MAKERERE UNIVERSITY

SCHOOL OF MEDICINE

DRUG RESISTANT TUBERCULOSIS IN KARAMOJA REGION: PREVALENCE, PATTERNS AND ASSOCIATED FACTORS

BY

NAKAFEERO BRENDA, BSc CS (MAK)

REGISTRATION NO: 2016/HD07/2438U

SUPERVISORS

DR. ACHILLES KATAMBA (MBChB, MS, PhD)

DR. WORODRIA WILLIAM (MBChB, M.Med, PhD)

A DISSERTATION SUBMITTED IN PARTIAL FULFILMENT OF THE REQUIREMENT FOR THE AWARD OF MASTER OF SCIENCE IN CLINICAL EPIDEMIOLOGY AND BIOSTATISTICS OF MAKERERE UNIVERSITY

JULY 2018

DECLARATION

I hereby declare that all the work in this dissertation is original unless otherwise acknowledged and has not been previously submitted for another academic award at any other institution of higher learning.

Signature:  Date……5th oct 2018……

Nakafeero Brenda (Principal investigator)

This dissertation has been submitted for examination with the approval of the following supervisors

1. Dr. Worodria William

Signature:  Date……5th Oct 2018……

1. Dr. Achilles Katamba

Signature…….. Date……..

DEDICATION

This book is dedicated to all persons whose lives have been affected by Tuberculosis especially those in Karamoja region and all those in the struggle to alleviate the problems associated with Tuberculosis in Uganda.

ACKNOWLEDGEMENTS

I wish to extend my sincere appreciation to the following people and or groups of people whose direct and or indirect contributions enabled me to have a successful and fruitful undertaking of this research project. First, I acknowledge my supervisors Dr. William Worodria and Dr. Achilles Katamba for their timely guidance and input into this project right from the proposal development stage to submission of the dissertation. For this I will forever be grateful.

Secondly I thank my parents Mr. Ssali K Joseph and Mrs. Ssali Anne Martha for making my education their priority and for a perfect upbringing. To my husband and best friend Francis E Simbwa and my children Ariella Ruth and Benjamin Gold for always enduring with me. To my sisters Beatrice, Betty, Susan, Stella, Esther and Hilda, for the daily financial, spiritual and moral support. Thirdly I thank Associate Professor Joan Kalyango, the Director Makerere University Clinical Epidemiology Unit, Professor Charles Karamagi and all the staff and students of the CEU especially my classmates, Elizabeth, Eva, Sandra, Mercy, Ghisilain, Fabrice, Emmanuel, Alex, Yvette, Paul, Denis, Kakeeto, Winnie, Immaculate, Juliet, Rose and Tobias for the timely guidance and encouragement. I thank CUAMM, Doctors with Africa for the financial support in form of a scholarship to allow me undertake this research and the CUAMM team Dr. Jerry, Dr. Ambrose, Dr. Denis, Victor, Simone and Veronica. I wish to say that I would not have managed to undertake and or participate in this project without your very significant contributions, may the Almighty God bless you abundantly. Finally, am forever grateful to the Almighty God for making it possible for me to successfully undertake this project.

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LIST OF ACRONYMS

AIDS Acquired Immune Deficiency Syndrome

CBTBC: Community-based tuberculosis (TB) Care

CEU Clinical Epidemiology Unit

CI Confidence Interval

DOT Directly Observed Therapy

DR-TB Drug Resistant Tuberculosis

DST Drug susceptibility test

DTLS District Tuberculosis and Leprosy Supervisor

FGD	Focus Group Discussion
HIV	Human Immuno-Deficiency Virus
IQR	Interquartile Range
MDRTB	Multidrug Resistant Tuberculosis
MOH	Ministry of Health
MSF	Medecins Sans Frontieres International
NTLP	National Tuberculosis and Leprosy Programme
SOMREC	School of Medicine Research Ethics Committee
TB	Tuberculosis
UNCST	Uganda National Council of Science and Technology
WHO	World Health Organization

OPERATIONAL DEFINITIONS

Drug susceptibility testing: Testing of a strain *of Mycobaterium tuberculosis* for its resistance to one or more anti-TB drug.(MOH, 2017a)

Extensively drug-resistant tuberculosis (XDR-TB): defined as MDR-TB plus resistance to a fluoroquinolone and at least one second-line injectable agent: amikacin, kanamycin and/or capreomycin).(MOH, 2017a)

Gene Xpert MTB/RIF: an automated molecular test for synchronized detection of tuberculosis and rifampicin resistance.(Meawed & Shaker, 2016)

Manyatta: Traditional semi-permanent family habitat of the Karamojong, consisting of huts and granaries.(SaferWorld, 2010)

Mono-resistance: resistance to one first-line anti-TB drug only. First-line drugs include isoniazid and rifampicin, Ethambutol and streptomycin.(MOH, 2017a)

Multidrug resistance (MDR): resistance to at least both isoniazid and rifampicin(MOH, 2017a)

Patterns: different diagnostic grouping of drug resistant Tuberculosis (MOH, 2017a)

Poly-resistance: resistance to more than one first-line anti-TB drug, other than both isoniazid and rifampicin(MOH, 2017a)

Rifampicin resistance (RR): resistance to rifampicin detected using phenotypic or genotypic methods, with or without resistance to other anti-TB drugs. It includes any resistance to rifampicin, in the form of mono-resistance, poly-resistance, MDR or XDR(MOH, 2017a)

ABSTRACT

Introduction: Tuberculosis (TB) remains a major public health problem in Uganda especially in Karamoja. Drug-resistance has been a major setback in fighting this infectious disease. The prevalence of MDR among new cases is 0-4.5% in Uganda, and among recurrent cases it is 12.1% - 17.7%. Karamoja is the region with the highest incidence of TB in Uganda; with some 3,500 new cases identified and treated annually including increasing cases of MDR. This study aimed at determining the prevalence, the patterns and factors associated with drug resistant Tuberculosis among TB patients in Karamoja region in the period from January 2015 to April 2018.

Methods: We conducted a cross sectional study to determine the prevalence and patterns of DR-TB in Karamoja region during the months of January 2015 to April 2018. To determine the factors associated, we conducted a matched case control study with 41 cases and used

random by sampled 164 controls. Three Focus group discussions (FGD), ten in-depth interviews and Key informant interviews were used to collect qualitative data. Adjusted Conditional logistic regression was used to determine associated factors. Ethical approval for this study was obtained from School of Medicine Research Ethics Committee and the Uganda National Council for Science and Technology.

Results: The prevalence of DR-TB in Karamoja was found to be 0.1% and 0.6% among the new and previously treated TB patients respectively. The patterns found in the region were Rifampicin Resistance and Multi Drug Resistant Tuberculosis. The major factors associated with Drug resistant Tuberculosis were Type of patient (P=0.004) and Drug stock out (P=0.001. The community was aware of high burden of TB and had positive perception of the values of TB treatment but nomadic lifestyle, use of substances, congested homesteads and poor attitudes of the health workers were a great challenge to effective treatment of TB.

Conclusion: Karamoja is still a low DR-TB prevalence region but with the highest TB incidence, the numbers are likely to increase if not handled early. History of TB treatment, and Drug stock out use were associated with DR-TB. Treatment adherence interventions targeting susceptible TB patients and infection control for their close contacts with poor socioeconomic status is recommended with more emphasis on improving the Directs Observed Therapy (DOTs).

CHAPTER ONE: INTRODUCTION

1.0 Background to the study

TB is the ninth leading cause of death worldwide and the leading cause from a single infectious agent, ranking above HIV/AIDS. A World Health Organization (WHO) 2017 comprehensive report involving 198 countries reports an alarming 6.3 million new cases of TB reported (up from 6.1 million in 2015), equivalent to 61% of the estimated incidence of 10.4 million. The latest treatment outcome data shows a global treatment success rate of 83%, similar to recent years In 2016, there were an estimated 1.3 million TB deaths among HIV-negative people (down from 1.7 million in 2000) and an additional 374 000 deaths among HIV-positive people (WHO, 2017a).

Globally, Uganda is among 30 countries with the highest TB/HIV burdens. Although Uganda has made some progress to control tuberculosis and leprosy, a lot more needs to be done to achieve the national and global targets for TB and to prevent the emergence of extreme TB control challenges such as drug-resistant TB.

Karamoja is the region with the highest incidence of TB in Uganda; every year there are some 3,500 new cases identified and treated, and they include increasing cases of MDR. Unfortunately, this may be due to people who stop their treatment early. An estimated 40% fail to complete their course of treatment and abandon health care facilities (Lochoro, 2016). Regarding the economic burden, treating a patient for drug-susceptible TB in Uganda costs around 200 dollars, however treating MDR TB costs more than 1,500 dollars, yet Ugandas per capita icome is approximately $700. Some of the specific risk factors in this region include poor living (small and crowded Manyattas), working conditions associated with high risk of TB transmission and factors that impair the host's defence against TB infection and disease, such as HIV infection, malnutrition, smoking, diabetes, alcohol abuse, and indoor air pollution (LochoroDP, 2016).The aim of this study was to determine the

prevalence, describe the patterns and determine the factors associated with and factors influencing drug resistant tuberculosis in Karamoja region, Uganda.

1.1 Problem Statement

Karamoja, in north-eastern Uganda has the highest incidence of TB in Uganda with 3,500 new cases identified and treated every year, and they include increasing cases of MDR. Unfortunately this is because the rate of people who stop their treatment early reaches peaks of 40%.

The region is considered by many a “hard to reach” and “hard to live in” sub-region. It is characterised by cattle rustling, insecurity from armed nomadic tribes, a semi-arid climate and the sub-region with high poverty levels upto 60.8% (UBOS, 2016) (UNHS, 2017). For years, infrastructure including roads, healthcare facilities and adequate water has been solely lacking, making the sub-region the least socially and economically developed in Uganda(SaferWorld, 2010).

Karamoja presented a unique challenge due to the poor health of its people and overall low development indices. Insecurity and the mobile population difficult to give information of the Karamojong have led to the area being neglected and marginalised from mainstream development efforts. Health and the health infrastructure in Karamoja is poor. The region has the highest incidence of TB in Uganda with 3,500 new cases identified and treated every year, and they include increasing cases of MDR. Unfortunately this is because the rate of people who stop their treatment early can reach peaks of 40%.

Although a national survey on drug resistance prevalence, Patterns and associated have been done, in Karamoja the patterns and associated factors to the high incidence of DR TB has not been clearly documented. There still exist substantial knowledge gaps on anti TB-drug resistance that ought to be addressed. It’s therefore important that its magnitude and risk

factors in Karamoja region are identified for better control the global Drug resistant TB epidemic.

1.2 Justification

In Karamoja there's more that 40% people who stop their anti-TB treatment early and abandon health care facilities. Resistance to effective drugs is becoming an increasing problem in Karamoja region (Lochoro, 2016), which complicates treatment and increases mortality and long-term morbidity. From 2001, the Ministry of Health through the Nation Tuberculosis and Leprosy Programme adopted the End TB Strategy, a policy of eliminating TB as a public health problem at the global level by 2035. One of the strategy pillars, integrated patient-centred care and prevention including treatment of all people with TB and patient support but does not cover the management of TB patients who are "lost to follow up" due to poor food security and nomadic lifestyles and may develop resistance to anti TB drugs. This study aimed to provide an insight on the prevalence and possible risk factors associated with and factors influencing drug resistance among TB patients in Karamoja. The study will inform policy on where to optimize implementation, promote innovations specific to this region and take actions on found determinants of DR-TB in Karamoja.

1.3 Research Questions

1. What is the prevalence of drug resistant Tuberculosis in Karamoja region between January 2015 to April 2018?

2. What are the patterns of drug resistance among Drug resistant TB patients in Karamoja between January 2015 to April 2018 ?

3. What are the factors associated with drug resistance among tuberculosis patients in Karamoja between January 2015 to April 2018?

1.4 Study Objectives

1.4.1 General Objective

To determine the prevalence, the patterns and factors associated with drug resistant Tuberculosis among TB patients in Karamoja region in the period from January 2015 to April 2018

1.4.2 Specific Objectives

1. To determine the prevalence and patterns of drug resistance in Karamoja region from January 2015 to April 2018.
2. To determine the factors associated to drug resistance among Tuberculosis patients in Karamoja region between January 2015 and April 2018.

