Assessment of treatment outcomes of registered tuberculosis patients in Laquintinie Hospital of Douala, Cameroon: a retrospective cohort study

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ABSTRACT

Background

Globally, tuberculosis is a major public health problem and especially in low-income settings where resources are limited for proper treatment. The disease is managed by control programs that follow patients throughout the treatment with outcomes routinely assessed and reported to promote successful TB treatment and survival of patients. However, Cameroon still records a large proportion of TB-related fatalities and studies have also shown a low treatment success rate of TB patients.

Objectives

We assessed treatment outcomes and factors associated with unsuccessful treatment outcomes on registered TB patients enrolled in the DOTS program in Laquintinie Hospital of Douala (LHD), Cameroon

Methods

A hospital-based retrospective cohort study was carried out by reviewing the TB registers of all TB patients enrolled in the DOTS programme at LHD from 2016-2019. Data was collected from all registered TB patients of all ages. Double data entry was done. For analysis we used crosstabulations and logistic regression to assess the determinants of unsuccessful treatment outcomes.

Results

Among the 3,321 registered cases with complete treatment outcome data, 86.9% were newly diagnosed. Males made up 53.9% of the new and 58.1% of the retreatment cases. Seroconversion was recorded in 33.8% of the new and 47.1% of the retreatment cases with 10% deaths among those HIV positive. New cases had 84.4% success. Retreatment cases had 74.5% success, 1.4% failure, 6.9% death, 6.2% lost-to-follow-up and 11.1% transferred out. For new cases, increased risk of unsuccessful treatment outcome was high in patients aged ≥55years (aOR 1.53, 95% CI: 1.07 - 2.18), having initial smear results of (+) (aOR 1.57, 95% CI: 1.10 - 2.22) and (++) (aOR 2.01, 95% CI: 1.43 - 2.83), being diagnosed and treated in the years 2017 (aOR 1.85, 95% C.I: 1.25 – 2.73) and 2019 (aOR 2.13, 95% C.I: 1.48 – 3.06) and with double risk in those HIV positive (aOR 2.26, 95% CI: 1.75 - 2.92). The risk of unsuccessful treatment was almost double if being diagnosed and treated in the years 2017(aOR 0.53, 95%CI: 1.05 - 6.10), and 2019 (aOR 2.93, 95% C.I: 1.34 – 6.43) for the retreatment cases.

Conclusion and recommendation

Treatment success of the retreatment cases (74.5%) was lower than the NTB program and WHO target. Proper tracing and follow-up of the “failed” and “lost-to-follow-up” retreatment cases is therefore needed to address concerns for MDR.

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ACRONYMS AND ABBREVIATIONS

AIDS	Acquired Immune Deficiency Syndrome
CDC	Centers for Disease Control and Prevention
CNTBP	Cameroon National Tuberculosis Program
COVID-19	Coronavirus Disease 2019
DOTS	Directly Observed Treatment, short course
DRTB	Drug Resistant Tuberculosis
E	Ethambutol
EPTB	Extra-pulmonary Tuberculosis
HIV	Human Immunodeficiency Virus
H/INH	Isoniazid
IUATLD	International Union Against TB and Lung Disease
LHD	Laquintinie Hospital of Douala
MDR	Multi Drug Resistant TB
MoH / MoPH	Ministry of Health / Ministry of Public Health
Mtb	*Mycobacterium tuberculosis*
NACC	National AIDS Control Committee
NTCP	National Tuberculosis Control Program
PLWHIV/AIDS	People Living with HIV/AIDS
PTB	Pulmonary Tuberculosis
RR-TB	Rifampicin-Resistant Tuberculosis
S	Streptomycin
SDGs	Sustainable Development Goals
TB	Tuberculosis

UN	United Nations
UNHCF	United Nation High Commissioner for Refugees
WHO	World Health Organization
Z	Pyrazinamide

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CHAPTER ONE

1.0 INTRODUCTION AND LITERATURE REVIEW

1.1 Tuberculosis – causation, transmission, and site of infection

Tuberculosis (TB) is a disease that people have for long battled with before the causative agent – *Mycobacterium tuberculosis (Mtb)* was discovered by Robert Kock in 1882 [1].

The disease is contagious and primarily airborne, acquired by inhaling airborne droplet nuclei of bacilli expelled by someone with active Pulmonary Tuberculosis (PTB), for example by coughing, spitting, sneezing, speaking, or laughing [2, 3].

Though the lungs is the primary site of *Mtb* infection (PTB), the infection can however spread to other secondary sites such as the pleura, lymph nodes, spine, other bones and joints, genitourinary tract, nervous system, abdomen through the blood stream, lymphatic system, the airway or by direct extension to other organs (Extra-Pulmonary Tuberculosis – ETB) [4]. Pulmonary tuberculosis is the most common comprising of about 80% of the total cases [2, 5]

1.2 Tuberculosis – determinants of transmission

People who are infected with *Mtb* but do not have an active TB disease cannot transmit TB. Children are less contagious than adults probably due to weaker cough mechanism, less sputum productivity and lower bacillary load [6]. Not everyone who is exposed to an infectious TB patient will become infected with *Mtb*. The probability of transmission depends on some variety of factors.

