in surveys aiming for the generation of spirometric reference equations [2].

Finally, 57 out of 212 participants (26.9%) did not have a valid spirometry result, either due to their inability to pass validity criteria or due to the presence of contraindications such as high blood pressure before the test. Those had to be excluded from the final analysis. There were no statistically significant differences between the included and non-included subjects for assessed risk factors including age, sex, height, weight, smoking status and self-reported HIV status. However, other risk factors than those measured might have been differently distributed among the two groups and, thus, could have introduced bias.

Acknowledging the recent calls for the adoption of the GLI reference values in clinical practice worldwide [29], our study is still very relevant. In the Mozambican context, our data suggest that the GLI equations may not apply to the Mozambican population, mainly because they did not include data from this country, and that the newly generated prediction equations may be an important reference for local clinicians and researchers to critically appraise the lung function of their patients with and without respiratory symptoms to avoid diagnostic errors.

5. Conclusions

To our knowledge, this was the first study to obtain local population spirometric equations in Maputo, Mozambique. Our results support the assumption that the GLI-based reference standards (category "Others") may not be appropriate for our population, because too few data from African populations were included in the equation modelling process. This may result in diagnostic errors in asymptomatic persons as well as in patients with respiratory symptoms. Therefore, the study results will contribute, in addition to other published standards such as GLI, a valuable comparison for future analysis of spirometry results from patients with pulmonary TB or other lung diseases that were recruited into different clinical studies from a similar urban environment. This study was performed in line with GLI and ERS Task Force recommendations that are calling for data collections in non-Caucasian, particularly African and Latin American, populations, including ethnic minorities [2].

Supplementary Materials: The following are available online at http://www.mdpi.com/1660-4601/17/12/4535/s1, Figure S1: association between the observed spirometry outcomes (FVC and FEV1) according to sex; Figure S2: relationship between the ratio of FEV1/FVC with age and height; Figure S3: goodness of fit for Mozambican (local) standards predictions and that based on GLI or South African standards when compared to the observed data; Figure S4: differences between z-scores of Mozambican standards and z-scores based on GLI or South African standards; Figure S5: comparison of performance of local Mozambican, GLI and South African standards on a data set of a TB cohort during and after TB treatment from Maputo, Mozambique. Table S1: likelihood ratio test results for selecting the regression model covariates; Table S2: absolute numbers of participants with different spirometry outcomes and severity grades depending on the applied reference standard (Mozambican, GLI—Others or South African Black prediction equations); Table S3: sensitivity analysis of the prediction equations based on the observed Mozambican data; Table S4: summary from 10,000 non-parametric bootstraps sensitivity analyses on the healthy adult's data from Mozambique; Table S5: comparison of lung impairment prevalence in the own Mozambican TB cohort using Mozambican, GLI and South African prediction equations.

Author Contributions: A.R., C.K. and E.S. designed the study; C.K. and I.M. performed all the study procedures; A.B. performed statistical analysis with input from E.S., O.I., C.K. and A.R.; N.B., I.J. and M.H. supervised and advised on the overall conduct of the study; O.I. and A.R. drafted the manuscript. All authors have read and agreed to the published version of the manuscript.

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Conflicts of Interest: The authors declare no conflicts of interest.

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4.5.2 Publication II

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Reproductive Health

RESEARCH Open Access

A cross-sectional mixed-methods study of sexual and reproductive health knowledge, experiences and access to services among refugee adolescent girls in the Nakivale refugee settlement, Uganda

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Abstract: Background: Humanitarian crises and migration make girls and women more vulnerable to poor sexual and reproductive health (SRH) outcomes. Nevertheless, there is still a dearth of information on SRH outcomes and access to SRH services among refugee girls and young women in Africa. We conducted a mixed-methods study to assess SRH experiences, knowledge and access to services of refugee girls in the Nakivale settlement, Uganda.

Methods: A cross-sectional survey among 260 adolescent girls 13–19 years old was conducted between March and May 2018. Concurrently, in-depth interviews were conducted among a subset of 28 adolescents. For both methods, information was collected regarding SRH knowledge, experiences and access to services and commodities. The questionnaire was entered directly on the tablets using the Magpi® app. Descriptive statistical analysis and multinomial logistic regression were performed. Qualitative data was transcribed and analysed using thematic content analysis.

Results: A total of 260 participants were interviewed, with a median age of 15.9 years. The majority of girls were born in DR Congo and Burundi. Of the 93% of girls who had experienced menstruation, 43% had ever missed school due to menstruation. Regarding SRH knowledge, a total of 11.7% were not aware of how HIV is prevented, 15.7% did not know any STI and 13.8% were not familiar with any method to prevent pregnancy. A total of 30 girls from 260 were sexually active, of which 11 had experienced forced sexual intercourse. The latter occurred during conflict, in transit or within the camp. A total of 27 of 260 participants had undergone female genital mutilation (FGM). The most preferred sources for SRH information was parents or guardians, although participants expressed that they were afraid or shy to discuss other sexuality topics apart from menstruation with parents. A total of 30% of the female adolescents had ever visited a SRH service centre, mostly to test for HIV and to seek medical aid for menstrual problems.

Conclusions: Adolescent refugee girls lack adequate SRH information, experience poor SRH outcomes including school absence due to menstruation, sexual violence and FGM. Comprehensive SRH services including sexuality education, barrier-free access to SRH services and parental involvement are recommended.

Keywords: Adolescent, Girls, Refugee, Migrants, Sexual and reproductive health, Experiences, Access, Africa

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Plain English summary

Although it is known that humanitarian crisis makes girls more vulnerable to unwanted pregnancies, HIV, maternal death and sexual violence, there is still a dearth of research on sexual and reproductive health (SRH) outcomes and access to SRH services among refugee girls in Africa. We conducted a study to assess SRH experiences and knowledge of refugee girls in the Nakivale settlement in Uganda using quantitative and qualitative methods. A total of 260 girls aged 13–19 participated in the survey and 28 of them took part in the in-depth interviews. Data analysis showed that many girls lacked knowledge about sexually transmitted diseases including HIV and contraception. A total of 27 of 260 girls had undergone female genital mutilation. Among 30 sexually active girls, 11 had experienced forced sexual intercourse which occurred during conflict, in transit or in the camp. The most preferred sources for SRH information were parents or guardians, although girls shared that they were afraid or shy to discuss other sexuality topics with parents apart from menstruation. In conclusion, our study showed that refugee girls lack adequate SRH information and experience poor SRH outcomes including school absence due to menstruation and sexual violence. Comprehensive SRH services including sexuality education, barrier-free access to SRH services and parental involvement are recommended in order to improve their SRH knowledge and outcomes.

Background

In 2018, there were 68.5 million people in the world who were forced to leave their homes, and among them, 25.4 million became refugees [1]. Crisis increases the vulnerability of women and girls to unwanted pregnancies, HIV and sexually transmitted infections (STIs), maternal death and sexual violence. Out of the 830 women and adolescent girls who die every day due to complications during pregnancy and childbirth globally, 507 are those from the displaced population [2]. Refugees and migrants are considered to be at high risk of sexual victimization [3–5].

The unprecedented fact is that more than half of the refugee population are under the age of 18 [1]. Despite these numbers, there is no satisfactory prioritization of sexual and reproductive health (SRH) challenges faced by the adolescents (10–19 years old) in humanitarian settings, and their SRH needs are often neglected. For instance, knowledge of refugee girls in African countries regarding contraceptive methods, STIs and HIV/AIDS is limited [6]. This population often has limited access and availability of SRH services due to distance, costs and stigma [6].