1.5 Conceptual framework

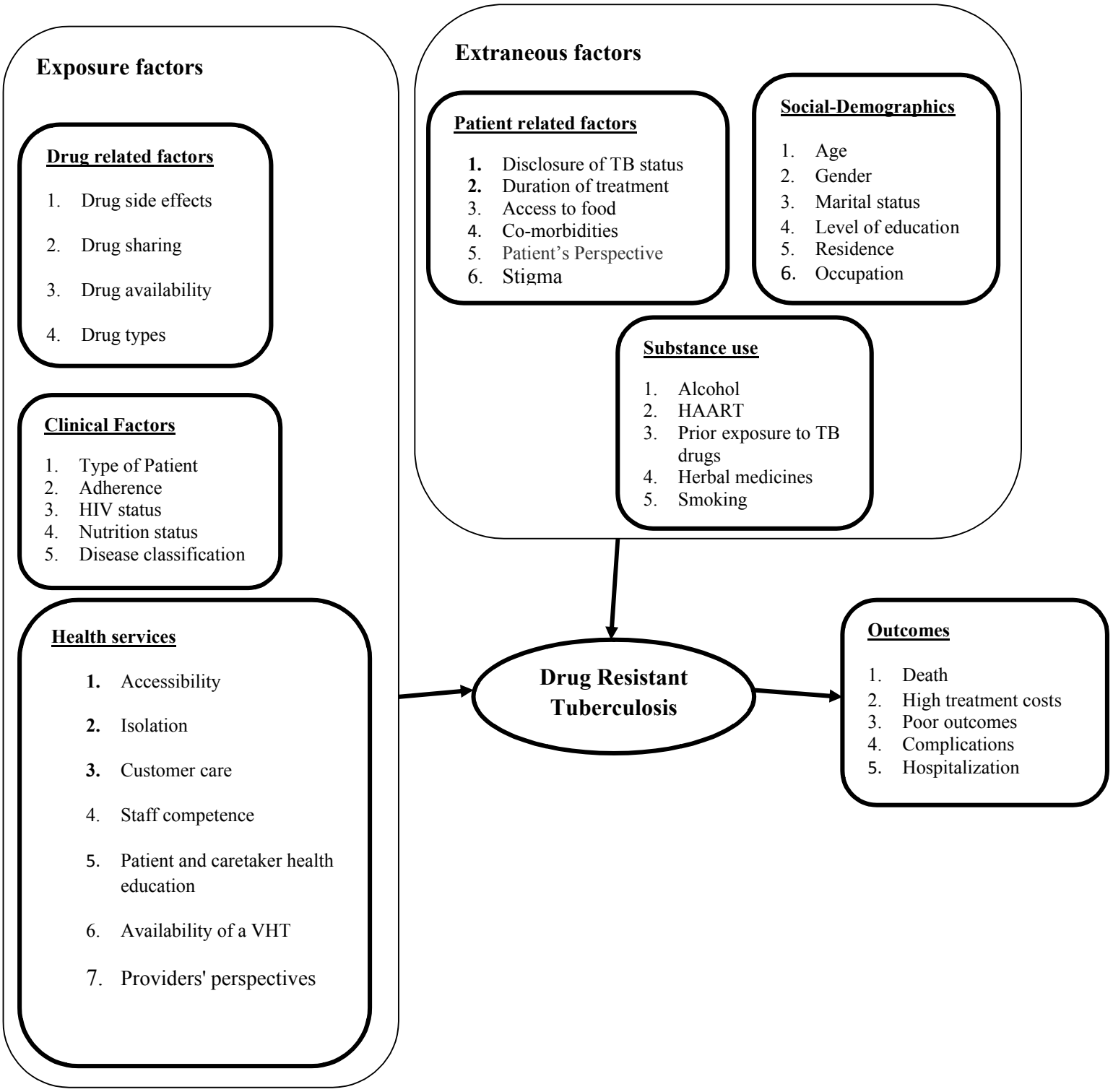

Figure 1.Conceptual framework showing the possible factors associated with Drug resistance

1.5.1 Scope of the study

Figure 1 above shows the various factors predicting drug resistance as well as its consequences. The factors that will be assessed in the study include Patient's Social demographics, Substance use, Patient related factors, drug related factors, Clinical factors and Health services.

CHAPTER TWO: LITERATURE REVIEW

2.1 Definitions

Tuberculosis (TB) is an infectious disease caused by the bacillus *Mycobaterium tuberculosis.* It typically affects the lungs (pulmonary TB) but can affect other sites as well (extra pulmonary TB). The disease is spread in the air when people who are sick with pulmonary TB expel bacteria by coughing. In general a relatively small proportion of people infected with *Mycobaterium tuberculosis* will go on to develop disease; however, the probability of developing Tb is much higher among people infected with HIV. TB is also more common among men than women, and affects mostly adults in the economically productive age groups; around two thirds of cases are estimated to occur among people aged 15-59 years(WHO, 2017a).

A defined case of TB is identified from clinical specimen, either by Gene X-pert or culture. In countries with poor laboratory infrastructure to routinely identify Mycobacterium tuberculosis, a pulmonary case with one or more initial sputum specimens positive for acids-fast bacilli (AFB) is also considered to be a definite case, provided that there is functional external quality assurance with blind rechecking. Drug susceptibility Testing (DST) is the testing of a strain of *M. tuberculosis* for its resistance to one or more anti-TB drugs. (MOH, 2017b).

A person with active TB disease has drug resistant TB if the TB bacteria that the person is infected with, will not respond to, and are therefore resistant to, at least one of the main TB drugs(National Cancer Institute). It includes the following patterns; Mono-resistance which has been defined as resistance to one first-line anti-TB drug only(First line anti-TB drugs are: isoniazid, Rifampin, Ethambutol, Pyrazinamide and Streptomycin); Rifampicin resistance (RR) which is resistance to rifampicin detected using phenotypic or genotypic methods, with or without resistance to other anti-TB drugs. It includes any resistance to rifampicin, in the

form of mono-resistance, poly-resistance, MDR or XDR. Multidrug resistance (MDR) which is resistance to at least both isoniazid and rifampicin. Poly-resistance which is resistance to more than one first-line anti-TB drug, other than both isoniazid and rifampicin. Extensively drug-resistant tuberculosis (XDR-TB)defined as MDR-TB plus resistance to a fluoroquinolone and at least one second-line injectable agent: amikacin, kanamycin and/or capreomycin) (MOH, 2017a). In 2016, there were 600 000 new cases with resistance to rifampicin (RRTB), the most effective first-line drug, of which 490 000 had multidrug-resistant TB (MDR-TB) (WHO, 2017a)

The cornerstone of tuberculosis management is at least a 6-month course of combination of first line drugs: Isoniazid, Pyrazinamide, Ethambutol and Streptomycin. Rifampicin and Isoniazid both form an integral part of the initiation and continuation phase of anti- tubercular treatment regimens in all defined categories of patients (MOH, 2017b). Compliance with the treatment regimen however is a challenge because of the long duration of treatment and the associated adverse drug reaction and yet it is crucial for curing the disease and prevention of drug resistance.

Results of a national DR-TB survey carried out in 2010 (limited to smear-positive samples) indicate an MDR-TB prevalence of 1.4% and 12.1% among new and retreatment cases, respectively(Lukoye et al., 2013). Every year in Uganda there are some 61,000 new cases of TB and 10,900 TB-related deaths, half of which of people co-infected with TB and HIV. The emergence of multi-drug resistant tuberculosis (MDR-TB) has become a major public health concern that threatens advances made in both global and local TB control efforts (the incidence of DR-TB is going higher posing a big challenge to the wiping out TB from the country). The prevalence of MDR among new cases is 0-4.5% in Uganda, and among recurrent cases ranges it is 12.1% - 17.7% in Uganda. There is a gap of 5,948 cases between

the estimated number of MDR-TB cases in East Africa and the number actually diagnosed. The only confirmed risk factors for MDR-TB are prior treatment for TB and refugee status (Kidenya et al., 2014).

2.2 Prevalence of Drug Resistant Tuberculosis

In 2016, there were an estimated 10.4 million cases and 1.3million deaths from TB. The End TB partnership aims that by 2020 there is a 35% reduction in TB deaths and a 20% reduction in TB incidence, compared with levels in 2015, and that no TB patients and their households should face catastrophic costs as a result of TB disease. This can only be achieved through effective National Tuberculosis Programmes (NTP). The SDG's targets can be achieved in all WHO regions with the exception of the African Region. This can be partially explained by the increase in incidence TB cases with drug resistance Mycobacterium strains(WHO, 2017a).

Approximately 600,000 DR-TB cases occur annually worldwide, representing nearly 5% of the world's annual TB burden. In sub-Saharan Africa countries with high burden of TB and HIV infection, DR-TB is estimated to occur respectively in 7.9% and 10% of new and previously treated TB cases with burden of XDR-TB increasing mostly due to lack of laboratory infrastructure for reliable drug susceptibility testing(WHO, 2017a).

The First National DR-TB Survey patterns in Uganda conducted from December 2009 to February 2011 as part of the global drug-resistance surveillance program. Among the 1537 patients (1397 new and 140 previously treated) enrolled in the survey from 44 health facilities using complete drug susceptibility testing (DST) results, of the 1209 isolates from new cases, any anti-TB drug resistance was 10.3%, 5% were resistant to isoniazid, 1.9% to rifampicin, and 1.4% were multi drug resistant. Among the 116 isolates from previously treated cases, the prevalence of resistance was 25.9%, 23.3% to isoniazid, 12.1% to rifampicin and 12.1%

were multi drug resistant. Of the 1524 patients who had HIV testing 469 (30.7%) tested positive(Lukoye et al., 2013).

The geographic distribution of predicted burden of MDR-TB by district in Uganda (using the 2010 national survey results, which predicted MDR-TB among new as [1.4%] and retreatment as 12.1%] cases) shows Karamoja as a region with a potential to have heavy burden of MDR-TB. With an estimated 20 MDR-TB incident cases predicted mostly because of its worryingly high prevalence of Tuberculosis and very poor adherence which are the main risk factors of drug resistance. To date only 15 DR-TB treatment initiation facilities have been started in the highest-burden districts. In Karamoja, St. Kizito Matany hospital is the only approved DR-TB treatment initiation facility serving patients from all the seven districts in the region and other surrounding districts (MOH, 2017a).

HIV is still prevalent in Uganda and has been associated with high TB burden globally (Berhan, Berhan, & Yizengaw, 2013; WHO, 2014, 2017a). There are still no conclusive studies regarding HIV association with anti-TB drug resistance especially among new cases of TB. In Uganda *Lukoye et al* found no association between anti-TB drug resistance with HIV infection since the MDR cases were few and this limited the precision of their estimate(Lukoye et al., 2013).

Uganda is one of the world's 30 high burden countries of TB. Despite having a national treatment program for drug sensitive TB, the existence of drug resistant strains of the disease present an urgent threat to people's health. By the year 2016, treatment success rates in Uganda were 75% compared to the WHO global targets of 85%(WHO, 2017b).

The treatment of the resistant TB forms comes at cost 5 times higher than the associated with the drug susceptible form.(Laurence, Griffiths, & Vassall, 2015) Furthermore, patients with Drug resistance have and more drug related toxicities, lower cure rate and higher mortality

than do patients with drug susceptible TB(Chung-Delgado, Guillen-Bravo, Revilla-Montag, & Bernabe-Ortiz, 2015)

2.3 Detection of Resistance

Culture and drug susceptibility tests for all cases of tuberculosis are considered the gold standard for diagnosis and surveillance of drug resistance. However, such tests are not feasible in most settings(WHO, 2017a). In most parts of the world, less than 5% of TB patients are tested for drug susceptibility. The diagnosis of DR-TB requires that people with TB are tested for susceptibility to first-line and later second line anti-TB drugs. The End TB Strategy calls for universal access to drug susceptibility testing (DST), that is, DST for at least rifampicin for all TB cases, plus DST for at least fluoroquinolones and second-line injectable agents among all TB cases with rifampicin resistance. DST methods include both phenotypic (conventional) and genotypic (molecular) testing methods. The most widespread technology currently available to test for drug resistance is Xpert MTB/RIF.

However WHO intensified efforts to track progress in the programmatic response to drug-resistant TB. In 2016, 1.4 million (39%) of the 3.6 million new bacteriologically confirmed and previously treated TB cases notified globally were tested for rifampicin resistance (up from 31% in 2015), with coverage of 33% for new TB patients and 60% for previously treated TB patients. There was an improvement since 2015, when 25% of new and 53% of previously treated TB cases had a test result for rifampicin resistance. They also represent major progress since 2009, when the figures were 2.9% and 5.9%, respectively. DST coverage increased in five of the six WHO regions between 2015 and 2016, with a high of 84% in the WHO European Region in 2016 however there was a reduction in coverage in the WHO African Region.(WHO, 2017a)

Conventional methods used to diagnose resistance rely on culturing of specimen followed by DST. The results take weeks and not all laboratories with capacity to perform DST for first

line drugs have the capability to perform DST for second line drugs (Bwanga, Joloba, Haile, & Hoffner, 2010). The landscape of TB diagnostics is rapidly evolving which has resulted in the endorsement of a new rapid test kits. These kits have different operation techniques as prescribed by the manufacture hence varying sensitivity and specificity. LPAs use multiplex polymerase chain reaction (PCR) amplification and reverse hybridization to identify *M. tuberculosis* complex and mutations to genes associated with Rifampicin and Isoniazid resistance(Albert et al., 2010).

Culture on Lowenstein-Jesen (LJ) medium and the method for DST are the most frequently used laboratory methods. Field demonstration studies found that Xpert MTB/RIF can detect Rifampicin resistance with 95.1% sensitivity and exclude resistance with 98.4% specificity (WHO, 2017a). The nitrate redictase assay (NRA) ia based on the ability of M. tuberculosis to reduce nitrate to nitrite when grown on LJ medium containing potassium nitrate and the test drug. Addition of the detection reagent causes a colour change (pink purple), indicating mycobacterial growth and thus resistance to the drug.

In a study to evaluate seven rapids tests kits using well characterized isolates for detected of MDR-TB in a Ugandan setting; nitratre reductase assay (NRA), Mycobaterium growth indicator tube 960 (MGIT 960) and Genotype MTBDR*plus* gave excellent detection of MDR-TB, with significantly shorter time to results compared to conventional testing(Bwanga et al., 2010).

2.4 Predictors of Resistance

Drug resistant TB is on the rise and controversies do exist on factors that may be associated with its development. Prior exposure to anti-TB drugs may lead to development of resistant strains (Caroline Deutschendorf, 2012). Similarly inadequate anti-TB treatment is an important factor that can contribute to the development of drug- resistant TB strains. The factors causing inadequate anti-TB treatment can be grouped into Health care providers,

(adequate treatment regimens, wrong dose or combination of drugs by prescribers, Poor DOT or lack of proper treatment monitoring and Non-compliance with guidelines), drug factors (Stock-outs (at all levels) or interrupted supply of drugs, Poor storage conditions at peripheral facilities, Poor quality of drugs and Poor regulation of medications) and patient factors (Lack of patient health education on TB, Poor adherence, Lack of transport/long distances to facilities, Side effects, Malabsorption, Social barriers, denial, cultural issues substance dependence/abuse and Co-morbidities (HIV, diabetes, malnutrition, psychiatric condition) (MOH, 2017a)

Studies have shown that Resistant TB strains can be acquired or new resistant TB strains can emerge due to different factors: previous use of quinolones, inappropriate TB treatment, and poor adherence to anti-TB drugs, long-lasting illnesses, and previous TB treatment. Very recently, WHO concluded that people living with HIV are facing the emerging threats of drug resistant TB (4). Nevertheless, most studies emphasized the role of HIV and previous TB treatment in the development of drug resistant TB infection.(Berhan et al., 2013)

Although several factors can contribute to the development of drug-resistant TB strains, inadequate anti-TB treatment is probably the most important. Situations of inadequate anti-TB treatment include: inadequate drug regimen, inadequate duration of treatment and drugs not taken regularly by the patient (MOH, 2017a).