- **Contagiousness of the source being the greatest factor.** Bacteriologically smear-positive cases are the most infectious.
- **Virulence of the strains**. Certain strains are very transmissible and more likely to cause active disease [5].
- **The environment where the exposure has occurred.** Open air and sunlight are conditions that will reduce transmission while settings with no ventilation are most likely to lead to transmission. The proximity to a patient with active TB is also important.
- **Duration of the exposure**. People who are close contacts such as family member, roommates, friends, co-workers, or other who spend multiple hours per day with an active TB patient are at high risk of becoming infected with the *Mtb* [4, 6].

1.3 Tuberculosis – evolution and development in humans

1.3.1 Tuberculosis evolution

Upon inhalation of the infectious droplets containing the bacteria, most of the larger droplets stay in the upper respiratory tract (nose and throat) where infection might not develop. On the hand, little droplet nuclei may reach the small air sacs of the lungs (the alveoli) and in which case infection may occur. Thus, following exposure to the bacteria, one of the natural courses occurs:

i. Latent TB infection. This is observed when the host immune response is strong and capable to kill the bacteria, thus preventing bacterial growth. Usually, the host has a low probability of experiencing TB disease in the future.
ii. Develop into an active/a primary TB infection, which is characterised by active bacterial growth and multiplication, leading to the clinical stage of the disease, for example, military TB and TB meningitis
iii. Post-primary TB. A clinical stage where the dormant bacilli get a chance to multiply and grow, a process known as reactivation [3].

1.3.2 Tuberculosis development in humans

There are two main stages in which TB develops in humans: TB infection and TB disease. In the first stage, an infectious case of TB spreads the bacteria to another person who is exposed to and then becomes infected. Then second stage, TB occurs when the infected individual develops the disease [5].

1.3.2.1 Primary infection

Following transmission on the bacteria into the body, it multiplies slowly mainly in the terminal alveoli of the lungs and in the lymph nodes. After one to two months, because of cellular immunity, the primary focus (defined as “small area of granulomatous inflation in the alveoli, which is not detectable on chest x-ray unless calcifies or grows substantially” [7]) will be contained and encapsulated with a central zone of parenchymal necrosis. At this moment, specific TB immunity appears and positive skin reaction to tuberculin is observed. This stage is usually asymptomatic though hypersensitivity reaction may occur in rare cases [7, 8].

1.3.2.2 Active TB disease

Bacilli from the primary infectious focus or from a near-by lymph node can be transported and disseminated throughout the body via the lymph system or bloodstream before immunity is established. This may result to secondary foci containing bacilli in other areas of the body particularly in the lungs, lymph nodes, serous membranes, meninges, bones and kidneys. However, when immune response is mounted, most of these foci are resolved but a number of bacilli may remain latent in the secondary foci for months or even years [9].

A variety of factors can reduce immunity and thus lead to reactivation of the bacilli and their proliferation in one or more of these foci. Active TB disease then results from reactivation or progression of the primary or secondary foci. Half of the cases of active TB appear in the year following infection though active TB cases may occur after months or even after years without clinical signs following primary infection [7, 8].

1.4 Tuberculosis - risk factors for developing active TB disease

The risk of developing to active TB disease depends on several factors including: factors that affect or weaken the immune systems, factors that damage the lungs, the intensity and duration of exposure [9].

1.4.1 Factors that affect the host immune defences

Infection with human immunodeficiency virus (HIV) is one of the main factors that greatly affects the immune system, specifically the white blood cells called CD4 cells. People living with the virus develops the acquired immunodeficiency syndrome (AIDS) which makes them disease prone including developing TB disease [5, 10]. The immune system prevents the development of TB following tuberculous infection. However, when this protection provided by the immunes systems is reduced by HIV infection, the microbe introduced from the new infection or that which was dormant in the body of someone previously infected can begin to multiply and cause TB [5]. The risk of coming down with active TB in someone with HIV infection is multiplied 20 – 40 times [11].

Other factors that weaken the host immune defences include diabetes mellitus (risk multiplied by 3-5 times) [9] and also associated with increased risk of developing primary multi drug resistant (MDR) TB [12]. Moreover, malnutrition; prolonged therapy with corticosteroids (such as prednisolone); other immunosuppressive therapies; certain types of cancer such as

leukaemia, Hodgkin's lymphoma, cancer of the head and neck; several kidney diseases; alcoholism; substance abuse; pregnancy also weaken the immune system and increase the risk of developing TB [11]. Furthermore, young children and persons over sixty years have greater risk due to immune system not fully developed for the former and comorbidities for the later [13].

1.4.2 Factors that enhance damage the lungs

Chronic alcoholism has been associated with acute respiratory distress syndrome (ARDS) and lung injury [14, 15]. Also, studies show risk of developing active TB is greatly increased in people who drink daily more than 40g of alcohol or have alcohol disorder [16], and heavy alcohol consumption /alcohol use disorder (AUD) being a risk factor for TB incidence and re-infection [17]. Consistence and subsistence evidence from several reviews show strong association between lung damage, lung cancer and smoking tobacco, waterpipe tobacco smoking, marijuana smoking [18-20]; TB and tobacco smoking, including passive smoking and indoor pollution exposures [21, 22] and in some studies causal association between smoking and TB disease [23]. "Dose-response" analysis in systematic reviews show strong association between Silicosis with lung cancer [24] and even low doses of silica increase the risk of developing TB [25].