Uganda, ranked as Africa's largest and the world's third largest refugee hosting country after Ethiopia and Kenya, is currently home to 1,252,470 refugees and asylum seekers [7]. Twenty-seven percent of these refugee populations are girls under the age of 18 [8]. As a hosting country, Uganda has the youngest population in the world with a median age of 15.2 and adolescents comprise 24% of the population [9]. The median age at first sexual intercourse is 16.9 years [10] and the teenage pregnancy rate in Uganda is 25%, one of the highest in Sub-Saharan Africa [9]. The knowledge and use of contraceptives seem to be limited in this age group. The modern contraceptive prevalence among women age 15–24 is 21.8% [11]. Seventy-five percent of unmarried women aged 15–19 reported having received gifts or money in exchange for sex [12]. However, there is a limited body of evidence on the SRH of refugee girls living in Uganda. Women's Refugee Commission and UNHCR report (2011) showed that girls in the Nakivale refugee settlement reportedly become sexually active at a very young age; often exchange sex for money starting by age 10, in some instances without having access to any family planning methods [13]. According to this report, there were four health facilities operating in the settlement, all of them provided some family planning methods. Staff was trained in these facilities, however reported some gaps in skills regarding long-acting contraception methods and often stock-outs. Youth-friendly services were absent, and girls were afraid to be seen and judged while visiting the maternity wing of a health facility [13].

This study aims to fill the knowledge gap and provide an overview of the situation on sexual and reproductive health experiences, knowledge and access to services among adolescent refugee girls living in a humanitarian setting in Uganda.

Methods

Study setting

Nakivale refugee settlement is located in Isingiro District in Southwest Uganda. It is the oldest and largest settlement in Uganda, currently hosting a diverse refugee population of more than 113,000 refugees. It was established in 1962 for refugees from Burundi and became predominantly Rwandese in 1994. This was followed by a large influx of Congolese refugees and a dramatic increase in the Somali population in the 1990s [13]. Women and girls comprise almost half (46.8%) of Nakivale's total population and half of the population (50.2%) are below 18 years of age [14]. Many children and youth in Nakivale do not attend school, according to UNHCR household survey 54% of households with school aged children have at least one child not enrolled in school [15]. Main barriers to education are high school fees for secondary school, overcrowding and long travel distances [16]. There is limited access to water sources in

the camp. Scares environmental resources cause tensions between refugees and the host community, for example, ccollecting firewood for cooking outside of the settlement puts women and girls at risk of sexual violence [16].

Study design

We selected a mixed-methods design for this study, linking common themes across the survey and semi-structured interviews in order to facilitate comparison of qualitative and quantitative data. Data were collected from March to May of 2018.

Quantitative data collection and analysis

A total of 260 girls were enrolled in the quantitative study. The selection criteria for respondents were age between 13 and 19 years old, willingness to participate in the study, informed consent from parent/caregiver and assent for minors. Unaccompanied adolescents below 18 years of age (without a parent or a legal caregiver who could provide an informed consent) were excluded from the study. Respondents comprised a convenience sample of girls recruited in the different camp communities, e.g. Burundi or Congolese communities, and schools with the help of local community mobilizers and teachers.

The questionnaire consisted of four sections: demographic characteristics, e.g. age, country of origin and education; SRH knowledge, e.g. ways of HIV transmission and prevention, list of contraception methods (modern and traditional) and STIs; SRH experiences, e.g. forced intercourse, FGMs and pregnancy; and access to SRH services. Validated tools were used to develop this questionnaire - Reproductive Health Assessment Toolkit for Conflict-Affected Women, CDC, 2007 [17] and Adolescent Sexual and Reproductive Health Toolkit for Humanitarian Settings, UNFPA and Save the Children, 2009 [18].

A research team of four field workers was trained in research ethics and administering of the structured questionnaire. Data were collected using the tablets in a private setting without parents or caregivers been present. The questionnaire was programmed using the Magpi® application. It allowed for a data collection in an off-line mode. The completed questionnaires were uploaded directly to the central database when connected to the internet and immediately extracted in Excel format.

The statistical package - STATA version 14 and R 3.5.1 were used for the analysis. We performed descriptive statistics to present the findings from the questionnaire. We also evaluated the knowledge on SRH through four question-based components namely, 1- "Ways of HIV transmission", 2- "Methods of HIV prevention", 3- "Knowledge of STIs" and 4- "Knowledge of contraception". Each of them was evaluated on an ordinal scale increasing from zero to three. Summary statistics on these outcomes have been described in the results for the observed data. We also combined these four components to obtain a univariate unweighted sum describing overall knowledge about SRH. This outcome of overall knowledge would range between zero and 12, on the ordinal scale. We categorized this outcome to low (average score up to one across four components), medium (average score between one and two across four components) and high (average score two or more across four components) levels for evaluation of individual explanatory variables (risk factors or covariates e.g. age, education) using a multinomial logistic regression. This method allowed us to evaluate the differential association of the individual candidate risk factors, and the outcome levels high and medium compared to low describing the score for overall SRH knowledge. Relative risk ratios (RRRs) describe this association outcome. RRRs are similar to the outcomes observed in a simple logistic regression; however, the above method allows us to joint comparison across more than two categories, which is an advantage over using simple logistic regression [19].

Qualitative data collection and analysis

Of the 260 girls who answered the questionnaire, 28 girls were purposively selected for the qualitative interviews to broadly represent different countries and age groups. Five interviews were excluded from the analysis because of a low quality, e.g. very short or unclear. The interviews were performed in English, Swahili or Runyankole by four field workers who were proficient in these languages. A guide for semi-structured interviews had been developed to guide the interviews but it allowed for flexibility. The guide was based on the topics addressed in the questionnaire and adapted to different age groups. For instance, young girls who were not sexually active yet discussed menstruation experiences, relationships with friends and family, SRH information sources etc. Same field workers who administered questionnaire, later performed in-depth interviews, which helped to build the trustful relationships with the participants. Interviews were performed in a private environment, e.g. in the classroom during the break when other children were outside, without a parent/caregiver/teacher been present. During the interviews, notes were taken and field workers checked them to ensure accuracy of the records. The interviews were recorded with voice recorders and transcribed. Interview transcripts were translated to English where applicable. Data were coded manually using colour coding and, primarily, deductive coding was applied. Two researchers reviewed all the transcripts and generated a codebook and themes based on the literature, our quantitative data and qualitative guide. We employed thematic content analysis for this research [20]. The findings are presented with original supporting source quotations from the 23 participants.

Results

Demographics characteristics of the participants

Two hundred and sixty girls participated in the survey and of them twenty-three girls participated in the interviews as well. The mean age of participants was 15.9 (SD 0.11, 95% CI 15.6, 16.0). The highest number of the girls were born in DR Congo (29.6%) and the lowest number came from Kenya, with only 1 participant out of the 260. The majority (about 37%) of the participants had been living in Uganda for more than 5 years or between 1 and 3 years (28.9%). Few of them (0.7%) could not recall or relate the duration of stay in Uganda and also a minority of them (4.2%) were staying in Uganda for less than a year. Seventy-one percent of girls had completed at least primary education and about 26% of them had completed secondary education. A total of 63.5% of girls were also currently in school. The demographic characteristics of the participants has been presented in Table 1.

Table 1 Demographic characteristics of the survey respondents

	Number (n = 260)	Percentage
Age		
Younger girls (13–15 years old)	119	45.8
Older girls (16–19 years old)	141	54.2
Country of Origin		
DR Congo	77	29.6
Burundi	45	17.3
Rwanda	35	13.5
Ethiopia	33	12.6
Somalia	25	9.6
Uganda (refugee born in Uganda)	21	8.1
South Sudan	13	5.0
Tanzania	8	3.1
Eritrea	2	0.8
Kenya	1	0.4
Duration of Stay in Uganda		
Less than 1 year	11	4.2
1–3 years	75	28.8
3–5 years	60	23.2
More than 5 years	96	36.9
Since birth	16	6.1
Don't know	2	0.8
Education		
Primary	185	71.1
Secondary	67	25.8
Never attended school	5	1.9
Tertiary	2	0.8
Adult learning	1	0.4
Religion		
Protestant	167	64.2
Catholic	45	17.3
Jehovah's witness	32	12.2
Orthodox	8	3.1
Muslim	6	2.3
Traditional	2	0.8
Currently in School		
Yes	165	63.5
No	95	36.5

Sexual and reproductive health knowledge among girls

We assessed the knowledge of SRH topics, e.g. ways of HIV transmission, STIs and family planning via survey. A total of 23 out of the 260 (8.8%) participants did not know about the ways of acquiring HIV and 30 of them did not know about the method of HIV prevention. Similarly, 41 (15.7%) of the participants could not name any of the STI's and 36 (13.8%) did not know about a single method of contraception. Among the girls knowledgeable about HIV acquisition, sexual intercourse with infected person was the most popular reason (85.8% of them had chosen this option). In the same manner, 80.4% of girls selected abstinence as a way of preventing HIV transmission. The SRH knowledge of the girls described through the four components has been presented in Table 2.