Previous episodes of TB is also a very important predictor of drug resistance; in a systematic review done in Nigeria, 34 anti-TB drug surveys were identified with 8002 adult TB patients consisting of 2982 new and 5020 previously-treated cases.

A study done in Karakalpakstan, shows that abandonment of treatment is another factor that is highly associated to drug resistance and this can be caused by many reasons including those that are patient specific like Struggle with prolonged treatment, Strive against stigma and toward support and Divergent perceptions and practices including Drug related factors

like Daily injections, pill burden, DOT, migratory work, social problems, prior TB treatment, and adverse drugs effects being major barriers to treatment adherence and retention-in-care by patients and providers.

Many studies have also reported that poor treatment adherence and irregular treatment are the strongest risk factors for development of MDR-TB, also the rate of MDR-TB is higher among patients who donot adhere to the proper treatment during intensive and continuous phase.(Mulu, Mekonnen, Yimer, Admassu, & Abera, 2015)

Providers too feel that despite their best efforts, Lost to Follow Up patients remain. Patient movements between private practitioners and traditional healers also further influences Lost to Follow Up(Shringarpure et al., 2016).

In addition Alcohol consumption and substance misuse have been noted to be associated to resistance in a way that the symptoms of TB can be masked by drink and drugs and someone with a substance misuse problem may also find it difficult or be reluctant to access healthcare, or take their medication regularly if they do. This means they then pose an increased risk of passing infectious TB on to others and/or developing drug-resistant TB.(TBAlert)

Some socio demographic factors have like age and size of household are associated with the occurrence of MDR-TB. Patients with MDR-TB were found to be younger than patients who are drug-sensitive, and showed association of young age and MDR-TB and a national surveillance study in Switzerland indicated existence of an increased risk of resistance to any first line drug with being <35 years of age.(Workicho, Kassahun, & Alemseged, 2017).

2.5 Conclusion

Though many studies have been conducted on the prevalence and factors associated to DR-TB, there still exists information gap on karamoja specific factors. Majority of studies done, focus on other regions especially central regions. In instances were studies focused on TB in

karamoja, DR-TB has not been fully explored. No studies have been conducted to elucidate the prevalence, patterns and determinants of DR-TB in Karamoja region. It is this gap that this study sought to bridge by determining the prevalence, patterns and factors associated to Drug Resistance among tuberculosis patients in Karamoja region.

CHAPTER THREE: MATERIALS AND METHODS

3.1 Study Design

The study employed mixed methods; two quantitative study designs and a qualitative study design.

A baseline cross-sectional study was carried out in Matany hospital to determine the prevalence of drug resistant tuberculosis between January 2015 and January 2018 in Karamoja region. A case control study and qualitative study were then carried out to determine the factors associated with drug resistant tuberculosis in Karamoja region among TB patients in the period of January 2015 to January 2018.

3.1.1 Study Setting

Karamoja region has 7 districts with 37subcounties and an estimated population of nine hundred eighty eight thousand four hundred twenty nine. Of the 7 districts, Nakapiripirit has the highest prevalence of DR-TB followed by Napak district. However Nakapiripirit has no Hospital but only health centre IVs, so the DR-TB treatment initiation program was started in Napak district.

The study was conducted at St. Kizito Hospital Matany in Napak district. Matany Hospital is the only DR-TB treatment initiation site in Karamoja region. The Hospital with the help of Doctors with Africa, CUAMM received a GeneXpert machine in 2015, which made Matany Hospital a diagnostic centre for MDR tuberculosis. The program handles all DR-TB patients from the region including adults and children.

3.1.2 Populations

Target Population

All TB patients in Karamoja region.

Accessible Population

All TB disease patients from Karamoja who visited the Hospitals and health centre IVs for treatment in the 7 districts of Karamoja region from January 2015 to April 2018

3.1.3 Study Population

All TB disease patients from Karamoja who visited the Hospitals and health centre IVs for treatment in the 7 districts of Karamoja region from January 2015 to April 2018. The patients must have fulfilled the eligibility criteria.

3.2 Cross-Sectional Study

For Objective 1: A baseline cross-sectional study was carried out in Matany hospital to determine the prevalence of drug resistant tuberculosis between January 2015 and April 2018 in Karamoja region.

3.2.1 Eligibility criteria

Inclusion criteria

Patient with confirmed TB and was within Karamoja region between January 2015 to April 2018 whose results from drug susceptibility testing (DST) of their sputum collected post screening indicated resistance to any anti- TB drug and are available in the database.

Exclusion Criteria

Patients with the outcome of Drug resistant Tuberculosis but are not residing in Karamoja region.

3.2.2 Sample size estimation

To determine sample size that is sufficient to compute the prevalence of Drug resistant tuberculosis in Karamoja region we used the kish Leslie formula (Steven R. Cummings, 2007). A national survey conducted from December 2009 to February 2011 in TB diagnostic centres in Uganda that reported TB cases to the NTLP estimated any anti-TB Drug resistance among new cases to be 10.3% and 25.9% from previously treated cases. (Lukoye et al., 2013)

$$n = \frac{Z^2 P(1 - P)}{d^2}$$

Z = The level of confidence at 95% = 1.96

P = The estimated prevalence of drug resistance 10.3% among new cases and 25.9% among previously treated cases. (Lukoye et al., 2013)

d = level of precision 5%

Substituting for the respective values into the Kish Leslie formula, the minimum numbers of subjects needed to determine the prevalence of drug resistant TB was 142 new cases and 295 previously treated cases. However The Entire database containing patients treated for TB was used since the data already existed in the DHIS2 database.

Sampling Procedure

The Entire database containing patients treated for DR-TB was used to determine the prevalence of DR-TB in the whole region.

3.2.3 Data Collection

Data to determine the prevalence and patterns of DR-TB was extracted from the District Health Information System (DHIS2) online tool. Data of all TB patients between January 2015 and April 2018 was extracted and analysed by the PI.

3.2.4 Data Analysis

Descriptive analysis

Descriptive characteristics of the prevalence and patterns of Drug resistance amongst the study population was described using percentages for categorical data and median and inter-quartile range for continuous data.

3.3 Case control study

A matched case-control study among DR-TB patients was conducted retrospectively. Cases were matched with controls by Location (Place of residence) at Sub-county level. We matched to control for Sex, Age and area of residents.

3.3.1Eligibility criteria

Cases

Definition

A case was a patient with an episode of tuberculosis disease who has / had a mono resistance, multi-drug resistance or extensively drug-resistance DST result between January 2015 and April 2018.

Inclusion criteria

Patient with confirmed TB and was within Karamoja region between January 2015 to April 2018 whose Drug susceptibility testing (DST) results of their sputum collected post screening indicated resistance to either isoniazid or rifampin, to more than one first-line anti-TB drug other than both isoniazid and rifampicin, to both isoniazid and rifampicin or to any fluoroquinolone and at least one of three second-line injectable drugs (capreomycin, kanamycin and amikacin.

Exclusion criteria

Patients with missing information.

Controls

Definition

A control was a patient with initial episode of tuberculosis disease, whose DST results showed no drug resistance at all to any anti-TB drugs. Four controls were selected per each case identified.

Inclusion criteria

Patient with confirmed TB and was within Karamoja region between January 2015 to January 2018 whose the drug susceptibility testing (DST) results of their sputum collected post screening indicated no resistance to any anti- TB drug.

Exclusion Criteria

Patients with missing information.

3.3.2 Sampling procedure

All cases at Matany hospital initiation site were enrolled in the study since the numbers of cases were few (41). Four controls were randomly enrolled per case identified from the sampling frame containing eligible controls. Simple random sampling procedures using computer generated random numbers were used to select controls who presented around same time of two months as the case identified. In the event that random number was repeated or control died or migrated, then immediate next was considered.

Sample size estimation

To compute the minimum analytical sample size, the formula for difference in proportion of two groups will be used.

$$n = \frac{[Z_{\alpha/2}\sqrt{((1+1/c)\,p'q'} + Z_{\beta}\sqrt{(p_1q_1 + (p_2q_2/c))}]^2}{(p_1 - p_2)^2}$$

p_1 = Proportion of case with previous Tuberculosis episode (0.259)

p_2 = Proportion of controls with previous Tuberculosis episode (0.733)

q_1 = Proportion of subjects in group 1 (cases) (0.2)

q_2 = Proportion of subjects in group2 (controls) (0.8)

n = number of cases

c = number of controls per case (4)

$Z_{\alpha/2}$ = 1.96 at 95% confidence interval

Z_{β} = 0.84 at 80% power

The figures from the previous study (Lukoye, 2013) give us the number of cases 120 that were to be used in this study but we used the 41 that were in Karamoja region.

Study Variables

Outcome

The Primary outcome in this study is Drug resistance to anti – TB drugs

Predictor Variables

1. **Patient Socio-demographic factors**: Age, sex, marital status, residence.
2. **Clinical factors**: Type of patient, HIV status, Nutrition status, Disease classification
3. **Drug related factors**: Drug stock out
4. **Substance use: use of** Alcohol, HAART, Antibiotics, Herbal medicines, smoking
5. **Patient related factors:** Nutrition status.

3.3.3 Data Collection

The research assistants extracted data from the patient files and TB registers using a pre designed data abstraction tool. This was used to collect the quantitative data. Prior to the

beginning of data collection, the questionnaires were pretested in a sample of 30 records in OPD and all inconsistencies noted in the line of data collection were corrected. Research assistants were trained on the methods of data collection to extract the data from the databases.

Triangulation of the information from the different sources was undertaken to ensure accuracy.

3.4 Data analysis

Univariate analysis

The baseline characteristics were summarised in forms of proportions and at Univariate level, patient characteristics between the two groups (cases and controls) were compared using Chi-square (X^2) or Fisher's exact tests as appropriate.

The McNemar's test (chi-square test for matched-pair data) was used to compare if the cases are significantly different from the controls

A bivariate analysis was conducted using chi- square tests to determine association with individual risk factors. Predictor Variables that had a p-value < 0.2 were carried on for the multivariate analysis.

A conditional Logistic regression model was used to determine the factors associated with drug resistance tuberculosis. The Odds Ratio was used as the measure of association and p-values less than 0.05 suggested statistical significance.

Predictors were entered in a stepwise model using a backward method with removal p-value of .05. Interaction terms were formed for those that remained but none was found to be significant.

To assess for confounding, the effects of the confounding variables were modelled in a multivariate equation which included the other significant exposures of interest. A

confounder was considered as any variable that led to >= 10% difference in the odds ratio. The final model was then checked for goodness of fit with link-test goodness of fit. Odds ratios, standard errors, P-values and Confidence intervals were presented.

3.5 Qualitative study

The qualitative study was conducted with the aim of assessing the social cultural-factors influencing and associated with drug resistant tuberculosis among Tuberculosis patients in Karamoja region from January 2015 to April 2018.

3.5.1 Key informant interviews

10 Key informant interviews were carried with Health workers in Karamoja region to assess heath related factors influencing drug resistant tuberculosis. The participants included Medical officers in charge of the TB wards, District Tuberculosis and Leprosy Supervisors, Health Inspectors, Nurses, Clinical Officers, data managers and District Health Officers. These were carried out by the PI in English. They were all recorded and notes were taken during the interviews. These were for 10 minutes.

3.5.2 In-depth interviews

10 in depth interviews were carried out with TB patients to determine social – cultural factors influencing and associated to drug resistance. These were carried out in both English and the local language. An in-depth interview tool guide was used to guide the discussion and the discussion points in the guide were those that could help to describe the socio-cultural factors influencing Drug resistance among TB patients. The interviewers were required to be thoroughly familiar with the in-depth interview tool as it allowed the moderator to be more engaged during the discussion and to rephrase questions that were unclear to participants, or to spontaneously think of follow-up questions and probes. The interview took 20 – 30 minutes

3.5.3 Focus group discussions

3 FGDs were carried out to collect data on social – cultural factors influencing and associated to drug resistance. This method is known to be effective in eliciting the social norms of a community or subgroup, as well as the range of perspectives that exist within that community(Natasha, Cynthia, Kathleen, Greg, & Emily, 2005). We used Purposive sampling to include participants in a FGD and a homogeneous groups that brings together people of similar backgrounds and experiences was considered. Two skilled moderators conducted the FGDs; one person acted as the moderator of the discussion and the other recording using a voice recorder. An FGD guide was used to guide the discussion and the discussion points in the guide were those that could help to describe the socio-cultural factors influencing Drug resistance among TB patients. The FGD moderators were required to be thoroughly familiar with the FGD guide as it allowed the moderator to be more engaged during the discussion and to rephrase questions that were unclear to participants, or to spontaneously think of follow-up questions and probes (Natasha et al., 2005). The discussions was audio taped, and notes taken during each session lasting between 45 to 60 minutes. A total of 10 participants were allowed for each FGD session and the FGDs conducted until there was data saturation therefore preliminary was data reviewed and analysis was done in conjunction with data collection.

3.5.4 Eligibility criteria

Inclusion criteria

1. Patient with confirmed DR-TB and was within Karamoja region between January 2015 to April 2018 whose results from drug susceptibility testing (DST) of their sputum collected post screening indicated resistance to any anti- TB drug and are available in the database. The patient must have been alive and available
2. Health workers in Karamoja region.

Exclusion criteria

Patients who could not provide correct information such as DR-TB patients with mental illness or alcohol abuse patients. The information about these patients was picked from their medical files.