1.4.3 Intensity of exposure

This refers to the number or quantity of inhaled bacilli [26]. Factors such as the contagiousness of the source, the environmental and proximity in which the exposure took place, duration of the exposure and residents of high-risk areas do affect the risk of developing active TB. [9, 11]. Studies in Brazil show increased risk of TB infection with intensity of exposure to patients with pulmonary TB [27]; case control study showed increase exposure may serve as a very good indicator of increased risk of progression to TB disease in Canada [28]; and exposure to PTB cases indicated strong risk of TB transmission to other inmates in Aba federal prison, Nigeria [29].

1.5 TB diagnosis and treatment

TB diagnosis can be done using sputum smear microscopy (developed more than 100 years ago), rapid molecular tests (first endorsed by WHO in 2010) and culture-based methods [2]. The culture-based takes up to 12 weeks to provide results but remain the reference standard. TB that is resistant to first line and second-line anti-TB drugs can be detected using rapid tests, culture methods and sequencing technologies.

The WHO recommends essential formulations of anti-TB drugs and fixed-dose combinations for the treatment of tuberculosis comprising of two main phases: intensive and continuation phase. The intensive phase consist of four (4) anti-TB drugs for two month with the main purpose of killing the bacteria rapidly, render the patient less infectious, disease control, prevent emergence of drug resistance and the continuation phase to sterilize by killing dormant and semi-dormant bacilli and prevent relapse of TB [30]. Essential anti-TB drugs are isoniazid (H, INH), rifampicin (R, RMP), ethambutol (E), pyrazinamide (Z) and Streptomycin (S) [30]. WHO recommends standard regimen and dosing frequency for new TB patients for intensive phase (2 months of HRZE) and for the continuation phase (4 months of HR) and whereas for countries with high levels of isoniazid resistance in new TB patients, and where isoniazid drug susceptibility testing in new patients is not done (or results are unavailable) before the continuation phase begins the recommendations are: intensive phase (2 months of HRZE) and for the continuation phase (4 months of HR) [5, 30].

In Cameroon, TB treatment is provided only by the National Tuberculosis Control Program (NTCP) at no cost with the combinations in line with the WHO recommendations [31]. The patients to be treated as tuberculosis cases are determined based on:

- The bacteriological status
- The localization of the disease – pulmonary or extra-pulmonary
- Past treatment history of the patient – never treated or previously treated for TB [32].

These patients are thus classified as new or retreatment cases.

New cases

Patients who have never been treated before or have been treated for less than one month with anti-TB drugs. They include:

- Pulmonary TB confirmed bacteriologically or my microscopy, molecular test (Xpert or TB-LAMP) and or culture (PTB+)
- Bacteriologically unconfirmed pulmonary TB (PTB-)
- Extra-pulmonary TB (EPTB)

Retreatment cases

These patients fall under three main treatment groups: relapse, treatment failures, return after default and should be rifampicin sensitive.

Relapses: patients who previously had received anti-TB treatment for active TB (bacteriologically confirmed or not) and were declared "cured" or "treatment completed" but later developed bacteriologically confirmed PTB.

Treatment failures: PTB patients on treatment who are still sputum smear positive 5 months or more after starting anti-TB treatment.

Return after default: new TB patients who had been in treatment for 1 month or longer and have returned with symptoms of PTB and positive sputum smear after having interrupted treatment for 2 months or more [32].

A new regimen was to put in place by 2020 in which Streptomycin was removed from the regimen for retreatment adult cases [32]. Treatment regimen up to the years 2019 and from 2020 are shown in the table 1.1 below and table 1.2 in the next page.

Table 1.1: Drug regimen for the treatment of new and retreatment TB cases in Cameroon before 2019

	Intensive phase treatment	**Continuation phase**
New cases	2-months of rifampicin (R, RMP), isoniazid (H, INH), ethambutol (E) and pyrazinamide (Z) (2RHEZ)	4-months with RMP and INH (4RH)
Retreatment cases	2 months of RHEZ and streptomycin (S) (2RHEZS)	1 month of RHEZ and 5 months of RHE (1RHEZ/5RHE)

Source: TB technical guide for health personnel in Cameroon, 2020 (pg. 145)

Table 1.2: Drug regimen for the treatment of new and retreatment TB cases in Cameroon from 2020

	Intensive phase treatment	Continuation phase
New cases	2-months of rifampicin (R, RMP), isoniazid (H, INH), ethambutol (E) and pyrazinamide (Z) (2RHEZ)	4-months with RMP and INH (4RH)
Retreatment cases (adults)	3 months of rifampicin (R, RMP), isoniazid (H, INH), ethambutol (E) and pyrazinamide (Z) (3RHEZ) *("Under very strict DOT observation on outpatient or in the hospital in case of severe clinical status of patient or if difficult to supervise patient on outpatient basis")*	3 months of rifampicin (R, RMP), isoniazid (H, INH), ethambutol (E) and pyrazinamide (Z) (3RHEZ)

Source: TB technical guide for health personnel in Cameroon, 2020 (pgs. 50, 145)

1.6 The Directly Observed Treatment (DOTS) program

According to WHO, the best curative method and most cost-effective way to stop the spread of TB in communities with high incidence is known as DOTS. The Directly Observed Treatment Short Course (DOTS, also known as TB-DOTS) is the name given to the TB control strategy recommended by the WHO [33].

The five main components of the DOTS program include:

- Government commitment (including political will at all levels, and establishment of a centralized and prioritized system of TB monitoring, recording, and training).
- Case detection by sputum smear microscopy.
- Standardized treatment regimen directly of six to nine months observed by a healthcare worker or community health worker for at least the first two months.
- Drug supply.
- A standardized recording and reporting system that allows assessment of treatment results.