A multinomial regression analysis showed that age, education level and teachers/school as a main source of SRH information were associated with better SRH knowledge. Results are presented in the Additional file 1.

These quantitative findings were confirmed by individual interviews. With respect to the route of HIV transmission, the girls frequently talked about sexual intercourse and sharing of sharp objects with an HIV infected person as risk factors. The other routes, such as mother to child transmission or breastfeeding, were not much discussed by them:

> *"… don't have sex or play with someone who has it* [HIV]. *Because if you have sex with someone who has HIV, it can be passed on to you. And still if you fight with an infected person, you may scratch him or he may scratch and your blood can easily mix."*(15 years old).

Similar results were seen for the ways of HIV prevention. The majority of girls during the interviews mentioned abstinence as an important method for preventing HIV acquisition or pregnancy. For the girls that knew more than one way of prevention, the next most well-known method was by the use of condoms.

The knowledge of girls about STIs was limited to HIV and syphilis for a vast proportion (80 and 31% of girls respectively). Some of them also talked about Hepatitis B

Table 2 Sexual and reproductive health knowledge among girls

	Number ($n = 260$)	Percentage
Ways of HIV transmission		
0	23	8.8
1	73	28.0
2	145	55.7
3 and more ways	19	7.5
Methods of HIV prevention		
0	30	11.7
1	166	63.8
2	54	20.7
3 and more methods	10	3.8
Knowledge of STIs		
0	41	15.7
1	134	51.5
2	48	18.4
3 and more STIs	37	14.4
Knowledge of contraception		
0	36	13.8
1	115	44.4
2	69	26.5
3 and more methods	40	15.3

and *Neisseria Gonorrhoea*, however, the symptoms of STIs were not clear to the girls.

The contraception methods often mentioned by girls were abstinence and condom use. Other than these methods, injection and pills were mentioned by few girls who had knowledge about two or more contraceptive measures:

> *"The methods of preventing pregnancy are like this: when you are still a student, you must abstain from sex. Then when you are a woman and you want to have sex without producing, you can use pills, injections and self-control."* (17 years old).

Misconception about family planning methods was also present:

> *"… I cannot use family planning methods because they are not good. They can affect life."* (17 years old, not sexually active and has not used contraception yet).

Menstrual hygiene and commodities

Out of the 93% of participants that had already experienced menstruation, the average age for the start of menstruation was found to be 13.4 years (95% CI, 13.2, 13.6, SD 0.7). While most of the girls began menstruation at either 13 or 14 years, one of them had at nine and some at 16. A total of 78% of menstruating girls had access to disposable pads (distributed by the UNHCR) and used them followed by cotton cloth (made from rags) - 18%. There was also one case of using plant leaves during menstruation.

The challenges in accessing menstrual hygiene products were also discussed in the interviews. The participants reported that the UNHCR distributed 5–6 packets of pads per women on an average of 6 months which sometimes even had to be shared with other female family members. When lacking pads, the adolescents used old clothes, and these were often reused after washing:

> *"Sometimes when it's not there* [pad], *we use clothes."* (16 years old).

> *"For me here, when I get money, I buy some pads and, when I fail to get money, I tear clothes and use them."* (19 years old).

> "*We hang them* [clothes] *there outside. And then sit around to keep them until they dry, or else other people will steal them."* (16 years old).

A total of 43% of the menstruating girls missed school during their menstruation due to multiple reasons. The main reason was pains during menstruation – named by 74% of girls. The girls were also afraid of staining (22%) and some had no product to manage menstruation (16%). Minority of them (2.8%) were afraid of being teased and the same proportion were also prevented from attending schools because of religious barriers or social taboos related to menstruation. During the interviews, the participants were frequently mentioning that they missed schools mainly because they had either severe pains or bleeding during the menstruation. This statement is also supported by the fact that one of the most common reasons to access health facilities was to seek help for menstrual problems.

Sources of information and access to SRH services

For many participants (38.5%), the most important source of SRH information was schools or teachers. The second most important source (34%) was parents or guardians. Television, internet, books or magazines and male relatives were not considered as an important source by any of the girls. Although radio was mentioned as an important source of information by few of them (1.5%), none of them preferred radio as a source of SRH information. The important and preferential sources of SRH information by the participants ordered by ranking has been elaborated in Table 3.

Table 3 Sources of information on sexual and reproductive health topics

	Main source *n*, %	Second main source *n*, %	Preferred source *n*, %
School/teachers	100 (38.4)	37 (14.2)	36 (13.8)
Parents/Guardians	93 (35.7)	89 (34.2)	100 (38.4)
Friends/peers	26 (10.0)	50 (19.2)	30 (11.5)
Doctor/Nurse	20 (7.6)	20 (7.6)	44 (16.9)
Other female relatives	6 (2.3)	21 (8.0)	18 (6.9)
Sister	5 (1.9)	20 (7.6)	11 (4.2)
Radio	4 (1.5)	2 (0.7)	0 (0.0)
Religious organisations	3 (1.1)	5 (1.9)	4 (1.5)
Brother	1 (0.3)	1 (0.3)	1 (0.3)
Neighbours (community)	1 (0.3)	5 (1.9)	3 (1.1)
Partner (boyfriend)	0 (0.0)	3 (1.1)	1 (0.3)
Organizations/seminars	0 (0.0)	4 (1.5)	3 (1.1)
TV	0 (0.0)	0 (0.0)	0 (0.0)
Internet	0 (0.0)	0 (0.0)	0 (0.0)
Books/Magazine	0 (0.0)	0 (0.0)	1 (0.3)
Male relatives	0 (0.0)	0 (0.0)	0 (0.0)
Any reliable person (whom they trust of having SRH knowledge)	0 (0.0)	0 (0.0)	7 (2.6)
Total	260	100%	

During the interviews, girls mentioned that even though their mothers were obviously the first and the closest person they could approach for sharing and discussing the SRH problems, they hesitated to do so. Some of them because of shame and some of them due to fear. The discussions with their mothers were limited to menstrual problems and its management. Mothers also frequently advised them to abstain from sex until they were married without discussing other topics, such as contraception. The participants stated that they sometimes discussed HIV and pregnancy with their friends:

> *"I talk to my mother, of course, but mostly I don't share with my mother because I feel shy. So, I have to ask friends who have experienced those things. I can consult them about how you do abortion, prevent HIV and ways through which one can acquire HIV. That's what I ask them."* (17 years old).

With this regard, the schools and teachers were the major source of SRH information for them. Teachers explained girls about menstruation hygiene and mostly promoted abstinence:

> *"… also teachers always teach us how to use pads while having periods."* (15 years old).

> *"… .at school they* [teachers] *taught us to abstain from sex until we finish our studies and get married."* (19 years old).

While did sometimes discuss other SRH topics, such as condom use and STIs, coverage of these topics was seen as poor or unsatisfactory by the students. One of the participants in the interview also mentioned that she learned about contraception methods by overhearing the women in the neighbourhood talking about them.

Access to health services among refugee girls was also found to be low with a total of 68.8% of participants who had never visited health centres to seek SRH services. Among the remaining 31.2%, the reasons for a visit were mostly HIV testing (22.7%) and menstrual problems (20.2%). About 83% of girls who ever visited a health care facility were willing to come back in the future. Some girls who did not want to return to the facilities pointed out the lack of privacy and mentioned the lack of resources, e.g. medicines in the centres due to which their problems could not be solved by the health workers. The girls also mentioned distance to the centres and mistreatment (e.g. judgments and impoliteness) by the health personnel as reasons for non-return.

When discussing the access to SRH services during qualitative interviews, the majority of girls did not know where to seek care related to SRH and were not aware about the location of the health centres. This could also be a reason for low number of visits to the SRH services. Interviewed girls who have already been living in the camp for longer had more knowledge about the existence of such services. Even then, they mentioned the distance to the facilities, lack of privacy and lack of health personnel as barriers to seek care for SRH problems. The issue of privacy was not only relevant to the health centres but also to schools, e.g. when girls wanted to discuss SRH aspects with teachers they were discouraged to do so knowing that they might share this information with others:

> *"… .some of them* [teachers] *are tough. Some of them* [teachers] *when you tell them some problems of yours they also go to speak with fellow teachers."* (16 years old).