3.5.5 Sampling Procedures

Sample size estimation

Interviews were done with DR-TB patients until we reached a point of saturation. To determine this point we interviewed DR-TB patients in the St. Kizito Hospital Matany database since the TB patients with the outcome are few. As recommended by Creswell (1998) a sample size of 5 to 25 and is needed to reach a point of saturation. 10 interviews were carried out.

3.5.6 Data Collection

For quantitative data, a predesigned data abstraction tool was used to collect the data from the registers, patient files and the DHIS2 by 8 trained research assistants. In-depth interviews using a translated interview guide (Ng'aa Karamojong) were carried for each of the TB patients for assessment of the social factors. Focus Group Discussion and Key informant interviews were used for qualitative data collection. Prior to the beginning of data collection, the data collection tools were pretested in a sample of 10 files and 10 patients in OPD and all inconsistencies noted in line of collection were corrected. The qualitative data was collected by research assistants that included University Interns and Student nurses.

Research assistants who would administer the questionnaires to the participants were trained on the methods of interview administration. The information was assessed using TB patients' self-report where applicable, further verification of the self reported information was made

using the patient files and registers. Triangulation of the information from these sources was undertaken to ensure accuracy.

3.5.7 Data analysis

A thematic-data analysis approach was utilised. Interviews were recorded, transcribed and themes generated to draw meanings. A qualitative package, Open code version 4.2.1 was used to generate themes from the interviews and followed by interpretation of the data generated.

Both raw data and the analysed data were kept both electronically and hardcopy for further reference later.

3.6 Quality Control

The data extraction tools were pretested by the principal investigator and amendments made to improve their validity and reliability. The research assistants and data managers were oriented before data collection. The team had 2 Medical doctors, TB focal person from CUAMM to regularly cross check the clinical data collected to ensure study is scientifically valid. Regular cross checking and inspection of collected data was done by the principal investigator to ensure the accuracy, consistency and uniformity, Data cleaning was done to further minimize errors

3.7 Data Management

The principal investigator checked the filled abstraction tools for completeness and correctness at the end of each day of data collection. All the collected quantitative data was be double entered, cleaned, and edited in a statistical software Epidata version 3.1 and thereafter exported to STATA version 13.0. Adjustment was made for the effect of clustering in the data and all statistical analysis performed using STATA version 13.0. We undertook regular saving and backup of the data on Google drive. The data management tools and instruments including the filled questionnaires were kept securely under lock and key.

3.8 Ethical Considerations

Approval to carry out this research was sought from School of Medicine research and Ethics committee and UNCST. Permission to collect data was sought from Clinical Epidemiology Unit and each of the 7 district authorities in Karamoja. Signed informed consent and assent was sought from the study participants including Patients with TB, Health workers, District leaders in both the quantitative and qualitative components. A waiver to assess secondary was got from SOMREC. To ensure patient protection and confidentiality, any possible patient identifiers were eliminated by use of serial numbers. A transport refund of ten thousand shillings (10,000/=) was given to all the participants in the qualitative study.

3.9 Dissemination of Results

Results from this research will be disseminated at the various forums, including but not limited to Makerere University, Clinical Epidemiology Unit, Sir Albert Cook Library, Directorate of Research and Graduate training, Doctors with Africa CUAMM, St. Kizito Hospital Matany, and District authorities in Karamoja region. Findings will also be published in a peer reviewed journal. Oral presentations at both local and international conferences will be made.

CHAPTER FOUR: RESULTS

4.1 Description of the study profile for objective one

A total of 6890 TB patients were reported in the DHIS in the period of January 2015 to April 2018 in Karamoja region. This included 41 patients with DR-TB and 6849 with susceptible TB. Of these 4134 were new TB patients while 2715 were recurrent cases, these include treatment failures, relapses and lost to follow ups. All 6890 patients were analysed for prevalence and patterns of DR-TB in Karamoja.

4.2 Description of the study profile for objective two

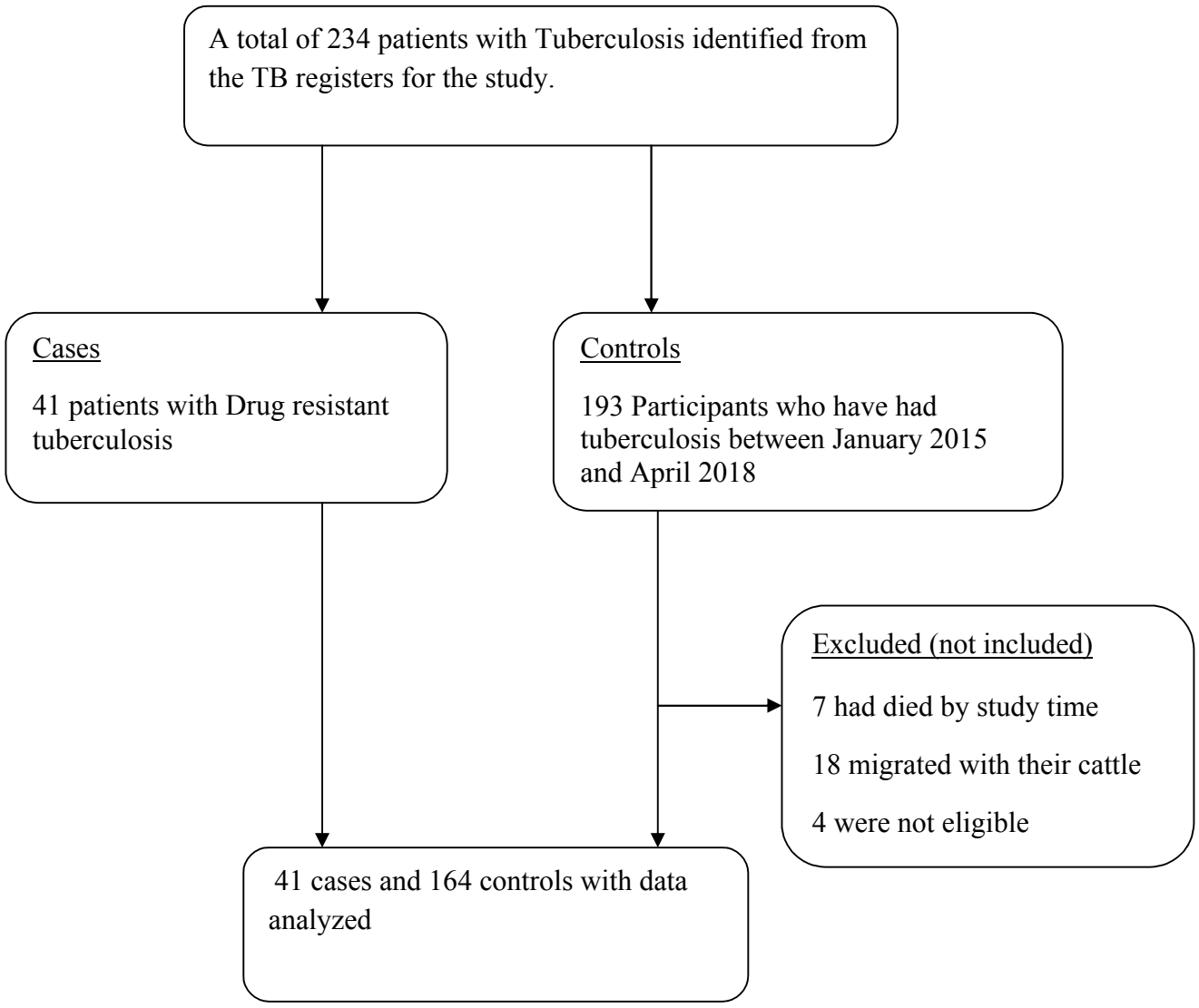

Figure 2.The study profile showing the flow of the participants in Karamoja region

A total of 234 patients with Tuberculosis were identified for the study. A total of 41 cases and 164 controls who participated had their date analysed.

4.3 Prevalence of Drug resistant tuberculosis

Table 1.Prevalence of Drug resistant tuberculosis among Patients with Tuberculosis in Karamoja region.

Variable	Frequency(n)	Percentage (%)	95%CI
Overall			
N = 6890	41	0.60	0.15 – 0.26
According to Patient type			
New	4	0.1	0.71 – 0.83
Previous TB treatment	37	0.5	0.17 – 0.28
Age			
<= 9 years (n = 756)	1	0.1	0.02 – 0.07
10 – 19 years (n = 1268)	5	0.4	0.08 – 0.17
20 – 59 years (n = 4134)	29	0.7	0.61 – 0.74
>= 60 years (732)	6	0.8	0.12 – 0.22
Sex			
Male (n = 4479)	19	0.4	0.39 – 0.53
Females (n = 2411)	22	0.9	0.47 – 0.61
Place of Residence			
Abim (n = 584)	2	0.03	0.02 – 0.08
Amudat (n = 150)	1	0.07	0.01 – 0.58
Kaabong (n = 823)	4	0.05	0.06 – 0.15
Kotido (n = 721)	6	0.08	0.11 – 0.21
Moroto (1523)	2	0.01	0.03 – 0.09
Nakapiripirit (n = 1161)	16	0.14	0.33 – 0.46
Napak (n = 1928)	10	0.05	0.19 – 0.31
DR pattern (N = 41)			
RR	28	68.3	0.52 – 0.81
MDR	13	31.7	0.19 – 0.48

The study found that the prevalence of drug resistant tuberculosis among patients with TB in Karamoja region in the period between January 2015 and April 2018 was 0.6%. The majority of the patients with Drug Resistant Tuberculosis were coming from Nakapiripirit district. Results of Drug Resistant tuberculosis are summarised in Table 1.

The proportions of Drug resistance in region were; 28 (68.3%) with Rifampicin resistance while 13 (31.7%) confirmed to have Multi Drug Resistant Tuberculosis in Karamoja as summarised in Table 2.

4.4 Patterns of drug resistant Tuberculosis in Karamoja region

Table 2.Patterns of drug resistance among patients with Tuberculosis in Karamoja region.

Characteristics	RR n (%)	MDR n (%)
Overall		
Frequency (n)	28 (68.3)	13 (31.7)
Age		
<= 9 years	1 (3.6)	0
10 – 19 years	4 (14.3)	1(7.7)
20 – 59 years	21(75.0)	8 (61.5)
>= 60 years	2 (7.1)	4 (0.3)
Sex		
Males	13 (46.4)	6 (46.2)
Females	15 (53.6)	7 (53.8)
Districts		
Abim	0	2 (15.4)
Amudat	1(3.6)	0
Kaabong	2 (7.1)	2 (15.4)
Kotido	4 (14.3)	2 (15.4)
Moroto	1(3.6)	1(7.7)
Nakapiripirit	13 (46.4)	3(23.1)
Napak	7 (25)	3 (23.1)

Table 3.Characteristics of Demographic, Social Economic, and health services-related factors for 41 Cases and 164 Controls in Karamoja region between January 2015 and April 2018

Characteristics	Frequency (n)	Percentage (%)	Pvalue
Characteristics and Category	**Cases (N = 41)**	**Controls (N = 164)**	
Marital status			
Married n (%)	26 (63.4)	126 (76.8)	0.034
Not married n (%)	15 (36.6)	38 (23.2)	
Personal Health-related factors			
Type of Patient			
New n (%)	4 (9.8)	156 (95.1)	<0.001
Previous TB treatment n (%)	37 (90.2)	8 (4.9)	
HIV status			
Negative n (%)	39 (95.1)	156 (95.1)	1.000
Positive n (%)	2 (4.9)	8 (4.9)	
Malnutrition			
Yes n (%)	24 (58.5)	82 (50.0)	0.363
No n (%)	17 (41.5)	82 (50.0)	
Disease classification			
PTB n (%)	40 (97.6)	120 (73.2)	0.011
EPTB n (%)	1 (2.4)	44 (26.8)	
Substance use			
Yes n (%)	40 (97.6)	95 (57.9)	0.001
No n (%)	1 (2.4)	69(42.1)	
Health services factors			
Drug Stock out			
Yes n (%)	36 (87.8)	36 (22.0)	<0.001
No n (%)	5 (12.2)	128 (78.0)	

The analysis was completed on 41 cases and 164 controls. Age of participants varied from 6 to 80 years with more females reported to have TB. Most of them were coming from Nakapiripirit district and were married. A big percentage of the participants had a previous history of TB and were malnourished. Substance use was high in the participants however very few of them had HIV. Also most of the participants received services from a health centre that had at least one TB drug stock-out as shown in Table 3.

4.4.1 Bivariate analysis between independent factors and Drug resistant tuberculosis

Table 4.Unadjusted association between socio-demographic factors, Clinical factors, drug related factors and Substance use related factors and Drug resistant tuberculosis among the TB patients in Karamoja region in the period between January 2015 and April 2018.

Variable	DR-TB		OR	95% CI	P-value
	Cases n (%)	Controls n (%)			
Socio-demographic factors					
Marital status					
Married	26 (63.4)	126 (76.8)	1		
Not married	15 (36.6)	38 (23.2)	3.16	1.09 – 9.14	**0.034**
Clinical factors					
Disease Classification					
PTB	40 (97.6)	120 (73.2)	1		
EPTB	1 (2.4)	44 (26.8)	0.058	0.006 – 0.527	**0.011**
Type of patient					
New	4 (9.8)	156 (95.1)	1		
Previous TB treatment	37 (90.2)	8 (4.9)	7.20	3.47 – 14.91	**<0.001**
HIV status					
Negative	39 (95.1)	156 (95.1)	1		
Positive	2 (4.9)	8 (4.9)	1	0.16 – 6.22	1
Malnutrition					
Yes	24 (58.5)	82 (50.0)	1		
No	17 (41.5)	82 (50.0)	1.44	0.66 – 3.16	0.363
Substance use					
Yes	28 (68.3)	126 (76.8)	1		
No	1 (2.4)	31 (18.9)	0.026	0.003 – 0.230	**0.001**
Health services factors					
Drug stock out					
Yes	36 (87.8)	36 (22.0)	1		
No	5 (12.2)	128 (78.0)	0.023	0.005 – 0.997	**<0.001**

Marital Status (OR = 3.16, 95%CI = 1.09 – 9.14), Disease classification (OR = 17.09, 95%CI = 1.99 – 153.88), Type of patient (OR = 7.199, 95%CI = 3.475 – 14.915) and Substance use (OR = 1.798, 95%CI = 1339 – 2.412) and were found significantly associated with Drug resistant Tuberculosis. Among the Health services factors, only Drug stock out (OR = 0.023,

CI = 0.005 – 0.997) was found significant as shown in table 4. Patients who were not married were 3.16 times more like to get DR-TB compared the the married participants.