Dr Karel Styblo of the International Union Against TB and Lung Disease (IUATLD) developed the technical strategy in 1970s which was then taken by the WHO and made into a Global strategy and dubbed DOTS [34]. Later the strategy is named STOP TB strategy and End TB strategy and all of them still include the 5 DOTS main components. Almost all countries had adopted the strategy, and there was considerable progress towards global targets established for 2005 [35]. However, the growing HIV epidemic represents a great challenge for the National Tuberculosis Programs (NTPs), which are seeing an increase in HIV infection among TB cases and the appearance of new TB cases among persons infected with HIV. This is compromising health system performance and NTP efficiency due to increased TB incidence, case-fatality, treatment abandonment, and challenges for the comprehensive treatment of both diseases [5]. It is important to notice that the direct observation (DOT) is just one of the several components of the "DOTS" strategy, this is sometimes comprehended.

1.7 Factors affecting TB treatment outcomes

The goal of TB treatment is to ensure relapse-free cure while presenting the emergency of drug resistance. Thus, sterilization, elimination of the bacilli from the sputum and not only about healing of lesions could be used to judge the effect of treatment. Mindful of the fact that *Mtb* is a slow-growing aerobic organisms and can remain dormant for a prolonged time, prolonged treatment with multiple drugs is needed to ensure cure without relapse and also prevent the emergence of resistance [36]. Bacteriology, environmental (anatomical and biochemical) and pharmacological factors play a major role of determining the treatment effect [37].

1.7.1 Bacteriological factors

1.7.1.1 The numerical factor

The number of tubercle bacilli varies widely with the type of lesion present. Data from lung specimen resected from untreated patients show that the number of bacilli in a medium-sized cavity communicating with the bronchi is about 100 million whereas the number in an encapsulated nodular lesion of the same size with no bronchial communication be as low as one hundred. The larger the bacterial population, the higher the probability of resistant mutant strains that might be present even before treatment [36].

1.7.1.2 The metabolic factor

Medications do kill organisms that metabolize actively and continuously, but in each bacterial population there are bacilli with low metabolic rate. This slow metabolic rate might be enhanced by low pH or some bacteria might just be dormant. The organisms are called “persisters” and even survive in the presence of isoniazid and streptomycin. However, rifampicin or pyrazinamide may attack and effectively kill these bacilli under certain conditions. This explains why to some extent why not all bacilli are killed during treatment, and why drug-susceptible bacilli are coughed out for some time even after treatment [36].

1.7.2 Environmental factors

1.7.2.1 The anatomical factors

The type of tissue harbouring tubercle bacilli may affect drug action because not all drugs are able to penetrate all tissues and cells or permeate biological membranes, including the normal blood-brain barrier. Isoniazid, rifampicin, and pyrazinamide readily cross biological membranes, whereas streptomycin fails to enter many cells and in much less effective against intracellular than extracellular bacilli [36].

1.7.2.2 Biochemical factors

Partial oxygen pressure, environmental pH are important biochemical factors that influence the antimicrobial effect of a drug [38]. In a cavity wall, at neutral pH, all the bactericidal antituberculosis drugs are highly effective. However, streptomycin is at most active in a slightly alkaline environment, whereas pyrazinamide acts largely in an acidic medium such as that found inside cells [39, 40]. With respect to factors relevance to dormancy of bacilli, it is stipulated that dormant organisms survive within the cells or in necrotic areas of old encapsulated lesions that do not communicate with the bronchus.

The partial oxygen is an important factor, shown by the small number of bacilli found in closed extrapulmonary lesions [26].

1.7.3 Pharmacological factors

1.7.3.1 Dosage

The dosage of drugs should be large enough to produce inhibitory concentration at the site where bacilli are found, but not necessary to keep the concentration constant [26].

1.7.3.2 Combination of drugs

Regimens should contain a combination of three or more drugs, particularly in the initial phase of TB treatment. In the early days of treatment, patients were given one drug; if that failed, further drugs were successively substituted or added, one at a time with the results that these people eventually became chronic patients with organisms resistant to all the drugs they had received. Thus, treatment of tuberculosis disease should never be attempted with a single drug, nor should a single dug be added to a failing regimen [5, 36].

1.7.3.3 The "lag period" factor

From experiment, when the tubercle bacilli are exposed to a drug for a short time (6-24 hours) and after careful removal of the drugs, are transferred to a drug-free medium, the surviving bacilli start to grow again after an interval of several days. This interval called the "lag period" varies with the type of concentration of the drug and with the length of exposure [36].

1.7.4 HIV/AIDS

TB is the most common opportunistic disease in PLHIV in countries with high prevalence of the two diseases. The immunological effect of HIV is manifested mainly on cell-mediated immunity, the part of the immune system vital in the response against *M. tuberculosis*. Thus, the immune deficiency caused by HIV infections greatly reduces the capacity of the host to contain TB infections, prevent a new infection or re-infection by *M. tuberculosis*. HIV and TB have a bidirectional interaction as *M. tuberculosis* increases the replication of HIV in vitro and HIV speeds up the evolution of TB infection into active TB disease [32].

Thus, patients infected with HIV usually have a response to treatment like those who are not infected with HIV, with a few exceptions. However, they are more likely to die during the treatment, usually from causes other than TB. Also, they may be more likely to experience toxic

reactions to drugs than those who are not HIV-infected, increase pill burden with the possible impact on adherence, TB immune reconstitution inflammatory syndrome [5, 32, 36].