Sexual experiences including pregnancies and forced intercourse

Out of the total 260 female adolescents, 30 reported to be sexually active. The mean age for having the first sexual intercourse was 16 years (95% CI: 15.2, 16.8; SD 0.3). Among the sexually active girls, some (3) had intercourse between the age of nine and 12. A total of 36.6% of sexually active girls had forced intercourse and 23.4% of them had transactional intercourse. For the majority

of the girls (46.7%), the partner was 1–5 years older. About 6.7% of them even had partners who were 10 or more years older than they were.

Among the 30 sexually active girls, a total of 70% of girls reported not using a condom the first time they had sexual intercourse. About 6.7% of them had used pills and the rest did not use any methods of contraception. A total of 46.7% of sexually active girls had been pregnant and for all of them, the outcome was a live child. But the pregnancy was desired only for 42.8% of those pregnant girls. The sexual experiences of the girls have been summarized in Table 4.

When the sexual experiences in the past 3 months were considered, only 36.6% of girls were sexually active according to the survey. Among them 90.9% had single partner. The rest could not recall the number of partners. For 81.8% of them, the partner was a steady partner (boyfriend). However, only 18% of them reported using condoms during the last 3 months. About 63.6% of them did not know the HIV status of their partners and the rest were confident about the partner being HIV negative. Although not used, 54.6% of girls said to have discussed contraception with the last partner.

During the interviews, the participants often mentioned the fear of getting pregnant, as pregnancy before marriage was unacceptable in the society. This would cause a girl to be excluded from the community and even get expelled from school. This was a major factor that lead girls to abstain from sexual intercourse:

> *"... some people in our community just chase a girl who becomes pregnant out of her home even if the parents are not aware of the issue ..."* (16 years old).

> *"... she was dismissed from boarding section [at school] ... they expelled her."* (16 years old).

The girls in the refugee camp were also victims of forced sexual intercourse. As discussed in the interview, some were victims of sexual violence during the war in their home country, some of them were raped in the camp itself and some on the migration way to the camp:

> *"In Burundi there was a war, they would come and find you in the house, they mistreat [rape] girls and ladies and leave your father observing and later kill you ... on the way we met people who wanted to rape us ..."* (19 years old).

> *"... on the way, we met thugs, they run after us and raped all of us ... I came here with the pregnancy of my child which I acquired from Congo through rape."* (19 years old).

During the interviews, it was found that not only forced sex but also coerced sex was prevalent in the camp:

> *"... I had nothing to do, the man was very strong and older than me."* (18 years old).

> *"... men come to trick us and lie that they love us and may end up impregnating us."* (19 years old).

Transactional sex, which was prevalent among adolescent refugees, was also discussed in school as mentioned by a participant during the interviews. She mentioned that in school they are made aware that they should avoid transactional sex:

> *"We learn that students should avoid free gifts from men. "* (17 years old).

Not a majority of them used condoms or other contraceptives the first time they had sexual intercourse. This was, as stated by the participants during the interviews, because of the fear of the partner or because the partner forced them to bear a child:

> *"... I feared him and I didn't use any contraceptives to stop pregnancy because of the fear."* (18 years old).

Table 4 Reported sexual experiences

	Number	Percentage
Ever had sex (n = 260):		
Yes	30	11.5
No	230	88.5
Mean age (n = 30):	16	NA
Forced intercourse (n = 30):		
Yes	11	36.6
No	19	63.4
Transactional sexual intercourse (n = 30):		
Yes	7	23.4
No	23	76.6
Pregnancy (n = 30):		
Yes	14	46.7
No	16	53.3
Was the pregnancy desired (n = 14):		
Yes	6	42.8
No	8	57.2
Use of condom at first intercourse (n = 30):		
Yes	8	26.4
No	21	70.0
Don't know	1	3.6

Female genital mutilation

Female genital mutilation (FGM) was seen to be prevalent in this population. About 10% of the participants of the study had been circumcised. They were mostly from Somalia (21), DR Congo (3), Uganda and Rwanda (3). The mean age when the circumcision took place was 7.3 (95% CI: 5.4, 9.1). For 44.4% of them, their mother made the decision that they would be circumcised. Some of them even reported that the decision was made by a close friend (7.4%).

The interviewers also talked to the girls about their experiences with FGM. The girls could relate very little of their experiences since for the majority, it took place when they were very young. But the consequence of the circumcision lies with the girls and they are constantly being affected by it. They complained of severe problems and pain during their menstruation. Not only the problems during menstruation, but some of adolescents also have difficulty with urination because of the circumcision. Despite all these difficulties, some of girls accept FGM as a part of their tradition:

> *"…while in the menstruation periods they make me feel pain. I can urinate little, little not very well … but I am happy with it because all my friends, my mother, my sister, my aunts, we are all the same. So I don't feel like it's only me."* (18 years old).

Discussion

This study evaluated SRH knowledge, information sources and access to SRH services, existing sexual behaviour practices and experience of sexual violence among adolescent girls in a humanitarian setting in Uganda. Findings indicate that adolescent girls had limited comprehensive knowledge on SRH issues. Furthermore, school facilities offer an important source of SRH information for adolescents, however parents are a preferred source for these adolescents. Access to SRH services at health facilities are limited due to unfriendly services or lack of confidentiality. A few adolescents were sexually active (11.5%) and about 4.5% of girls overall had experienced sexual violence during the migration and settlement into the camp, describing situations that were unavoidable such as mass rape and "rite of passage". Few sexually active adolescents had risky sexual practices such as limited condom use and transactional sex, in case of consensual sexual intercourse.

The overall SRH knowledge apart from HIV was low. Compared to adolescent nationals of a slightly younger age group in a recent study in South Western Uganda, adolescents in this study demonstrate low scores on knowledge of at least one effective method of pregnancy prevention - 44% vs 55%, knowing at least one STI - 52% vs 95%; however, knowledge of at least one way of HIV transmission was higher - 91.2% vs 47% respectively [21]. A related study in the same study area by Harrison et al. 2009 that compared refugees to nationals, established similar knowledge levels of HIV among 15–24 years old - 33.5% that were in comparable range to the national estimates [22]. A recent review also described limited SRH knowledge among adolescents in humanitarian settings in Sub-Saharan Africa [6]. Interventions are needed to enhance the knowledge and understanding of SRH issues within the refugee population to ensure these adolescents are on par with in-country counterparts.

Important sources of information on SRH for these adolescent girls were school and teachers. However, adolescents pointed out a few inadequacies related to the range of SRH topics taught, which were usually limited to abstinence with very little information on contraceptives. Adolescents also described constraints such as lack of trust or confidentiality of information shared with school teachers. The current enrolment of girls in schools, although satisfactory (63.4%), was lower in comparison to the findings of a study in a similar humanitarian setting in Somalia, where 91.4% of the adolescents (male and female) were currently enrolled in school [23]. There could be gender differences in these studies resulting from poor menstrual health management, forced and coerced intercourse resulted in pregnancy, contributing to school dropout among female adolescents. However, school sources offer good opportunities for sexuality education and a more comprehensive approach, e.g. recommended by UNESCO, to increase the coverage of SRH topics should be adopted in order to realise better outcomes [24]. Furthermore, parents were named as a preferred source for SRH information and similar studies described parents as important facilitators for behavioural changes and better SRH outcomes for adolescents [25]. Although adolescents shared that they are shy to discuss a broad range of SRH topics (usually limited to menstruation management) such social constraints of adolescent-parent communication in Sub-Saharan Africa has been identified before including inadequate knowledge, skills and cultural taboos. To enhance this communication, there is a need for strengthening of this important source of SRH information and behavioural change [26].

Furthermore, health centres were underutilised sources in this study, where 7.6% of girls sought SRH related information, yet only approximately 2.5% of them obtained contraceptive methods. This is low compared to an estimate by UNHCR of 58% of women who obtain family planning services from the SRH centres [13]. Although the results of the UNCHR report are from non-segregated data, the finding that access of adolescents to SHR services is generally limited has been described before [27]. Constraints to access SRH services at health facilities

identified in our study were related to lack of knowledge about their location, fear of being judged/victimised by society and poor attitude of health workers - unfriendly or even rude.