4.4.2 Results of the multivariate analysis

After the bivariate analysis, independent factors that had significant relationship with drug resistant TB were considered for multivariate analysis. Conditional Logistic regression was used for the multivariate analysis

4.4.2.1 Results of multivariate analysis of independent factors and Drug resistant Tuberculosis.

Table 5.Adjusted association in the multivariate analysis of independent factors and Drug resistant Tuberculosis.

Variable	Cases n (%)	Controls n(%)	OR	95% CI	P- value
Predictors of DR-TB					
Type of Patient					
New	4 (9.8)	156 (95.1)	1		
Previous TB treatment	8 (19.5)	4 (2.4)	5.51	1.74 – 17.44	0.004
Drug stock out					
Yes	36 (87.8)	36 (22.0)	1		
No	5 (12.2)	128 (78.0)	20.18	3.62 – 112.57	0.001
Confounders					
Substance use					
Yes	28 (68.3)	126 (76.8)	1		
No	1 (2.4)	31 (18.9)	0.30	0.39 – 2.30	0.246

Multivariate analysis

In the CLR model, the aOR of two risk factors were found statistically significant namely, Type of patient and Drug stock out.

History of TB and Drug stock out in the health facilities were found statistically significant. The aOR of the previous history of TB was 5.51 (95%CI: 1.74 – 17.44) compared to no history. Thus the risk of DR-TB increased 5.5 times among the respondents who had TB in the past than the respondents whose histories were clean. Among these patients, people with The risk was 70% lower among people who were getting treatment from facilities with no TB

drug stock out compared to people who were getting treatment from facilities with TB drug stock outs .Substance use was found to confound Drug stock.

4.5. QUALITATIVE RESULTS

The key issues that emerged in relation to Drug Resistant Tuberculosis in Karamoja District are as outlined below.

4.5.1 Drug resistance still big.

Drug resistance is a big issue in Karamoja and the numbers reported are much less than the actual numbers. This was because of the long distances travelled to access health services, poor retention and nomadic life style.

"...most of the patients walk a long distance to the health centres to get medication. They stay in very remote areas with very bad roads especially in rainy seasons even rivers follow and block them." **Key informant from Nakapiripirit district.**

"....Karamojongs are pastoralists and yet the weather here is not very favourable so they usually travel in groups and make kraals where there's food for the cattle sometimes it is even in Kenya, we have failed to find such people" **Key informant from Napak district.**

4.5.2 Congested homesteads

Poor housing conditions in Karamoja have increased the exposure of disease to other people. The Karamojongs stay in closely enclosed homesteads with many people sharing poorly ventilated huts.

"...At my home we sleep 15 girls in my hut and in the manyatta we have very many families. All of us young girls have to sleep in one hut. Only those who are going to get married are given their own huts" **A participant during FGD with DR-TB patients in Napak district.**

4.5.3 Retention in care for susceptible TB patients.

Retention in care for susceptible TB patients is very poor. There rate of lost to follow up and treatment failure is very high in the region.

"...some of the problems we are facing with TB treatment here is lost to follow up most of our people don't have mobile phones so it is very hard to contact them when they don't come for appointments" **Key informant from Kotido district.**

"...The Pastoralists go to the kraals for months and return only if they are very sick or the dry season is done. Even then we do not know the exact time and period they go and yet they don't inform us." **Key informant from Moroto district.**

4.5.4 DOTs program is not well implemented

All the patients are on community based DOTs program and yet the incidence of TB is still high and so is the rate of lost to follow up.

"...here we use the community based DOT because we cannot afford Facility based but even the treatment supporters are not doing their jobs. Some of them drink and forget others like wives can't force their husbands to adhere to drugs if they refuse to." **A participant during FGD with Health workers in Karamoja.**

The DOTs program is also challenged by stigma as awareness is increasing people instead want to stay away from the patients so adherence is not closely monitored

"...the other problem faced by TB patients is isolation and stigma. One chairman told the whole village that a patient had Ebola so they chased him from the village because they didn't want to be infected too." **A participant during FGD with Health workers in Karamoja.**

4.5.5 Poor nutrition status

There is poor food security in Karamoja. Most of the patients are malnourished by the time they are diagnosed with TB.

"…here in Karamoja there's no food because the land is dry so when you get sick you can't take medication because you are hungry. Even if CUAMM gives us food, the given for only the patient, now how can I eat when my children are starving? We have to share this little food" **A participant during FGD with DR-TB patients in Napak district.**

4.5.6 Too much Substance use

Many of the adults take alcohol in their free time and community hours in the evenings while the pastoralists smoke a lot to keep warm. Also many believe you have you use traditional herbs to get well.

"…it is very hard to stop drinking especially when on medication. But when I go home a drink a little and take the medicine in the morning." **A participant during FGD with DR-TB patients in Napak district.**

4.5.7 Poor adherence to TB medication

There is very poor adherence especially when patients leave hospital to return home and when they go to the kraals.

"…in the kraals we sometimes sleep under one cow to protect them. We carry very little clothing. Sometimes the medicine gets lost and you can't find it." **A participant during FGD with DR-TB patients in Napak district.**

The long regimens and associated side effects make it very hard to finish the medication.

"The tablets are very many and for a long time. The problem is that you have to keep going to hospital to pick every month yet sometimes we have travelled far from our homes. Also the medication makes me weak and you can't work yet everyone depends on me" **A participant during FGD with DR-TB patients in Napak district.**

4.5.8 Attitudes in the Health workers

Some health workers avoid interacting with TB patients for fear of being infected. There Continuous Medical Education are lacking.

"Health workers here are not empowered to manage TB patients, they fear to treat them so they isolate the patients especially the recurrent ones." **Key informant from Moroto district.**

4.5.9 Lack of equipment and drug stock out

Most of the health facilities have had more than one episode of drug stock out and there's no equipment used for TB management like T95s and Gene Xpert.

"...sometimes the nearby hospital doesn't have the medicine that it is finished so we have to wait until they bring more. If you feel so sick you take some of our traditional herbs and they work" **A participant during FGD with DR-TB patients in Napak district.**

"...One of the problems we have is that NMS is not consistent with drug supplies so when we run out of anti TB drugs we borrow from nearby Health facilities however sometimes they also don't have some drugs so we send patients to other facilities, but some of course don't go and am sure these are the people who get resistance" **Key informant from Nakapiripirit district.**

"...We have equipment but they are not been serviced in a long time even after we have written emails and sent complaints. Sometimes the gene Xpert machine has no cassettes and it takes very long to get them. This decreases case detection". **A participant during FGD with Health workers in Karamoja.**

CHAPTER FIVE: DISCUSSION

5.1 Prevalence of drug resistant tuberculosis in Karamoja

The research started with finding the prevalence of DRTB which was 0.6% with 0.1% and 0.5% among new and previously treated sputum smear-positive TB patients respectively in the period between January 2015 and April 2018 in Karamoja region. Since settings with a DR-TB prevalence of less than 3% among new patients are classified as having a low DR-TB burden,(WHO, 2017a) we conclude that the prevalence of DR-TB among new and previously treated TB smear positive patients in Karamoja is low. These findings were consistent with findings of an anti-TB drug resistance survey in Uganda (Lukoye et al., 2013). The Low prevalence observed show that irrespective of the high incidence of TB in the region, much has been done to ensure high cure rates but TB being a major public health problem in Uganda, the prevalence of DR-TB should be reduced to zero. Also the low burden observed may be attributed to the intense case finding programs in the area like contact tracing and use of the Xpert MTB/RIF.

Nakapiripirit district had the biggest proportion of DRTB patients (0.14% of its TB patients reported in this period) followed by Napak and Kaabong districts.

However Karamoja being a region with the highest TB incidence in Uganda and 40% of these patients failing to complete their treatment and abandoning health care facilities due to their nomadic lifestyle (LochoroDP, 2016) and with only 2 rapid molecular diagnostic tests like Xpert MTB/RIF and no centres doing culture, the prevalence of Drug resistant tuberculosis maybe higher than observed.

5.2 Patterns of drug resistant tuberculosis in Karamoja

Out of the 41 DR-TB patients that were identified, 13/40 (31.7%) had MDR-TB while 28/40 (68.3%) patients were found to have resistance to rifampicin placing these patients just one step away from developing MDR-TB. These results are in line with the Global TB report

2017 that showed that there are more RR patients than any other kind of DR-TB patients(WHO, 2017a).

5.3 Factors associated to Drug Resistant Tuberculosis

5.3.1 Clinical factors

Previous history of TB treatment was significantly associated with developing DR-TB. Patients with a previous history of treatment for TB had were 2.4 times more at risk of developing MDR-TB than patients without a history of previous treatment for TB this is also consistent with findings from studies elsewhere (Workicho et al., 2017), (Mulu et al., 2015) and (Lukoye et al., 2013).

Similar to previous studies, HIV status had no significant association with DR-TB (Mulu et al., 2015) and (Lukoye et al., 2013). However this is contrary to the study in Ethiopia which found that patients who had HIV infection were three times three times at higher risk than those who had no HIV infection to develop DR-TB (Workicho et al., 2017). They noted that this association had a marginal statistical significance showing that HIV infection is not a strong predictor of DR-TB infection in TB patients. Karamoja is one of the regions with the lowest HIV prevalence of 3.4%.(MOH, 2017)

The nutrition status of TB patients was not significantly associated with DR-TB this may result from the fact that most of the participants were malnourished by the time they were diagnosed this resulted in no difference between the cases and controls and Karamoja has problems with food security.

5.3.2 Health services factors

One or more TB Drug stock outs in health facilities treating susceptible TB was significantly associated with risk of developing DR-TB and this has been noted as one of the factors contributing to poor outcomes and risk for development of DR-TB (MOH, 2017a).

5.3.4 Patient Related factors

In this study substance use was found to be significantly associated with DR-TB with substance use increasing the risk of developing DR-Tb by 30%. However with majority of the DR-TB patients (70%, n = 29) were found to consume alcohol. Therefore alcohol consumption was also one of the risk factor for the development of DR-TB. It might be associated with its significant role for default and failure rate among new TB cases. Hence, it increases the rate of DR-TB cases. In another studies also alcohol consumption was frequently reported as one of the risk factors for DR TB (Mulu et al., 2015).

At the Bivariate analysis, Marital status was found to be significantly associated with MDR-TB, patients who were not married were 3 times more likely have DR-TB and this could be due to lack of social support from a committed partner. This fact was also found in a study done while assessing for risk factors of MDRTB in Ethiopia (Workicho, 2017).

5.4 Qualitative Study

Evidence from the qualitative method in this study showed that DR-TB is a stigmatized disease in karamoja. However the incidence is only increasing due poor adherence, poor living conditions where families live in poorly ventilated congested houses in a very close community (Manyattas) with very little economic activity, poor infrastructure, excessive alcohol consumption, several drug stock outs in the health facilities and poor attitudes of health workers.

5.5 Strengths of the Study

The strengths of this study are; triangulation of information both at the data collection stage (using both the participants self-report and the TB patient files) and at the data analysis helped to give a richer depth of the answers to the research question.

5.6 Limitations of the Study

The study only represented patients diagnosed through the NTLP-supervised health facilities and does not account for drug resistance patterns among population without access to the health system and we did not have data about the size and characteristics of this patient population.

The study used patients' self-reports on some variables like Substance use which could have caused recall bias towards the null.

There could also have been selection bias in this study, as those who had died and those that had migrated and could not be accessed were eliminated. It is possible that these are the patients who had developed Drug resistant TB and could have changed the prevalence statistics. However, the impact of this may not have been big because other participants were identified and included in the study.

Health facilities with missing data on anti TB drug stock outs from their stock cards in the stores were left out of the study for objective two. It is possible that these facilities had more information on anti-TB drug stock outs that could significantly change our results.

5.7 Trustworthiness of FGDs and KIIs

The research assistants were interns from Universities working with CUAMM and student nurses from Matany nursing school, fluent in both Ng'aa Karamojong and English. The KIIs were done with DHOs and DTLS who are medical professionals, know widely about the different areas in the region and supervise TB related activities in the region, the Medical Officers, Nurses and Data managers were all from TB wards and have been dealing with TB patients for a minimum for a year. All data collected was reviewed by the PI and confirmed by the Medical doctor in charge of the TB ward in Matany hospital. The factors identified in the qualitative data were comparable to the quantitative results that showed anti TB drug

stock outs, Substance use and poor retention were the main risk factors to DR-TB in the region.

CHAPTER SIX: CONCLUSIONS AND RECOMMENDATIONS

6.1 Conclusion

In conclusion, Anti-TB drug resistance among the new and previously treated smear positive TB cases was low.

Secondly History of TB treatment and anti-TB drug stock out and were the only statistically significant risk factors for DR-TB.

Thirdly alcohol consumption nomadic lifestyle, congested homesteads and poor attitudes of the health workers were a great challenge to effective treatment of TB.

6.2. Recommendations

We therefore recommend that strengthening and implementation of appropriate interventions is critical to keep MDR-TB levels low in the country or to reverse the trends.

The TB control program should focus on improving patient's adherence to anti-TB drugs, further decreasing TB/HIV co-infection, and health promotion activities about TB plus focusing on means of transmission.