1.8 Factors that influence adherence to TB treatment

Adherence to treatment is needed to attain the maximum benefits from the drugs. However, factors ranging from the level of the patient, treatment-related and the therapeutic environment can influence the adherence treatment. It is possible to control the treatment and therapeutic-related factors but not always possible to control those related to the patient. These factors influence treatment adherence and abandonment, which affects the treatment out comes [32, 41, 42].

1.8.1 Patient-related factors

This includes:

- Socioeconomic factors like having a job, being stigmatized, being marginalized, family support [43].
- Psychological factors for example having the feeling discouragement or not.
- Knowledge and perception of the disease. For example, patient might continue treatment if there's improvement or abandoning if no improvement. Also, not taking treatment id disease is attributed to supernatural causes [44].

1.8.2 Factors related to the treatment

This includes:

- The simplicity of treatment such as fixed dose combinations simplifies the treatment by reducing the number of tablets.
- Adverse effects of the treatment
- Direct observation of treatment of the patient by health support staff [26]

1.8.3 Factors related to the therapeutic environment

This includes:

- Waiting time at the health facilities, the way patients are welcomed at the clinics, patient accommodation for hospitalised patients.

- The closeness of drug distribution centres to the patients
- Relationship between the health workers and the patients. A good patient health worker relationship will make patient more likely to follow instruction to take medication and vice versa.
- The co-management of HIV infection and TB requires coordination between the TB and HIV/AIDS programs at all levels [45].
- Subsidized or free health care (consultations, laboratory test, drugs, etc) reduces the number of dropouts.
- Drug availability, management, and supply. The drug supply process should be rigorous to avoid shortages, which can lead to treatment interruptions and of coz impact adherence and treatment outcome negatively.

The coordination for other diseases like diabetes, HIV and hypertension in the same health facility will decrease the burden on the patients [32, 42, 45].

1.9 Global and national burden of tuberculosis

Tuberculosis (TB) is still a major cause of ill health - among the ten top causes of death worldwide. It is the leading cause of mortality among PLW HIV and deaths related to antimicrobial resistance [2].

In 2019, WHO estimated 10 million people globally fell ill to TB, 5.6 million were men, 3.2 million were women and 1.2 million children. There were 1.4 million TB deaths among HIV-negative people and 208,000 TB deaths among HIV-positive people [46].

According to the World Health Organization (WHO) regions 44% of TB cases were reported in South-East Asia, Africa (25%), the Western Pacific (18%), the Eastern Mediterranean (8.2%), the Americas (2.9%) and Europe (2.5%) and with eight countries accounting for 66% of the new cases: India, China, Indonesia, the Philippines, Pakistan, Nigeria, Bangladesh and South Africa [46].

Drug-resistant TB accounted for about half a million new cases of rifampicin-resistant TB (RR TB) - of which 78% had Multidrug-Resistant Tuberculosis (MDR-TB). India (27%), China (14%) and the Russian Federation (8%) had the largest share of the global burden. Globally, 3.3% of new TB cases and 17.7% of previously treated cases had MDR-TB and RR-TB, with the highest proportions (>50% in previously treated cases) in countries of the former Soviet Union. The global treatment success rate for MDR/RR-TB stands at 57% [46].

In 2019, the estimated Disability Adjusted Life Years (DALYs) lost due to tuberculosis stood at the global level, for Sub-Saharan Africa and for Cameroon at 47,030,118, 17,547,389 and 291,908 respectively [47].

Cameroon is ranked in the top 30 countries with high TB/HIV burden countries in the world and in the top 20 countries with the highest estimated number of incident TB cases among PLW HIV in 2019 [48]. In 2019, the estimated rates per 100,000 populations were: TB incidence 179 (116–255), HIV-positive TB incidence 48 (31–69) and MDR/RR-TB incidence 3.6 (1.7–6.9). The HIV-negative TB mortality and HIV-positive TB mortality per 100,000 stood at 29 (17–43) and 19 (12–28) respectively [48].

1.10 The global plan to End TB 2016-2030

In the years 2014 and 2015, all Member States of the World Health Organization (WHO) and the United Nations (UN) committed to ending the TB epidemic. They unanimously endorsed the WHO's End TB Strategy at the World Health Assembly in May 2014, and by adopting the UN Sustainable Development Goals (SDGs) in September 2015. The SDGs were set up in 2015 by the United Nations General Assembly and are intended to be achieved by 2030 and SDG Target 3.3 includes ending the TB epidemic by 2030 [35].

The vision of this strategy is to ensure a world free of TB - ensuring zero deaths, disease and suffering due to tuberculosis and the goal is to end the global TB epidemic [35].

The global plan to End TB has milestones for 2025 and targets for 2035.

The milestones for 2025 include:

- 75% reduction in tuberculosis deaths - compared with 2015.
- 50% reduction in tuberculosis incidence rate (less than 55 tuberculosis cases per 100,000 population) – compared with 2015.
- No affected families facing catastrophic costs due to TB.

The targets for 2035 include:

- 95% reduction in tuberculosis deaths (compared with 2015).
- 90% reduction in tuberculosis incidence rate (less than 10 tuberculosis cases per 100,000 population).

- No affected families facing catastrophic costs due to tuberculosis [2, 35].