The low use of contraceptives as found in our study (around 30% of sexually active girls ever used contraceptives at first sexual intercourse) corresponds to the findings reported in the UNHCR report in 2011, where around 40% reported the use of contraceptives [13]. Similar findings were reported by the study in Northern Uganda where less than 40% used condoms the first time they had sexual intercourse [28]. Eighteen percent of adolescents in our study used a condom the last time they had sexual intercourse, which was very similar to the results of the study by Casey et al., 2006 in Sierra Leone where 16% of adolescents used condoms the last time, they had sexual intercourse [27]. A study by Okanlawon et al., 2010 in Nigeria with a similar setting showed a higher proportion - 32.8% [29]. This study illustrates stagnancy in utilisation of contraceptive services in the settlement camp in Nakivale, and it has not progressed much comparing to the similar settings in 2006.

International guidelines emphasize prioritisation of provision of SRH information and services in humanitarian settings including vulnerable adolescents [30]. Operationalisation of these guidelines require a multi-pronged approach linking school-based sexuality education initiatives with parental support as well as linkage of adolescents to a wide range of SRH services, such as antenatal care, emergency contraception, services for victims of gender-based and sexual violence at health centres. It is important to address gender inequalities and marginalisation among refugees with particular attention to addressing harmful cultural practices such as FGM, gender based sexual violence and promoting access to contraception information and services among this vulnerable group.

Sexual activity was surprisingly low at only 11% in our study. A study in a transit camp in Northern Uganda has reported that 30% of women were being involved in sexual activity before the age of 15 [28]. This might be due to social desirability bias which plays a role in the underreporting of the sexual activity. The mean age for having the first sexual intercourse was 16, however, among those with consensual sex, at least 23% reported having had transactional sex, and 70% practiced sex without condoms. Earlier studies in the same setting showed that refugees were more likely to practice risky sexual practices compared to nationals [22]. Reasons for no condom use among girls in our study were related to fear of their partner or lack of knowledge of the contraceptive methods.

Adolescent girls also reported cases of forced and transactional sexual intercourse. Such cases were also described by Iyakaremye et al., 2016 in their qualitative findings in a refugee camp in Rwanda [31]. The proportion in our study was higher - 36.6% forced intercourse and 23.4% transactional intercourse among sexually active girls, than that reported in the study by Harrison et al., 2006 performed in Uganda – 5 and 10% accordingly [22].

Study limitations

The study of sensitive SRH topics among adolescents has a lot of methodological challenges. The sampling method incorporated by the quantitative part of the study was a convenience sampling. It is easy and affordable sampling technic commonly used in research. However, it is likely to be biased, e.g. girls motivated towards or willing to obtain more information about SRH may have taken part in the interviews, which might sometimes not reflect the complete picture or miss hard-to-reach adolescents. Nevertheless, by targeting different communities and schools within the camp we tried to minimize potential bias. The attempt of the study was to include only the adolescent girls age 13–19 from the refugee camp. This was challenging as the reported age could not always be confirmed by valid documents for all cases. Because of this the study could have reporting bias in terms of age. Majority of the participants did not have knowledge of English; hence, an orally translated questionnaire was used. Nevertheless, questions which were back-translated may not always convey the exact and culturally adapted message. Underreporting is always a challenge when the study includes sensitive questions like sexual activity and contraception. Sexual activity was reported by very few participants. This might not reflect the real situation in the camp. Similarly, the girls might also have underreported transactional sex or sexual violence by their family members which is prevalent in studies in similar humanitarian setting. Thus, this study is not free from social desirability bias.

Conclusions

Adolescent girls in humanitarian settings such as Nakivale settlement remain with limited SRH knowledge and access to SRH services. Schools and parents offer important information sources, though limited in coverage and quality. A multi-sectoral approach incorporating provision of comprehensive sexuality education for adolescents in schools and out of schools, with family support and facilitating access to youth friendly services including SRH commodities at health centres is important to reduce potential vulnerability of this group. A longitudinal intervention study to assess effectiveness of targeted SRH educational interventions on utilisation of SRH services and sexual behaviours in this vulnerable group would be helpful.

Although a few adolescents were sexually active in this study, it's important to recognise and mitigate emerging effects of sexual violence and risky sexual practices by offering counselling and rehabilitation of adolescents who are victims of forced sexual intercourse during transit or within the camp.

Additional file

Additional file 1: Tabulated results from the multinomial regression analysis for each of the individual covariates and the corresponding Relative Risk Ratio's (RRR), Confidence Intervals (CI) and *p*-values. (DOCX 16 kb)

Abbreviations

AIDS: Acquired Immune Deficiency Syndrome; CDC: Centre for Disease Control and Prevention; FGD: Focused Group Discussion; HIV: Human Immunodeficiency Virus; IC: Informed Consent; NGO: Non-Governmental Organization; SRH: Sexual and Reproductive Health; STI: Sexually Transmitted Infection; UN: United Nations; UNFPA: United Nations Population Fund; UNHCR: United Nations High Commission for Refugees

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Availability of data and materials

The datasets and materials used during the current study are available from the corresponding author on reasonable request.

Authors' contributions

OI and EK conceptualized and designed the overall study. OI, EK, VN and WM were responsible for training and implementation at the field level. MR, OI and AB conducted the quantitative analysis. MR and OI conducted the qualitative analysis of the transcripts. OI oversaw writing of the paper with contributions from MR and EK. All authors reviewed and approved the final text.

Ethics approval and consent to participate

The study received approval from the Mbarara University of Science and Technology Research Ethics Committee, the Uganda National Council of Science and Technology and the LMU Ethics Committee, Munich, Germany. A letter of support for the study was obtained from the refugee desk officer and the Nakivale Camp commandant. Furthermore, informed consent to participate was directly from adolescents who were 18 and above, whereas obtained from parents, as well as assent from adolescents below 18 years.

Consent for publication

This manuscript does not contain any individual person's data in the form of image or video. Hence consent for publication is not applicable.

Competing interests

The authors declare that they have no competing interests.

Publisher's Note

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4.6 Prospects and conclusions

The conducted research intended to highlight the importance and relevance of health situation assessment (formative research) for design and implementation of targeted health interventions. Both situation analyses for this thesis contribute to future global health programming efforts and clinical practice.

Study I was the first study to obtain spirometric equations for the local population in Maputo, Mozambique. It confirms the assumption that the non-local reference standards, such as Global Lung Function Initiative (GLI) and South African equations, may not be appropriate for this population, because only few samples from African countries were incorporated in the equation development process by GLI [1,39]. This may lead to diagnostic errors in non-symptomatic persons, as well as in those with respiratory symptoms and morbidities. Thus, the study results will contribute a valuable comparison for future analysis of spirometry results from patients living in Maputo with pulmonary TB or other lung morbidities [1]. This study followed the call of GLI for data collections in non-Caucasian, particularly African and Latin American, populations, including ethnic minorities [29]. Its results will also be used to analyse the lung function of TB and post-TB participants in the multi-centre African study called TB Sequel [40].

Study II contributed to a body of evidence on adolescent girls in humanitarian settings. It demonstrated that girls have limited SRH knowledge and access to SRH services. To address these gaps, there is an urgent need for locally-adapted health and educational interventions. An inter-sectorial approach with provision of comprehensive sexuality education for adolescents in and out of schools, facilitation of access to SRH commodities at health centres and family support would be important to decrease the potential vulnerability of this population group [2]. An implementation study assessing effectiveness of targeted SRH educational interventions on sexual behaviours and utilisation of SRH services in young adolescents would be crucial [2]. Based on the study results, there is also a need to recognise and mitigate emerging effects of risky sexual practices and sexual violence by offering counselling and rehabilitation to adolescents who survived forced sexual intercourse or gender-based violence during transit or within camps [2]. We are currently working with colleagues in Uganda to develop a locally-adapted comprehensive sexuality education program for refugee girls and seeking funding for its implementation.