The Nation TB and Leprosy Program need to improve on ensuring vailability of anti TB drugs in hospitals and to expedite the process of decentralizing TB services to lower health facilities that is HCIIs to improve access to anti-TB services, enhance the DOT services and improve on retention and completion of treatment.

Health education programmes tailored towards health workers in the districts as means to close the information gap on DR-TB identified in the district during the study.

Further research should be done to help understand areas of retention in care e.g. the nomadic migrations, like where they usually migrate to and in what seasons they do so. This can aide in ensuring the patients still complete their treatment from the newly adopted home / areas.

The National TB program needs to carefully monitor directly observed therapy since the DOT program is already running in the region and adherence to therapy for all TB cases especially new TB cases and ensure completion if Drug resistance is to be eliminated.

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APPENDICES

Appendix 1.Consent for participation in the study on Tuberculosis in Karamoja region Informed Consent form

This consent form is to be administered by an interviewer on the research team.

Study title
Drug Resistant Tuberculosis in Karamoja Region: Prevalence, Patterns and Associated Factors

Principal Investigator
Brenda Nakafeero, BscCS. Makerere University College of health sciences, Clinical Epidemiology unit,
Mobile: +256 701763860 / +256-774038653,
Email nakafeerob@gmail.com

Introduction
TB is a serious disease and a leading cause of death worldwide. In Uganda, Karamoja is the region with the highest number of new cases of TB. You are being asked to volunteer to participate in this study that aims to better understand the factors increasing TB cases in Karamoja including Drug resistant TB to allow for improved control measures. Before you decide on whether to be in this study we would like it purpose, outline its risks and benefits, what is expected of you and what you can expect from us. You are allowed to ask anything you want to learn from us in relation to the study. Your participation in the study is voluntary. If you accept to participate, we shall use about 20 to30 minutes of your time.

Purpose of the study
The study intends to determine the prevalence, the patterns and factors associated with drug resistant Tuberculosis among TB patients in Karamoja region in the period from January 2015 to January 2018

Study Procedure
You will be asked some questions about yourself, your experiences during this period of sickness, your contacts and your household as part of the study

Who will participate in the study?
The study will engage all patients with Drug resistant tuberculosis and some patients with Tuberculosis, was within Karamoja region between January 2015 and January 2018 and can provide correct information.

Risk and Benefits
Utilising your time could delay your other activities of the day. There may be some temporary anxiety and discomfort while being interviewed. There are no direct benefits but the results of this study will provide information which can be of help early detection of DR-TB, elimination of DR-TB and improving TB health services in Karamoja region.

Cost and compensation

There will be no payment required for you to participate in this study. You will not be compensated for anything in this study. However you will be compensated with ten thousand (10,000/=) for your transportation to the hospital to participate in this study.

Confidentiality
If you accept to participate in this study, your record will be kept confidential. Your name will not appear on any study documents or publications. You will be known only by a study number.

Alternatives to participation
Participation in research is completely voluntary. You may refuse to participate in this study or withdraw your consent at any time for any reason and this will not affect you in any way. Some of the questions may be embarrassing to you. You have the right not to answer questions you may not be comfortable answering.

In case of problems or questions
If you have any questions, complaints or concerns regarding this study, you can contact the Principle investigators Brenda Nakafeero, Mobile Telephone 0701763860 / 0774038653: If you have any questions regarding the rights or any other ethical issues concerning your participation in this study, you may contact Prof. Ocama Ponsiano, chairman School of Medicine Research and Ethics Committee on mobile phone number; 0772421190

Dissemination of results
All participants and stakeholders will get routine feedback and progress of the study and new information that affects the study or data that has relevance to research participants (including incidental findings) will be made available to research participants and relevant stakeholders.

Ethical approval:
This study has been approved by the Makerere University School of Medicine Research and Ethics committee

Participants' statement of consent
I have read and/or someone has read and explained to me the information in this consent form. I understand why the research is being done, what will be done, the risk, benefits, and my rights regarding the study. I understand that by signing this form, I do not waive any of my legal rights nor relieve the investigator of any liability, but merely indicate that I have been informed about the research study in which I am voluntarily agreeing to participate. A copy of this consent form will be provided to me.

…….....
Name of participant Signature or Thumb print Date

…….....
Name of Witness Signature (if applicable) or Thumb print Date

…….....
Name of study staff / interviewer Signature or Thumb print Date

Appendix 2.Informed Consent for participation in Focus group Discussion

This consent form is to be administered by an interviewer on the research team.

Study title

Drug Resistant Tuberculosis in Karamoja Region: Prevalence, Patterns and Associated Factors

Principal Investigator

Brenda Nakafeero, BscCS. Makerere University College of health sciences, Clinical Epidemiology unit,
Mobile: +256 701763860 / +256-774038653,
Email: nakafeerob@gmail.com

Introduction

TB is a serious disease and a leading cause of death worldwide. In Uganda, Karamoja is the region with the highest number of new cases of TB. You are being asked to volunteer to participate in this study that aims to better understand the factors increasing TB cases in Karamoja including Drug resistant TB to allow for improved control measures. Before you decide on whether to be in this study we would like it purpose, outline its risks and benefits, what is expected of you and what you can expect from us. You are allowed to ask anything you want to learn from us in relation to the study. Your participation in the study is voluntary. If you accept to participate, we shall use about 20 to30 minutes of your time.

Purpose of the study

The study intends to determine the prevalence, the patterns and factors associated with drug resistant Tuberculosis among TB patients in Karamoja region in the period from January 2015 to January 2018

Study Procedure

You will be asked some questions about yourself, your experiences during this period of s

Who will participate in the study?

The study will engage all patients with Drug resistant tuberculosis, was within Karamoja region between January 2015 and January 2018 and can provide correct information.

Risk and Benefits

Utilising your time could delay your other activities of the day. There may be some temporary anxiety and discomfort while being interviewed. There are no direct benefits but the results of this study will provide information which can be of help early detection of DR-TB, elimination of DR-TB and improving TB health services in Karamoja region.

Cost and compensation

There will be no payment required for you to participate in this study. However you will be compensated with ten thousand (10,000/=) for your transportation to the hospital to participate in this study.

Confidentiality
If you accept to participate in this study, your record will be kept confidential. Your name will not appear on any study documents or publications. You will be known only by a study number.

Alternatives to participation
Participation in research is completely voluntary. You may refuse to participate in this study or withdraw your consent at any time for any reason and this will not affect you in any way. Some of the questions may be embarrassing to you. You have the right not to answer questions you may not be comfortable answering.

In case of problems or questions
If you have any questions, complaints or concerns regarding this study, you can contact the Principle investigators Brenda Nakafeero, Mobile Telephone 0701763860 / 0774038653: If you have any questions regarding the rights or any other ethical issues concerning your participation in this study, you may contact Prof. Ocama Ponsiano, chairman School of Medicine Research and Ethics Committee on mobile phone number; 0772421190

Dissemination of results
All participants and stakeholders will get routine feedback and progress of the study and new information that affects the study or data that has relevance to research participants (including incidental findings) will be made available to research participants and relevant stakeholders.

Ethical approval:
This study has been approved by the Makerere University School of Medicine Research and Ethics committee

Participants' statement of consent
I have read and or someone has read and explained to me the information in this consent form. I understand why the research is being done, what will be done, the risk, benefits, and my rights regarding the study. I understand that by signing this form, I do not waive any of my legal rights nor relieve the investigator of any liability, but merely indicate that I have been informed about the research study in which I am voluntarily agreeing to participate. A copy of this consent form will be provided to me.

…….....
Name of participant Signature or Thumb print Date

……..…….....
Name of Witness Signature (if applicable) or Thumb print Date

.....…….....
Name of study staff /interviewer Signature or Thumb print Date

Appendix 3.Consent form for Key Informant Interview

This consent form is to be administered by an interviewer on the research team.

Study title

Drug Resistant Tuberculosis in Karamoja Region: Prevalence, Patterns and Associated Factors

Principal Investigator

Brenda Nakafeero, BscCS. Makerere University College of health sciences, Clinical Epidemiology unit,
Mobile: +256 701763860 / +256-774038653,
Email: nakafeerob@gmail.com

Introduction

TB is a serious disease and a leading cause of death worldwide. In Uganda, Karamoja is the region with the highest number of new cases of TB. You are being asked to volunteer to participate in this study that aims to better understand the factors increasing TB cases in Karamoja including Drug resistant TB to allow for improved control measures. Before you decide on whether to be in this study we would like it purpose, outline its risks and benefits, what is expected of you and what you can expect from us. You are allowed to ask anything you want to learn from us in relation to the study. Your participation in the study is voluntary. If you accept to participate, we shall use about 20 to30 minutes of your time.

Purpose of the study

The study intends to determine the prevalence, the patterns and factors associated with drug resistant Tuberculosis among TB patients in Karamoja region in the period from January 2015 to January 2018.

Study Procedure

You will be asked some questions about yourself and your experiences during this period of management of TB as part of the study

Who will participate in the study?

The study will DHOs, TB ward in-charges of Matany Hospital, District TB focal persons and Health workers on the TB ward in Karamoja.

Risk and Benefits

Utilising your time could delay your other activities of the day. There may be some temporary anxiety and discomfort while being interviewed. There are no direct benefits but the results of this study will provide information which can be of help early detection of DR-TB, elimination of DR-TB and improving TB health services in Karamoja region.

Cost and compensation

There will be no payment required for you to participate in this study. However you will be compensated with twenty thousand (20,000/=) Uganda shillings to cater for your transport.

Confidentiality
If you accept to participate in this study, the record tapes, written notes and your written record will be kept confidential. The information gathered will only be used for the purpose of this study. Your name will not appear on any study documents or publications. You will be known only by a study number.

Alternatives to participation
Participation in research is completely voluntary. You may refuse to participate in this study or withdraw your consent at any time for any reason and this will not affect you in any way. Some of the questions may be embarrassing to you. You have the right not to answer questions you may not be comfortable answering.

In case of problems or questions
If you have any questions, complaints or concerns regarding this study, you can contact the Principle investigators Brenda Nakafeero, Mobile Telephone 0701763860 / 0774038653: If you have any questions regarding the rights or any other ethical issues concerning your participation in this study, you may contact Prof. Ocama Ponsiano, chairman School of Medicine Research and Ethics Committee on mobile phone number; 0772421190

Dissemination of results
All participants and stakeholders will get routine feedback and progress of the study and new information that affects the study or data that has relevance to research participants (including incidental findings) will be made available to research participants and relevant stakeholders.

Ethical approval:
This study has been approved by the Makerere University School of Medicine Research and Ethics committee

Participants' statement of consent
I have read and or someone has read and explained to me the information in this consent form. I understand why the research is being done, what will be done, the risk, benefits, and my rights regarding the study. I understand that by signing this form, I do not waive any of my legal rights nor relieve the investigator of any liability, but merely indicate that I have been informed about the research study in which I am voluntarily agreeing to participate. A copy of this consent form will be provided to me.

…….....
Name of participant Signature or Thumb print Date

……..…….....
Name of Witness Signature (if applicable) or Thumb print Date

.....…….....
Name of study staff /interviewer Signature or Thumb print Date

Appendix 4.Application for waiver of consent to access participants files in hospital archives

1st March 2018

The chair,
School of Medicine Research Ethics Committee
Makerere University College of Health sciences
P.O BOX 7072, Kampala Uganda

Through: The Director Clinical Epidemiology Unit
College of Health Sciences, Makerere University

RE: Request for a waiver of consent for a study titled; Drug Resistant Tuberculosis in karamoja region: prevalence, patterns and associated factors

I am writing to request for a waiver of consent to use retrospective data for the above mentioned proposed study. This will be for analysis to determine the prevalence of drug resistance in Karamoja region from January 2015 to January 2018. It involves no more than minimal risk to subjects. Moreover, no new medical procedures or interventions will be performed as part of this study and no new medical conditions that can increase economic, legal or social risks for study subjects will be discovered.

In an effort to protect patient confidentiality, each participant has a unique ID number. All study related data will be kept under lock and key with restricted access and no individual will be identified by any study reports or publications. Findings will be of potential benefit to society in general. The study will inform policy on where to optimize implementation, promote innovations specific to this region and take actions on found determinants of Drug Resistant Tuberculosis in Karamoja.
. Your consideration for a waiver of consent will be appreciated

Yours faithfully,

Brenda Nakafeero

Principal investigator

+256 774038653/701763860

Appendix 5.Translated Consent for participation. (Ng'aa karamojong version).

Abaruwa ngina ka acamunet.

Erai abaruwa na ngina einakini ka ekorakini ekengitingitan natun ngina ka aripirip.

Nguna epolok

Loukoi ngolo ipiyoroanakimukeo alokarimojong alalau keng ka nguna italalato inges alokarimojong.

Ekapolokiniton aripirip

Epolokinit aripirip na erai Brenda Nakafero, ngina ebunit alo Makerere, alosukul angolo ka angaleu enamba ka asimu erai +256-1763860/ +256 – 774038653. Kori nakafeero@gmail.com.

Akitoodiunet/ageunet

Erai loukoi edeke ngolo arononnooi ngolo eyaunit atwanare ngina alalalan alotooma akwap daadang. Alotooma akwap ngina a Uganda, Karimojong nooi elalaata ngikadiakak ngulu eripununuio eyakatar loukoi.

Ikingitakinitae iyong ka-arimaanut ayakau lokiyan lo ngolo elosikinitere aripun nguna italalato ngikadiakak aloukoi alokarimojong kaapei ka loukoi ngolo ipiyoro akimukeun. Erai nu daadang kotere epedorere aryamun epite ngolo iretakinere loukoi.

Eroko iyong nyecamuna ngun, ikingitakinit iyong aripun nguna epolok alokiyan alo, nguna ejokak, nguna eroko, nguna iitana anenei kon ka nguna iitanit iyong aneni kosi. Ipedori iyong akingit isuanguna icamit iyong aanyun aneni kosi totapito loukoi.