1.11 The National TB Control Program (NTCP) of Cameroon

The mission of the NTCP is to eliminate TB as a public health problem in Cameroon. The NTCP is organized at all levels of the health pyramid: the central level (the Ministry of Public Health, MoPH), the regional Level and the operational level [32].

Goal

The goal is to reduce the incidence of TB from 186 cases per 100,000 inhabitants to 130 cases per 100,000 by 2024 and to reduce TB deaths from 54 per 100,000 to 32 per 100,000 in the same period.

The specific objectives are:

- Intensify TB case finding especially among vulnerable and or at-risk population and increase the treatment success rate to 90% by 2024.
- Test 95% of TB patients for HIV and put 100% of coinfected cases on antiretroviral therapy by 2024.
- Increase to 95% the screening for HIV of TB patients and increase to 100% the treatment by ARVs of coinfected patients by 2024.
- Increase to 85% screening for multidrug resistant TB in the target populations and to 100% linkage to treatment for those patients detected with MDR-TB by 2024.
- Protect people living with HIV with isoniazid preventive therapy in collaboration with the National AIDS Control Committee (NACC)
- Improve on the management practices of the programme at all levels of the health pyramid [32].

The strategies for the implementation of the NTCP are:

- Screening and diagnosing of TB.
- Correct treatment of patients.
- Prevention of disease.
- Community participation.
- Training of health personnel.
- Epidemiological surveillance.

- Systematic screening for and management of HIV in TB patients and TB in HIV infected patients.
- Early detection and management of MDR-TB [32].

The Sustainable Development Goal (SDG) number 3 states: “Ensure healthy lives and promote well-being for all ages”. Target 3.3 by 2030, end the epidemics of AIDS, tuberculosis, malaria and neglected tropical diseases and combat hepatitis, water-borne diseases, and other communicable diseases [49].

The National TB Control Program of Cameroon (NTCP) aims to achieve TB treatment success rate of ≥87% by 2020 [50]. This target is in line with the End TB strategy which recommends ≥90% TB treatment success rate in 2025 latest [2].

1.12 TB and the Coronavirus disease 2019 (COVID-19)

Coronavirus disease 2019 (COVID-19 for short) is the name of the infectious disease caused by the newly discovered coronavirus (SARS-CoV-2 coronavirus) and declared a pandemic by the director of the World Health Organization (WHO), Dr Tedros Adhanom Ghebreyesus on March 11, 2020. It spreads primarily through droplets of saliva or discharge from the nose when an infected persons coughs or sneezes [51].

Some people infected with the virus have no symptoms. However, common symptoms include fever, body ache, dry cough, fatigue, chills, headache, sore throat, loss of appetite and loss of smell. In others, severe symptoms like high fever, severe cough, and shortness of breath could be present. The number of infected people changes very rapidly [51].

Recent progress in reducing the global burden of the TB disease is being threatened by the COVID -19 pandemic [46]. Based on modelling analysis, predictions have been made on the annual number of TB deaths to increase globally when compared to the era before Covid 19 due to decrease in detection, reporting and treating of TB cases, as a result of lock down, disruption of health services and people do not go to the health facilities [46]. Studies done by the Stop TB program and partners estimate between the years 2020 and 2025: 1.4 million TB deaths if long durations of lock down are implemented with delayed restoration of services [46, 52].

Moreover, key determinants of TB incidence (GDP per capita and under nutrition) have also been predicted to worsen because of the economic impact of the pandemic. Modelling predicts

unemployment/lost income, and increase number of people with TB./households facing catastrophic cost could cause a yearly increment of more than one million people developing TB between the years 2020-2025 [46].

As the Covid-19 pandemic continues, TB endemic countries reported reallocation of TB health care workers and other material resources from TB programs to combat Covid-19, as well as significant drop in TB notification implying that a huge number of people with TB are going on reported, untreated and are probably transmitting the infection. Global TB experts fear there could be is a great risk for a surge in TB cases and mortality after the Covid-19 pandemic and argue that if global responses to TB are not improved upon, catastrophic clinical and economic implications could be recorded in TB and could reverse the gains achieved in the TB control program before 2020 [46, 53].

1.13 Statement of the problem

TB remains a major public health problem globally and especially in resource-poor settings [2]. In Cameroon, it is reported that TB infection is among the ten top causes of death [47]. Moreover, Cameroon is ranked in the top 30 countries with high TB/HIV burden countries in the world and in the top 20 countries with the highest estimated number of incident TB cases among PLW HIV in 2019 [2, 54, 55]. A third of all TB cases in Cameroon were recorded in the two major cities of Douala and Yaoundé. Previous study done in 2013 to describe the clinical characteristics and outcomes of tuberculosis in the Laquintinie Hospital of Douala, Cameroon (HLD) showed a low treatment success rate of TB patients which might have accounted for fatalities [31]. Therefore, we wanted to assess any changes in treatment outcomes and to identify factors associated with unfavourable outcomes among registered TB patients in the Laquintinie Hospital of Douala, Cameroon; this may help the TB control programme how to further improve the treatment outcomes.

1.14 Objective

1.14.1 Main objective

To study the treatment outcome of registered TB patients enrolled in the DOTS programme from 2016 to 2019 in Laquintinie Hospital of Douala, Cameroon

1.14.2 Specific objectives

1) To describe the treatment outcomes of registered TB patients.
2) To identify the factors associated with unfavourable treatment outcomes.