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Supplementary Material: Publication I

Supplementary Materials:

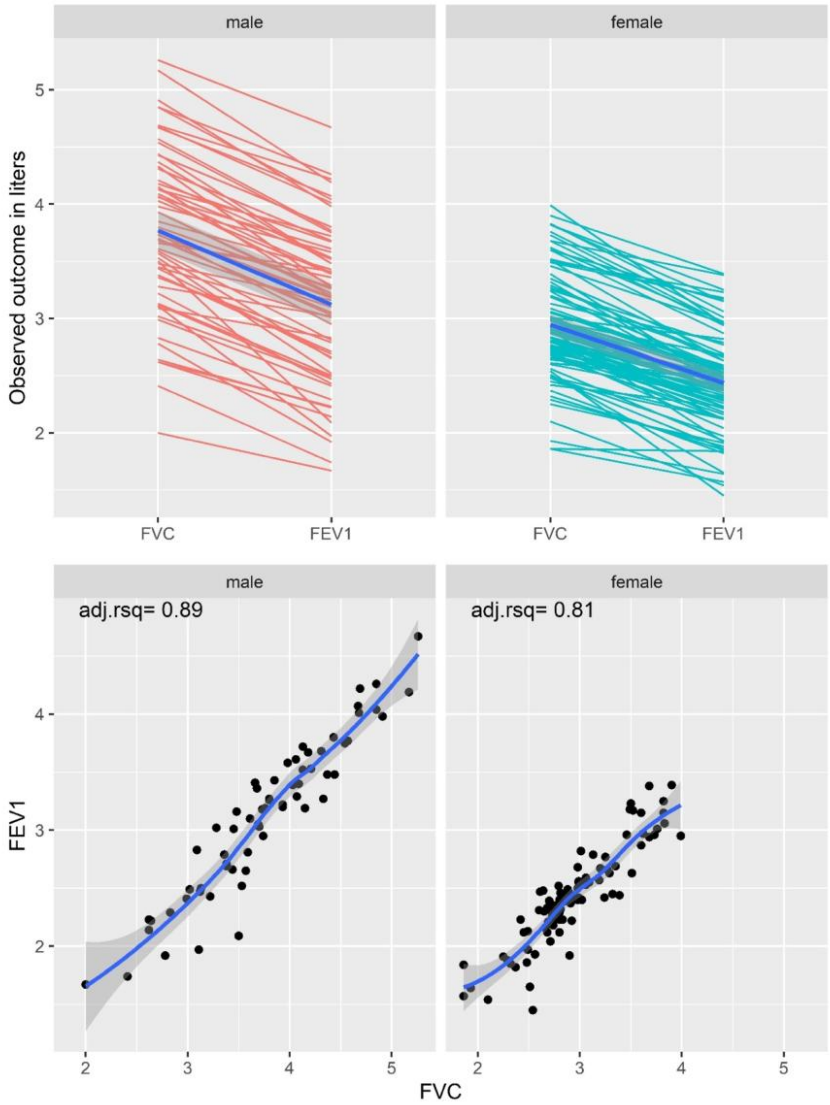

Figure S1. Association between the observed spirometry outcomes (FVC and FEV1) according to sex.

Legend: There is a strong association between the values for FVC and FEV1 in both sexes.

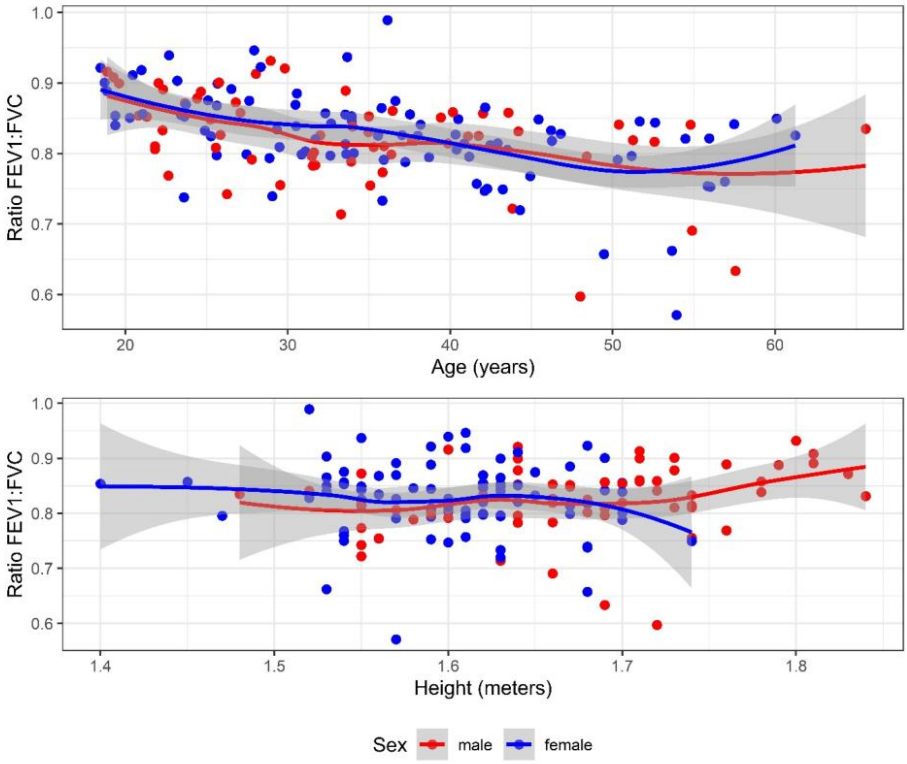

Figure S2. Relationship between the ratio of FEV1/FVC with age and height.

Legend: A decreasing trend (LOESS fit) with age (negative slope) is observed for the FEV1/FVC ratio; however, no particular trend with height is visible (almost flat line). No difference across sex is visible in both trends.

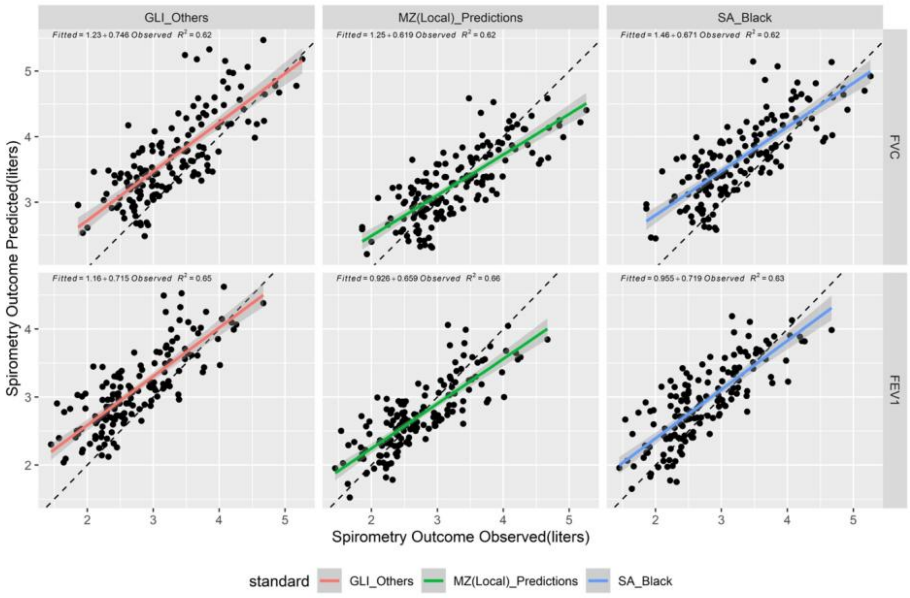

Figure S3. Goodness of fit for Mozambican (Local) standards predictions and that based on GLI or South African standards, when compared to the observed data.

Legend: This figure shows the performance of the standards in terms of fitting to the observed data. We depict the diagonal line (Fitted= 0+ 1* Observed), which would indicate values where observed is exactly equal to the fitted. The coloured lines represent the regression equation for Fitted based on the Observed data. For the South African Black and the GLI Others standards, we observe more points above the diagonal line indicating that the predicted values are higher than the observed values. This is more balanced for the Mozambican Local standard based predictions. In addition, we also demonstrate through this plot that the predictions based on Mozambican standards are lower than the South African Black and the GLI Others on average.