Erai akiyan na akoniinakina ka eyayi apak ngina edoli ngadakikae ngatomoniyarei (20) todolite ngatomoniuni (30).

Nguna elosikinitoe

Elosikinitoe aryamu etiae, alalau ka nguna italalato loukoi ngolo ipiyoro akimukeun alotooma ngikadiakak alokarimojong ageun elap ngolo ke-epei ekaru 2015 akitodol elap ngolo ke-epei ekaru 2018.

Epite ngolo eripiripiyere.

Ikingisyo iyong ngadi nguna etapito akonikuwan,nguna itami iyong apak ngina idiakar, ngulu irukitotor iyong kaapei ke-ekonikal.

Ngae ebeit toyakaun nakingitingito naga?
Alotooma akingitingito naga, erai ngikadiakak daadang ngulu eyakatar loukoi ngolo ipiyorit ngikito ikes ebeit toyakas ka nguluce dang ngulu eyakatar loukoi alokarimojong, ageun elap ngolo ke-epei ekaru ngalipyo ngatomoniyarei ka ngitomon angikan (2015) akitodol elap ngolo ke-epei ekaru ngalipyo ngatomoniyarei ka ngitomon angikanikauni (2018). Ebeit nai ngitunga lu topedorito ainakin ngakiro nguna iyookino kotere loukoi.

Ajokis ka nguna aronis ka akiyan ana.

Epedori aripirip na akisicaluwar iyong etic kon ece ngolo anakuwar ana. Eyakaun aceepak akuryanu neni kon abongonokin ngakingiseta. Emam etacit eyai kori icee-bore ikikorakinio. Nguna eripunio kori iyanunio ikes ikingarakinete iwon ayeun kori aryamun epite ngolo eripunere iwon loukoi ka epite ngolo kiretakinet, ka akitojokun ngipitesyo ngulu imukeere loukoi ngolo ipiyorit ngikito.

Akitalakaret

nyetacio akoniyakau nakiyan na ka emam ibore ikiinakinio iyong edaun akiyan na. iryamuni iyong nai ngisilinga ngalipyo ngatomon (10,000) ngulu doket amotoka paka lore kon.

Nguna etapito ngakiro nguna iyanio

Ani kicamu iyong akiyan naga, emam nyelimorio ekonikiro ka nguna ibongokini iyong daadang, mam nyibolorio kinga. Nai iwayio ka-akerit ani erae ikiyenio iyong ke-enamba bon mere ke-ekiro kon.

Ani pa kicamit akingito

Erae akingito na ainakinet ke-etau kon.ipedori iyong acamun kori akinger anguna iyeni iyong apak daadang. Iyakar iyong apedor akinger abongonokin nguna ikikarunito iyong.

Keya nguna etyoko kori ngakingiseta

Ani keya nguna etyoko kori ngakingiseta, todolok akaripiripan ngina apolon, Brenda Nakafero alonamba 0701763860/0774403853. Ani keya nguna etapito ngapedorosyo kon, toramak emalimu (prof.) Ocama Ponsiano, ekapolon alosukul angolo ka aripirip nguna kitetnguna etapito angaleu ka ngipitesyo ngulu itiyare ejok. Enamba 0772421190.

Epite ngolo elimorere nguna etakanunete alotooma ngabongokineta.
Eryamunete ngikabongonokinok daadang ka nguluce tunga ngulu eya nakiyan na abongokinetngina iyookino alotoomaepite ngolo elosyo akisyom kori aripirip ngakiro nguna aloukoi. Elimorio nabo nguna kitet nguna epedorete akilocokin ngabongokineta anikabongonokinok ka topolok alotooma aripirip nguna aloukoi. Ikekinio nu daadang lokabongonokiok ka nguluce dang.

Acamakinet ke-etic alo.
Ecamakinit akisyom kori aripirip na kori etic lo, erai esukul ngolo a Makerere, aryonget ngina epolokinit aripirip nguna etapito anagaleu.

Acamunet ngina ke-ekabongonokinon

Asyom ayong kori akasyomaki ayong iceetunganan ka eketecaik nguna eyakasi nabaruwa na. ayeni tokona ayong nguna elosikinitoe nguna kitiya, nguna edikino erokiata, nguna aryamuni ayong ka nguna angapedorosyo kang.ayenu kona ayong atemar ecemaki ayong nabaruwa na erai akaacamunet ngina ke-etau, ka emam nyerai ayiunia ekengitingitan. Ecamu alotau kang.

Ebeit naiabaruwa na kigurunoi oting ayong dang apei.

.....

Ekiro ke-ekabongonokinon Ethei (akicemakinet) (ngarwa nguna ke-elap)

.....

Ekiro ke-ethuuda Ethei (akicemakinet) (ngarwa nguna ke-elap)

.....

Ekengitingitan Ethei (akicemakinet) (ngarwa nguna ke-elap)

Appendix 6.Focus Group Discussion Guide

OVERALL QUESTIONS TO ANSWER IN FOCUS GROUP DISCUSSION:

Reminder to moderator:

The purpose of this focus group is to determine the following:

- What are the cultural factors that impact patients' perception of tuberculosis?
- How is health seeking behavior and adherence to TB treatment impacted by those perceptions?
- What are the barriers and obstacles to initiating and completing treatment for TB?
- How did this group overcome the barriers and obstacles to the initiate and complete treatment for TB?
- Do they know about DR-TB?

I. Introduction (10 m)

- Welcome participants and introduce yourself.
- Explain the general purpose of the discussion and why the participants were chosen.
- Discuss the purpose and process of focus groups
- Explain the presence and purpose of recording equipment and introduce observers.
- Outline general ground rules and discussion guidelines such as the importance of everyone speaking up, talking one at a time, and being prepared for the moderator to interrupt to assure that all the topics can be covered.
- Review breaks schedule and where the restrooms are.
- Address the issue of confidentiality.
- Inform the group that information discussed is going to be analyzed as a whole and that participants' names will not be used in any analysis of the discussion.
- Signing of the consent form by the participants.
- Read a protocol summary to the participants.

PART TWO: Discussion Questions

I. <u>Cultural Perceptions of Illness, Healing and Treatment &</u>

Barriers to Health Seeking

For the first part of our discussion we are going to talk about health and sickness.

Q1. What is your biggest health concern?

Q2. What do you think is the biggest health concern for your community?

Q2a. Where you go when you need to see a medical doctor?

PROBE: Personal physician, Veterans (VA) hospital? Health department? Hospital emergency room?

Q3. Has there been a time when you were sick and you thought it would be helpful to see a medical doctor but didn't go?

PROBE: Tell me about that. **What prevented you from seeing the doctor?**

Q3a. Other than seeing a doctor when your sick is there anything else you do to get well?

PROBE: Do you eat certain foods? Get more rest? Take vitamins?

Pray? Use medicinal herbs and plants? See a minister? healer? Other?

[Approx. 15 min.]

II. TB Information: Impact of Diagnosis, TB Treatment, Stigma, and Adherence

Q4. [1 min.] Is there another word people use for tuberculosis besides TB?

Q5. [2 min.] When I say *Tuberculosis,* what is the first thing that comes to your mind?

Q6. [5 min.] How do you think people get TB?

NOTE: If most say transmission through the air, ask: Are there other ways?

Q7. How would you know if you have TB?

Q8. Do you think TB is a serious disease??

Q9. Do you think TB can be cured?

Q10. Do you think people can be infected with TB germs and not be sick?

Q11. How worried are you about getting TB disease?

Q12. What do you think you can do to prevent yourself from getting TB?

Q13. Do you think some people are more likely to get TB than others?

PROBE: Who? Why?

Q15. I want you to think back to the time that you found out you were infected with TB germs. Briefly tell us what happened and what you did about it.

PROBE How did you feel about it?

PROBE Who did you tell?

PROBE Was there anyone you didn't want to know about your diagnosis? Why?

PROBE How did your close friends, family, and coworkers treat you when they found out you were infected with TB germs?

PROBE What questions did you have?

PROBE: Who answered those questions?

PROBE: Of the information you received, what was the most difficult part to understand?

PROBE: Did you ask anyone for advice about what to do? (friends or family)

PROBE: Did you go to someone besides a medical doctor for treatment? advice?

(healer, family, friend)

PROBE: Did you take medicine? Did you use other treatment? (medicinal herbs and plants, healer)

Q16. What does your family and friends know and think about TB?

Q17. Was there anything about your visit to the health centre (or visit with your doctor or other health worker) that you did not like or did not understand?

PROBE: Was there anything about the TB skin test you did not like or did not understand?

PROBE: Was there anything about the Chest x ray you did not like or did not understand?

PROBE: Was there anything about the examination you did not like or did not understand?

PROBE: Were you concerned that your friends and family may be at risk for TB?

PROBE: Did you understand the difference between TB infection and TB disease?

PROBE: Did you understand that you are not sick now, but you could get sick later if you don't take your medicine?

PROBE: What questions did you have about taking medicine?

Q18. How do you feel about coming to the health centre?

PROBE: How did the staff at the health centre treat you?

PROBE: Did the staff at the health centre try to help you with other concerns (transportation, financial issues, other medical care issues, substance abuse)? If not, would you have liked assistance for these issues? Others?

PROBE: Was the health centre open at convenient times for you?

PROBE: Were the health centre staff available when you needed them?

Q19. What are your thoughts about the taking medicines to treat TB infection?

Q19a What convinced you of the importance of taking TB medicines?

PROBE: Who explained to you the reasons why it important to take your TB medicines?

PROBE: What explanations did you receive about why it is important to take your medicine?

PROBE: What instructions did you receive about how to take your TB medicine?

PROBE: What are your thoughts about having someone watch you take your medicine

In the clinic (health centre)?

In your home?

In another location?

PROBE: What are your thoughts about taking your TB medicine when you are not feeling sick?

PROBE: What are your thoughts about the length of TB treatment?

PROBE: What are some reasons why people would not take their TB medicines?

PROBE: What do you think are some reasons people may not complete taking their TB medicines?

Q20. Do you feel that taking TB medicines prevents you from doing things in your life that you normally do?

PROBE: Hanging out with friends? Working?

PROBE: Were you told not to drink alcohol when taking your TB medicine? How do you feel about that?

PROBE: What do you think will happen if you take your TB medicines and drink alcohol?

Q21. For any of you who have taken TB medicines, did you have any problems?

PROBE: What were these problems?

PROBE: Where did you go for help with those problems?

PROBE: Did any of you stop taking your medicine? Why? Why didn't you seek out help?

Q21a. How do you remind yourself to take your TB medicines?

PROBE: A calendar? Notes? Reminders from family and friends.

Q22. What could your doctor or the health department have done to make it easier for you to take your medicine?

PROBE: Explained things in a different way?

PROBE: More support from the health care worker?

PROBE: Provided a different health worker? If so, what characteristics are important to you?

PROBE: Provide incentives such as food, food coupons? Transportation? Other?

Q23. Is there somebody who helps you (reminds you) to take your meds? If so,

who? Family? Friend? Health Dept. Staff? Church member? If not, is there

someone who could help you?

Q24. Can you think of anything else that would convince other people of the importance of taking TB medicines?

Let's take a five-minute break before we move to the last area of discussion. When we

come back we will have a short question and answer period for those of you who have

questions.

It is now_____. We'll start again at _____.

[Approx 1 hour and 30 min.]

PART THREE: <u>Question and Answer</u>

Note to Moderator: Invite participants to answer any questions that they may have about TB. These questions will be answered by TB experts in the room.

[Approx 20 min.]

PART FIVE: Conclusion

Summary

Q30. Is there anything we should have talked about but didn't? Is there anything else we need to know?

Acknowledgements

Thank you very much for coming here today. We appreciate your thoughts and ideas. They will be very helpful.

Appendix 7.Informed Consent for Focus Group Discussion (Ng'aa karimojong version)

ARIPIRIP KA AKIYAN ALOGURUPO KORI NGATUKETA.

NGAKINGISETA.

Nguna epolok kotere ekarikon ka-akingitingit.

- Ngaanu nguna ebasi ngitalio yok koterelouk oi?
- Anibo epite ngolo iwaritere iwon akimukeo aloukoi ka akilik ngikito, ebasi ngitalio yok ai?
- Yaanu nooi nguna iksipiyorito iwonageunun, akiricakin ka akirikanakin akimukeo aloukoi?
- Anibo kona atukot na, nyaanu nguna abu kitiya kotere epedoryata akirikakin akimukeo alokoi?
- Eyenio kona iyes loukoi ngolo ipiyoro akimukeun a?

Ageunet (ngadakikae ngatomon)

- Kiajau ngitunga ka kitoodiun neni kec
- Tolimok nguna itukokinitor iyong ikes.
- Tolimok ajokis ngina ka akimor ngakiro kori akiyan ikwa egurupkori atukot.
- Tolimok ajokis angiboro angulu itatamere ka ikamere nguna iyanio ka nabo kitoodiu ngikaripiripak nguluce ngulu yekasi.
- Kikobak nguna etupitae anakiyan angina ikwa akiyan kaapei, angipeipei, atupit esaa ka ngunace dang.
- Totap nguna ka akerit ka akiwait ngakiro nguna iyanio
- Tolimok ngitunga atemar nguna iyanio elosyo amisiyanar ka aripirip ejok ka nyelimorio ngirorwa angulu ebongonokinete.
- Icemio baruwa ngina ka acamunet
- Tosyomak nai ngimembae nguna daadang eyani kirikakin akiyan.

NGAKINGISETA

1. **Nguna angitalyo kotere edeke, angaleu ka akimukeo kaapei ka nguna ikisipiyorio akiwarit amukean.**

Elosyo iwon akirworo nguna etapito angaleu ka edeke.

Q1. Nyaanu nguna epolok nooi alotooma angaleu kon?

Q2. Anu itami iyong atemar epolok nooi alotooma angaleu alore kus?

Q3. Ai iloseneneete iyes icamitoakitangaleuno?