CHAPTER TWO

2.0 RESEARCH METHODOLODY

2.1 Study design, study site, and period

2.1.1 Study design

A hospital based retrospective cohort study aimed at assessing the treatment outcomes of registered TB patients enrolled in the DOTS program in Laquintinie Hospital of Douala (LHD), in the Littoral region of Cameroon from 2016 to 2019. The data was collected from December 01, 2020 to January 30, 2021.

2.1.2 Study site and period

LHD is found in the heart of Akwa, Deido health district of Douala, Littoral Region of Cameroon. It extends over nine hectares, and it is a reference hospital of second category [56]. The TB clinic of the LHD is the biggest in Douala and the second largest in Cameroon after the Yaounde Jamot Hospital [31].

Douala is the largest city and the economic capital of Cameroon. It is the headquarters of the Cameroon's Littoral Region and the home to Central Africa's largest port. As of 2018, the estimated population stood at 2,768,400 [57]. The city sits on the estuary of the Wouri River and has a tropical climate with warm and humid conditions with an average annual temperature of 27.0 °C (80.6 °F) and an average humidity of 83% [58].

After the end of the millennium development goals in 2015, the Cameroon National TB Control Program had as national baseline success rate of 82%. With the commence of the SDGs from 2016, projections were made for estimated treatment success rates from 2016-2020. Mbatchou *et al.,* 2013 reported treatment success rate of 75.2% at the HLD and made recommendations [31], however a follow-up study is yet to be done. Thus, looking at the treatment outcomes within this study period from 2016 – 2019 which happens to be the first quarter of the SDGs, from a major treatment centre like the LHD which help to address issues to at the hospital and also help in public health policy.

2.2 Source population

All patients registered for TB treatment at LHD from January 2016 – December 2019.

2.3 Study participants

All registered TB patients registered at the LHD and enrolled in the DOTS programs and had treatment outcome at from January 2016 – December 2019.

2.4 Inclusion and exclusion criteria

2.4.1 Inclusion criteria

i. Registered TB patients in the DOTS program at the LHD of all ages

2.4.2 Exclusion criteria

i. Patients who have more than one final treatment outcomes.
   There are six major final treatment outcomes which are mutually exclusive: cured/ completed treatment/ lost to follow-up/ failed/ died/ transferred out. Thus, if a patient had two final treatment outcomes for example cured and at the same time lost to follow up, then patient was excluded from the study.
ii. Patients with incomplete patient data

2.5 Data collection

The TB registers in the TB clinic was used get relevant information for the demographic information and treatment outcome of patients. The outcome / dependent variable is the treatment outcome which can take only one of six values: cured/ completed treatment/ lost to follow-up/ failed/ died/ transferred out to other health facilities.

The independent/exposure variables are demographic characteristics of patients including sex, age, date of registration; clinical characteristics of patients including type of TB (pulmonary/extrapulmonary), type of patient (new or retreatment), HIV status, antiretroviral and cotrimoxazole treatments; laboratory results at diagnosis and follow up, interruptions in treatment (yes/no).

2.6 Data entry, validation, analysis, and presentation

Data was entered in a template created in Epidata. Double data entry was done to ensure data quality assurance and validation.

Statistical Package for Social Sciences (SPSS) version 26 was used for data analysis and the results are presented in tables and figures in terms of group bases of the patients (new cases and retreatment cases).

Crude (bivariate) and adjusted (multivariate) logistic regression analysis was performed, and we regarded odds ratios an approximation for risk.

For objective 1, the results described using crosstabulation of the treatment outcomes (cured, completed, died, lost-to-follow-up, transferred out) by age, gender, HIV status, ART status, type of TB, type of patient, sputum smear result (Neg/+/++/+++).

For objective 2, the determinants of unsuccessful treatment outcomes were obtained from logistic regression.

2.7 Operational definition of key terms

TB infection: Infection with the bacilli of *Mycobacterium tuberculosis*.

Active TB disease: Presence of signs and symptoms of TB disease in an individual who is infected with the bacilli of *Mycobacterium tuberculosis*.

Case of tuberculosis: A definite case of pulmonary TB with one or more initial sputum smear positive for acid-fast bacilli or one in which a health worker has diagnosed TB and has decided to treat the patient with a full course of DOTs.

New case: without or with less than 1 month of previous treatment.

HIV infection: Infection with the Human Immune-deficiency Virus (HIV) that is confirmed by first line and second-line serologic tests.

HIV/TB co-infection: The presence of both HIV and TB infection in an individual patient.

TB treatment outcome: The final known status of a TB patient who was started on anti-TB treatment.

Cured: An initially sputum smear-positive patient who is sputum smear negative at or one month prior to, the completion of TB treatment and on at least one previous occasion (usually at the end of the second or fifth month).

Treatment completed: A patient who completed anti-TB treatment without evidence of failure but for whom sputum smear or culture results are not available in the last month of treatment and on at least one previous occasion.

Treatment failure: A patient whose sputum smear or culture is positive at the fifth month of treatment or later during the course of treatment. Also included in this definition are patients found to harbour a multi-drug resistant strain at any point of time during the treatment, whether they are smear-negative or positive.

Lost to follow-up: (formerly "Defaulter"): a patient whose treatment was interrupted for 2 months or more during the treatment period.

Died: A patient who died for any reason during the course of TB treatment.

Transfer out: A patient who started treatment and was transferred to another treatment unit and for whom the treatment outcome is not known at the time of evaluation of treatment results.

Treatment success: The sum of patients who were declared 'cured' and those who had 'completed' treatment [2, 5, 36, 59].