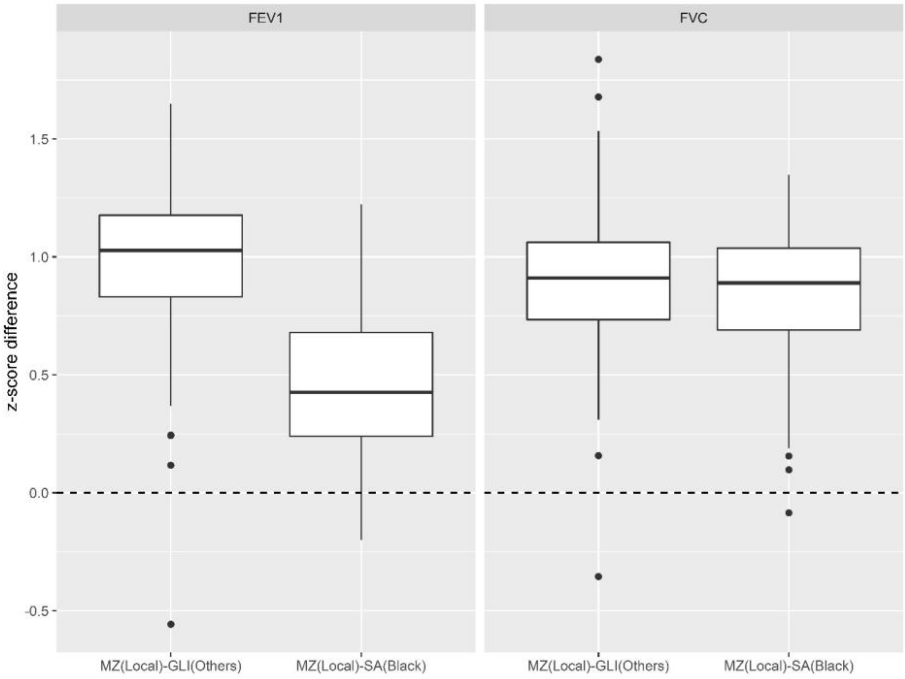

Figure S4. Differences between z-scores of Mozambican standards and z-scores based on GLI or South African standards.

Legend: The box plots show the distribution of the differences in z-scores for FEV1 and FVC based on the Mozambican prediction equation compared to GLI and South African equations, respectively. On average, the difference between Mozambican predictions and the other predictions is about one standard deviation (z-score difference=0.9) for FVC. For FEV1 the difference with GLI prediction is 1.2 standard deviations and only about 0.4 standard deviation compared to South African predictions.

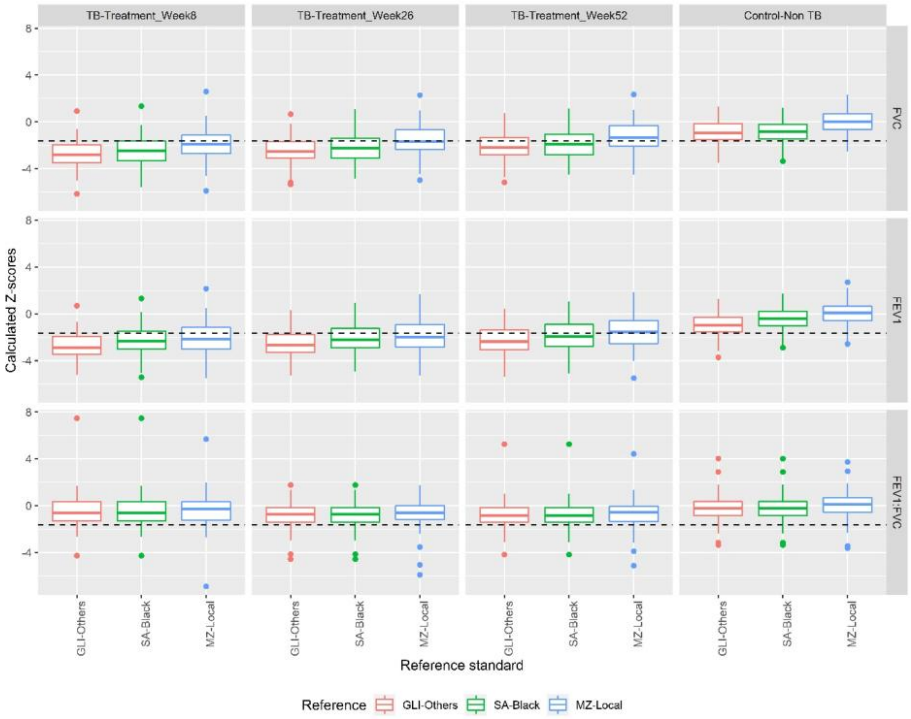

Figure S5. Comparison of performance of local Mozambican, GLI and South African standards on a data set of a TB cohort during and after TB treatment from Maputo, Mozambique.

Legend: The plot of the z-scores on the TB cohort (Week 8, Week 26 and Week 52 from TB treatment start) shows an improvement for FEV1 and FVC over time, as we would expect. The difference across the standards used (GLI - Others, South African-Black and local Mozambique) seen in the TB cohort is similar to the control group, which constitutes the healthy volunteer local population in Mozambique. The effect on the FEV1/FVC ratio does not differ across the different standards in both the TB cohort and in the control group, which is in accordance with the GLI guidelines (Quanjeer et al. 2012), where they describe the lack of ethnicity effect.

Table S1. Likelihood Ratio Test Results for selecting the regression model covariates.

```
Variables used in the model for FVC
Likelihood ratio test
Model 1: FVC ~ Sex + Baselineage + Height #Selected Model
Model 2: FVC ~ Baselineage + Sex * Height
Model 3: FVC ~ Sex * Baselineage + Sex * Height
Model 4: FVC ~ Sex * Baselineage + Sex * Height + Height.Sq
Model 5: FVC ~ Sex * Baselineage + Sex * Height + Sex * Height.Sq
  #Df  LogLik Df  Chisq Pr(>Chisq)
1   5 -88.436
2   6 -86.904  1 3.0626    0.08011 .
3   7 -86.508  1 0.7918    0.37356
4   8 -86.026  1 0.9651    0.32591
5   9 -83.721  1 4.6093    0.03180 *

Variables used in the model for FEV1
Likelihood ratio test
Model 1: FEV1 ~ Sex + Baselineage + Height
Model 2: FEV1 ~ Baselineage + Sex * Height # selected model
Model 3: FEV1 ~ Sex * Baselineage + Sex * Height
Model 4: FEV1 ~ Sex * Baselineage + Sex * Height + Height.Sq
Model 5: FEV1 ~ Sex * Baselineage + Sex * Height + Sex * Height.Sq
  #Df  LogLik Df  Chisq Pr(>Chisq)
1   5 -68.285
2   6 -64.985  1 6.6004     0.0102 *
3   7 -64.633  1 0.7045     0.4013
4   8 -64.522  1 0.2205     0.6387
5   9 -63.893  1 1.2588     0.2619

Interaction of age and sex is discarded because
Likelihood ratio test
Model 1: FEV1 ~ Sex + Baselineage + Height
Model 2: FEV1 ~ Sex * Baselineage + Height
  #Df  LogLik Df  Chisq Pr(>Chisq)
1   5 -68.285
2   6 -67.485  1 1.5995      0.206

Variables used in the model for ratio FEV1:FVC
Likelihood ratio test
Model 1: rfev1.fvc ~ Baselineage #Selected Model
Model 2: rfev1.fvc ~ Sex + Baselineage
Model 3: rfev1.fvc ~ Sex * Baselineage
Model 4: rfev1.fvc ~ Sex * Baselineage + Height
Model 5: rfev1.fvc ~ Sex * Baselineage + Sex * Height
  #Df LogLik Df  Chisq Pr(>Chisq)
1   3 226.95
2   4 227.32  1 0.7461    0.38773
3   5 227.35  1 0.0413    0.83892
4   6 227.35  1 0.0069    0.93374
5   7 229.02  1 3.3484    0.06727 .
```

Table S2. Absolute numbers of participants with different spirometry outcomes and severity grades depending on the applied reference standard (Mozambican, GLI - *Others* or South African Black prediction equations).