Kingit ejok. – lodakitar kon

- Lodakitarin ngulu Ngorok
- Lodakitarin ngulu imukeere ngulu edyakasi nooi.

Q4. Eyai apaki ngina idiakar iyong toripuatemar ejok alosit lodakitar nai nyilot a?

Kingit ejok. – nyo abu ikisipiyo iyong ? kitecau mono iyong ejok.

Q5a. akilo aanyun edakitar, eyai ibore ic ngini itiyaenene iyong angaleunio a?

Kingit ejok– akimuj ngamujangunaajokak

-akiyengunun

-akimat ebitamen

-akilip

-akimat ngataagor

- Alosenen lomurok

II nguna aloukoi aripunun ka akimukeunun loukoi, nguna ebasi ngitunga ka akiricanakin ekitoe.

Q4. Eyai mono epite ece enyaritere loukoi a?

Q5. Ani iirari iyong ekiro be loukoi, nyo ibore ngini emotun natameta kon atipei?

Q6. Alipite eryamununuiata ngitunga loukoi itamakini iyong?

Totamunite

Kebongokis ngikalalak atemar lokuwam,kingit keyakasi ngipiesyo kori ngiwaetin ngice ngulu etapununuyere loukoi.

Q7. Ikokini iyong iripuni atemar iyakar iyong loukoi ai?

Q8. Ani itamakini iyong, epatana mono loukoi a?

Q9. Ani itamakini iyong, imukeunun mono loukoi a?

Q10. Itamakini iyong, epedori itunganan aryamun ekurut aloukoi nyediakakin a?

Q11. Etya mono amaranu aneni kon kotere aryamun loukoi ai?

Q12. Nyaanu nguna itiyae iyong nyiryamunia loukoi?

Q13.Ani itamakini iyong, eya mono ngitunga ngulu epatanikinit kori epatana aryamun loukoi akilo nguluce a ?

Kingit ejok– atangae ikes?

-Kaninyo?

Q14. Totamak apak ngina iripunia iyong atemar iyakar iyong loukoi. Tolimokinai ngadi guna apotu kitiyaunos neni kon ka nguna ibu iyong kitiya apaki ngin.

Kingit ejok.

- Ibu iyong totamak anu kori anu apotu potu natameta kon?
- Ngae ibu iyong tolimok atemar iyakar iyong loukoi ?
- Ayai idyo tunganan ngini pa icamit iyong tooanyu ngakiro ngun a? ani keyai, kaninyo?

- Apotu ngitunga kon ikitinga iyong lopite ali eanyunete atemariyakar iyong loukoi ?
- Anu kingiseta iyakar iyong apaki ngin ?
- Ngae abu tobongok ngakonikingiseta?
- Alotooma ngabongokineta ngun, ngaanu nguna atyono akiirar nooi?
- Eyai idyotunganan ngini ibu iyong kingit akisirwor iyong nguna kitiya a? (ikwa ngikonei kangitunga ngulu ke-ekal).
- Ayai ice akilo edakitar ngini abu ikimukeu iyong a? (ikwa emuron, ngitunga ngulu ke-ekal kori edyokone).
- Ibu yong tomat ekitoe kon a?

Q16. Nyaanu nguna etamete ngikonei kon ka ekonikal kotere loukoi?

Q17. Eyai ibore ngini abu ikipiyo iyong ayenun kori abu ikikarunit iyong apaki ngina ilosio iyong lodakitar a?

Kingit ejok.

- Aya nguna atapito akipim ejamu kon kotere aripun loukoi a?
- Icamunit iyong kori ikikarunit iyong?
- Ani bo akinuak ekore, icamunit iyong kori ekaruna?
- Ayai ibore ikikarunit iyong kori ayai idyobore ngini abu ikipiyo iyong aanyun?
- Itami iyong atemar epedorete ngikonei kon ka ngitunga ngulu ke-ekal kon aryamun loukoi a?
- Ibu iyong toripu atemar nyidiaka iyong tokona, nai ipedori adiakakin erae pa kimat ekitoe kon a?
- Nyaanu nai nguna ingita iyong akitogogongio akimat ekitoe kon?

Q18. Nyaanu nguna itami iyong kotere abunenen lodakitar?

Kingit ejok.

- Ikitingito iyong ngidakitarin ikwaani ?
- Apotu ikingarakis angiboro angidi a? ikwa ngisilinga ngulu doket, etacit ngolo ka amukean, akimuj kangiboro nguluce dang ngulu iyeni iyong.
- Angaanario edakitar ngirwa ngulu iyookino a? ani bo ngisaae, eyookino a?
- Ayakasi ba ngidakitarin ngisaae daadang ngulu abeitor ikes ayakau?

Q19. Anu itami iyong kotere akimat ngikito ngulu itangaleunete loukoi?

Q19a. Anu apotu ikiinakis iyong acamun akimat ngikito ngulu itangaleunete loukoi?

Kingit ejok.

- Ngae abu ikitocaik iyong ajokis ka akimat ngikito ngulu itangaleunete loukoi?
- Nyaanu nguna apotu topoloto alorwor kus kotere loukoi ka ngikito keng ?
- Abookoi iyong emasio ekitoe ngol ikwaai ?
- Anutameta iyakar iyong alotooma akimat ekitoi aloukoi ikitee itunganan alodakitar, alore kori aiwace?

- Anibo akimat ngikito pa idiaka? Iyookino kori erono?
- Ani bo aoyau ka apaki angina emasere ngikito aloukoi, anu ilimuni iyong?
- Nyobo nyemaseneneata ngitunga ngice ekitoe aloukoi?

Q20. Itami iyong atemar ikisipiyori iyong akimat ekitoe aloukoi etic ngolo sek ityaenene iyong a?

Kingit ejok.

- Ikwa akipasat ka ngikonei
- Elejilej
- Abookoi iyong nyimasenene ngawe iliki ekitoe a?
- Anu itami iyong ebe ityaun neni kon erae kimasi iyong ngagwe tomasi nabo ekitoea aloukoi?

Q21. Kotere iyes ngulu imasitotor ekitoe aloukoi,eyakasi ngatyokisyo ipotu iyes toryamut a? Ani keyasi, area anu tyokisyo?

Kingit ejok.

- Ai ipotu iyes toloto aryamun akingarakinet?
- Eyai idyo ngini abu tojongo akimat ekitoe a? Ani keyai, area kaninyo?
- Nyo pa ingititar iyong adyokingarakinet?

Q21a. ikwaani itatamuununuia iyong akonikuwan akimat ekitoe aloukoi ?

Kingit ejok.

- Ngarwa nguna ke-elap
- Ngikonei
- Ngulu ke-ekal

Q22. Nyaanu nguna abeit edakitar kon akijaanakin kotere tojokunia epite ngolo iryamununuia iyong ekitoe?

Kingit ejok.

- Abongonokin ngakingiseta alopite angolo egelegelya
- Akingarakinet ngina elal a?
- Ayaunit ekemukean ece a?
- Ani kerai ikwangina, ngaani nginibore abu itonira iyong nooi ?
- Ikiinanakini idiobore ikwa akimuj kori ngisilinga a?

Q23. Eyai itunganan ngini ikitatamununui iyong akimat ekitoe kon a? Ani keyai, erae ngae? Ekal kori ngikonei kon? Ngidakitarin kori ngulu angkelesiyae/ngikanisae? Ani kemam, ngaekona itami iyong atemar epedori?

Q24. Totamu mono iyong idiobore ngini epedori ainakin agogongu ka abobou lotunga nguluce kotere aryamun ka akimat ekitoe ngolo aloukoi.

Elosiob kona mono akiyengun apaki ngina ewuruwana ido nai oloto ngaren anakiyan yok. Ani tokona ikibonguni, ikilosi abongonokin ngakingiseta erai keyakasi ngulu eyakatar.

Erae tokona ngisaae……., egeunio nai nabo iwon ngisaae……

(Edoli epei saa ka atutubet; 1hr 30mins).

III. Ngakingiseta ka ngabongonokineta.

Ecamakinio ngini eyakar abongokinet kotere nguna etapitoloukoi ka alimun akingiset ngina etapit edeke loukoi. Ebongokinete nai nugu ngulu eyenete ka esyomito nguna alalak kotere loukoi.

(Edoli apaki naga ngadakikae ngatomoniarei: 20mins).

Q30. - Eyakasi mono kona ngani nguna abeit kiyanae, nai edpara a?

-eya ngace nguna apolok nguna abeit ayenut a?

Akitalakaret.

Alakara nooi neni kus daadang aponare nege nakwarina. Ikilakara nooi kotere nguna ikiyan iwon, kotere ngakiniseta kus ka ngabongonokineta kus daadang anerai epolok nooi. Ikilakara nabo kotere ngatamanakineta kus anerain ikingarakinete iwon alemar loukoi alokarimojong. Nguna nai sek eyanio iwon daadang, mam nyerai ngakiro nguna ibolorio king kori irimitere ani ingadao ka akereru. Nyelimorio tar ekonikiro.

ALAKARA NOOI.

Appendix 8.Data Abstraction tool

TB Clinic ID	
Age	
Sex	
Marital Status	1. Single 2. Married 3. Divorced 4. Widowed
Place of Residence	District Sub-county LC1
Ethnic origin	
Health Worker	1. Yes 2. No
Immuno-suppression	
Nutrition status	**1.** (G) Normal **2.** (G)Moderate Acute Malnutrition **3.** (R) Severe Acute Malnutrition
TB/HIV Activities	**1.** (C) Counseled **2.** (CT) Counseled and Tested **3.** (CT1) HIV positive **4.** (CT2) HIV negative
If Positive, under care?	1. No 2. Yes (CPT) 3. Yes (ART No.)
Clinical Factors	
Type of Patients	1. N (New) 2. R (relapse) 3. F (failure) 4. L (LTFU) 5. THU (Treatment History Unknown)
Exposure	1. Exposure to drug-susceptible TB 2. Exposure to drug-resistant TB
Disease Classification	1. P-BC 2. P-CD 3. EP
Treatment Model	1. F – (Patient is Health Facility based DOTS)

	2. C – (Community based DOTS)
Duration of previous TB treatment in months	
Follow up	1. Category 1 Patient (remained sputum +ve at the end of 2 months & intensive care for 1month) 2. Category 2 Patient (Started on intensive phase for 3 months)
Diagnosed with DR TB	1. Yes 2. No
If Diagnosed with DR TB what type is it	1. Isoniazid-Resistance 2. RR 3. MDR 4. XDR

Appendix 9.Key informant interview Guide (Health worker)

1. What is your qualification?
2. How long is TB treatment?
3. How long do you take to detect DR TB in patients?
4. How do you deal with the patients as you wait to for the DR TB patients
5. what methods do you use to follow up on the patients and their families
6. Are there ways you are trying to overcome resistance in your health facility?
7. What resources and tools would be useful to communicate effectively with patients about the DR TB?
8. What logistical challenges have you had with DR TB in your health care setting? (Probes: human resources, training, laboratory support – i.e. please describe your interaction with the laboratory?)
9. What are some additional challenges that you think other health care providers might face in treating DR TB in their health care setting?
10. What additional information about DR TB would you like to share with us?
11. In TB, we talk a lot about issues surrounding diagnosis of DR TB. Please tell us about your experience with using the diagnosing DR TB.

Appendix 10.In-depth interview

Participant ID	
Social Economic Status	
Work status	**1.** Employed **2.** Self employed **3.** Non Employed
Type of work (for 1&2)	
Income	
Number of close family members	
Education Level	1. None 2. Primary 3. Secondary 4. Tertiary
Substance use	1. Smoking 2. Alcohol 3. Other, specify

Do you know what DR TB is?

.....

Is it your first time to get TB

.....

Do you have DR TB? When did you first know you had it?

.....

How Many people do you live within your home?

.....

What mode of transport do you use to come to the Health centre?

.....

When were you able to access health services?

.....

How is the service?

.....

Did you get any adverse drug and treatment effect what where they?

.....

What are the perspectives of your community about DR-TB?

.....

How has your family handled your situation?

.....

What is your source of income?

.....

Do have any other disease apart form TB?

.....

Is there any other kind of substance or traditional medicine you use?

.....

Appendix 11.Translated In depth interview (Ng'aa karimojong version)

Eyenitenekeekabongonokinon	
Eyakaeke- ekabongonokinon	
Etic	**4.** Itiyaenapis **5.** Eyakarekeetic bon **6.** Mam etic
Ali tic (kotere 1&2)	
Ngisilingangiyaieyakar?	
Enambaangitungaanguluke-ekal	
Asyomit	5. Mam 6. Ngakilasyangakanikarei 7. Sinia (ngakanikainipakangatomon ka ngauni) 8. Kidyamasiniaikwa Makerere
Ngimaten ka ngiboronguluemінaitunganan	4. Akimatethigara 5. ngagwe 6. ngice, kitochauejok

Iyeniiyongngadikotereloukoingoloipiyoroalokito a??

.....

Akisyakiniyongaryamunloukoina a?

.....

Woriisyakiniaiyongaripunatemariyakariyongloukoingoloipiyoro?

.....

Ngitungangiyaiirukitotoriyongalorekon?

.....

Ali piteiloseneneoiyonglodakitar?

.....

Aria anipakiryamuniaiyongakijaanakinalodakitar?

.....

Ikonikonaakijaanakinnginai?

.....

Ayaiiborenginiarononabukitiyaunnenikonirikakiniiyongakimatekitoealoukoi a??

.....

Nyaanungunaetemete ka ebasingitunga a lore kuskotereloukoingoloipiyoroalokito?

.....

Alipitekonaikitingitoriyongekalkonkoterengakiroaloukoi?

.....

Alipiteiryamunitoriyongngisilingakoriiboredaadangnginiingaranakinoriyong?

.....

Iyakariyongedekeeceakiloloukoi a?

.....

Eyaiekitoeeceisitiyaeiyongikwangikitonguluangirerya a?

.....