Mozambique (Local)		***GLI-Others***				***South Africa-Black***		
Impairment type	Normal	Obstruction	Restriction	Mixed	Normal	Obstruction	Restriction	Mixed
Normal (139)	113	1	23	2	116	2	20	1
Obstruction (9)	0	8	0	1	0	8	0	1
Restriction (7)	0	0	6	1	0	0	6	1
Impairment severity	Normal	Mild	Moderate	Severe	Normal	Mild	Moderate	Severe
Normal (139)	113	24	1	1	116	22	1	0
Mild (15)	0	4	8	3	0	7	7	1
Moderate (1)	0	0	0	1	0	0	0	1

Legend: Compared to the local Mozambican standard (139), a smaller number of participants was classified as having normal lung function if GLI (113) or the South African (116) prediction estimates were used as reference on the Mozambican sample. Also, compared to the local Mozambican standard (1), the number of participants with moderate and severe lung impairment was increased when GLI (14) and South African (10) references were applied.

Table S3. Sensitivity analysis of the prediction equations based on the observed Mozambican data.

Outcome	*Training 2/3; Testing 1/3 – 1 Random Draw*	*Leave One Out Cross Validation - LOOCV*	*10-Fold Cross-Validation*	*5 Repeated 10-Fold Cross-Validation*
FVC	Rsquared-0.63; RMSE-0.37; MAE-0.30	Rsquared-0.60; RMSE-0.44; MAE-0.35	Rsquared-0.62; RMSE-0.43; MAE-0.35	Rsquared-0.64; RMSE-0.43; MAE-0.35
FEV1	Rsquared-0.68; RMSE-0.33; MAE-0.27	Rsquared-0.67; RMSE-0.37; MAE-0.30	Rsquared-0.67; RMSE-0.37; MAE-0.30	Rsquared-0.66; RMSE-0.37; MAE-0.30
Ratio FEV1/FVC	Rsquared-0.26; RMSE-0.05; MAE-0.04	Rsquared-0.20; RMSE-0.06; MAE-0.04	Rsquared-0.28; RMSE-0.06; MAE-0.04	Rsquared-0.27; RMSE-0.06; MAE-0.04

Legend: Sensitivity analysis of the prediction equations based on the observed Mozambican data under different cross-validation methods for evaluating the predictive performance of the models. The predictions performances are consistent across different methods. These outcomes can be compared to the prediction outcomes based on 1-South African equations produce (Rsquared = 0.62; RMSE = 0.58; MAE = 0.47) for FVC, (Rsquared = 0.63; RMSE = 0.43; MAE = 0.34) for FEV1; 2-GLI equations produce (Rsquared = 0.62; RMSE = 0.60; MAE = 0.48) for FVC, (Rsquared = 0.65; RMSE = 0.54; MAE = 0.44) for FEV1 and (Rsquared = 0.21; RMSE = 0.06; MAE = 0.04) for the ratio of FEV1/FVC. The prediction efficacy is better than the South African and GLI for the outcomes of FEV1 and FVC. However, the prediction efficacy for the ratio FEV1/FVC is similar to that based on GLI.

Table S4. Summary from 10000 non-parametric bootstraps sensitivity analyses on the healthy adult's data from Mozambique.

Summary Measure	*Characteristics*	*FVC (95%CI)*	*FEV1 (95%CI)*	*Ratio FEV1/FVC (95%CI)*
Rsquare	Model Fit	0.62 (0.52, 0.69)	0.66 (0.57, 0.73)	0.22 (0.12,0.34)
Intercept	Coefficient	−2.27 (−4.01, −0.69)	−3.50 (−5.18, −1.45)	0.92 (0.89, 0.96)
Sex Female	Coefficient	-0.49 (−0.65, −0.34)	3.33 (0.77, 5.92)	-
Age	Coefficient	−0.02 (−0.03, −0.01)	−0.02 (−0.03, −0.02)	−0.003 (−0.004, −0.002)
Height	Coefficient	3.99 (3.03, 5.02)	4.43 (3.21, 5.79)	-
Sex Female: Height	Coefficient	-	−2.28 (−3.87, −0.72)	-

Legend: The obtained estimates are similar to those derived from the fitted regression equation to describe the observed data. The obtained confidence intervals are overlapping with the estimates reported in Table 2 for Mozambique.

Table S5. Comparison of lung impairment prevalence in the own Mozambican TB cohort using Mozambican, GLI and South African prediction equations.

	TB-Treatment Week 8 (N=62)	**TB-Treatment Week 26 (N=62)**	**TB-Treatment Week 52 (N=62)**
Impairment Mozambique (Local standard)			
- Impaired	39 (66.1%)	33 (54.1%)	28 (45.2%)
- Not impaired	20 (33.9%)	28 (45.9%)	34 (54.8%)
- Missing	3	1	0
Impairment South Africa (Black standard)			
- Impaired	46 (78.0%)	42 (68.9%)	40 (64.5%)
- Not impaired	13 (22.0%)	19 (31.1%)	22 (35.5%)
- Missing	3	1	0
Impairment GLI (Others standard)			
- Impaired	51 (86.4%)	46 (75.4%)	40 (64.5%)
- Not impaired	8 (13.6%)	15 (24.6%)	22 (35.5%)
- Missing	3	1	0

Legend: This table describes a lung function in a TB cohort (Week 8, Week 26 and Week 52 from TB treatment start) using different prediction equations. As expected, for all reference standards, the improvement of lung function under treatment is observed, with best lung function results at 52 weeks after TB diagnosis and treatment start. However, less lung impairment is described by the local Mozambican standard compared to South African Black and GLI - Others equations.

Supplementary Material: Publication II

Additional file 1

Tabulated results from the multinomial regression analysis for each of the individual covariates and the corresponding Relative Risk Ratio's (RRR), Confidence Intervals (CI) and p-values.

		Outcome of overall knowledge: Comparator **Low**					
		Medium			**High**		
Covariate	*Comparator*	*RRR*	*CI*	*p value*	*RRR*	*CI*	*p value*
Age group (>15 years)	<=15 years	1.20	(0.68,2.10)	0.53	**2.78**	**(1.29,5.98)**	**0.01**
Age (continuous)		1.14	(0.97,1.33)	0.12	**1.38**	**(1.12,1.69)**	**<0.01**
Living in Uganda							
3-5 years	< 3 years	0.72	(0.34,1.51)	0.39	1.13	(0.42,3.09)	0.80
> 5 years	< 3 years	1.10	(0.57,2.12)	0.77	1.94	(0.82,4.61)	0.13
Education							
Secondary/ Tertiary	Primary	**8.21**	**(2.43,27.79)**	**<0.01**	**45.92**	**(12.55,167.94)**	**<0.01**
Religion							
Catholic	Protestant	0.69	(0.32,1.51)	0.36	1.08	(0.69,4.10)	0.25
Others	Protestant	1.69	(0.51,2.28)	0.85	1.26	(0.48,3.32)	0.65
In School							
No	Yes	0.76	(0.43,1.35)	0.35	0.61	(0.28,1.30)	0.20
Ever had sex							
No	Yes	0.30	(0.10,0.91)	0.03	0.28	(0.08,1.00)	0.05
Country of birth							
Burundi/ Rwanda	DR Congo	1.97	(0.94,4.12)	0.07	0.97	(0.37,2.49)	0.94
Eritrea/ Ethiopia	DR Congo	0.66	(0.27,1.63)	0.37	0.71	(0.24,2.11)	0.54
Somalia/ South Sudan	DR Congo	1.61	(0.63,4.15)	0.32	1.70	(0.57,5.05)	0.34
Others	DR Congo	2.18	(0.80,5.94)	0.13	0.66	(0.15,2.89)	0.58
Main source of knowledge							
School Teachers	Parents	**2.60**	**(1.27,5.34)**	**0.01**	**8.80**	**(3.40,22.80)**	**<0.01**
Others	Parents	1.05	(0.54,2.05)	0.89	1.12	(0.37,3.40)	0.84

The outcome is obtained as a categorical classification of low, medium and high, based on the sum of the scores from the knowledge on prevention measures and transmission methods for HIV/AIDS as well as knowledge on STIs and methods of contraception (see Table 3 in the manuscript). The statistically significant covariates or covariate categories at 5 % level of significance are shown in bold values of RR, CI and p value.