Favourable/successful outcome: "Cured" and "completed".

Unfavourable/unsuccessful outcome: All outcomes that are not "successful" i.e., "failure" "died", "defaulted" and "transferred out".

2.8 Administration ethical considerations

Administrative authorisation was obtained from the director of the Laquintinie Hospital of Douala, Cameroon (appendix 1).

Ethical approval was obtained from the Faculty of Health Sciences Institutional Review Board (FHS-IRB) - University of Buea, Cameroon (appendix 2).

The Norwegian Ethical Committee in Bergen (REK) responded that ethical approval was not needed from them (appendix 3).

CHAPTER THREE

3.0 RESULTS

In this study, patients that were newly diagnosed and who have never been treated before or have been treated for less than one month were classified as new cases while those who had a relapsed or returned after default were categorised as retreatment cases.

3.1 Demographic characteristics

This study recorded a total of 3615 TB patients registered at Laquintinie Hospital of Douala, Cameroon from 2016 to 2019. Amongst these, we analysed 3321 cases with complete treatment outcome data, in which 2887 (86.9%) were new cases and 434 (13.1%) were retreatment cases. There were more adults (between 25-54 years), fewer young (aged 0-14) and old patients (aged ≥55 years) in both the new and retreatment groups. Males represented 53.9% of new and 58.1% of retreatment cases, shown in seen in **Figure1**.

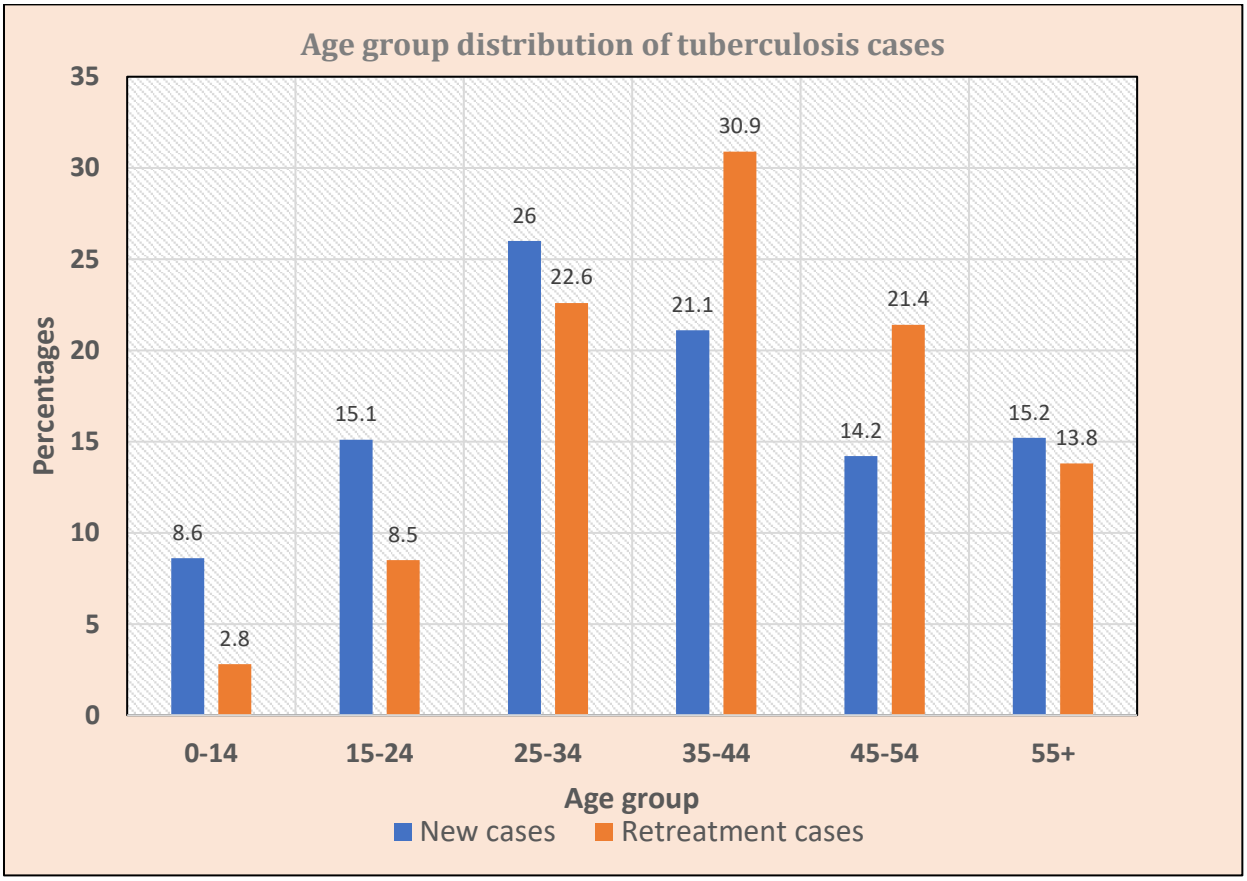

Figure 1: Age distribution of patients with tuberculosis at Laquintinie Hospital Douala, Cameroon from 2016 to 2019: new and retreatment cases

Pulmonary TB (PTB) was recorded in 36.9% of the new cases and 51.4% in the retreatment cases; EPTB was recorded in 32.6% of the new cases and 17.5% of the retreatment cases, while 30.5% of new cases and 31.1% of the retreatment cases presented both PTB and EPTB, **Figure 2.**

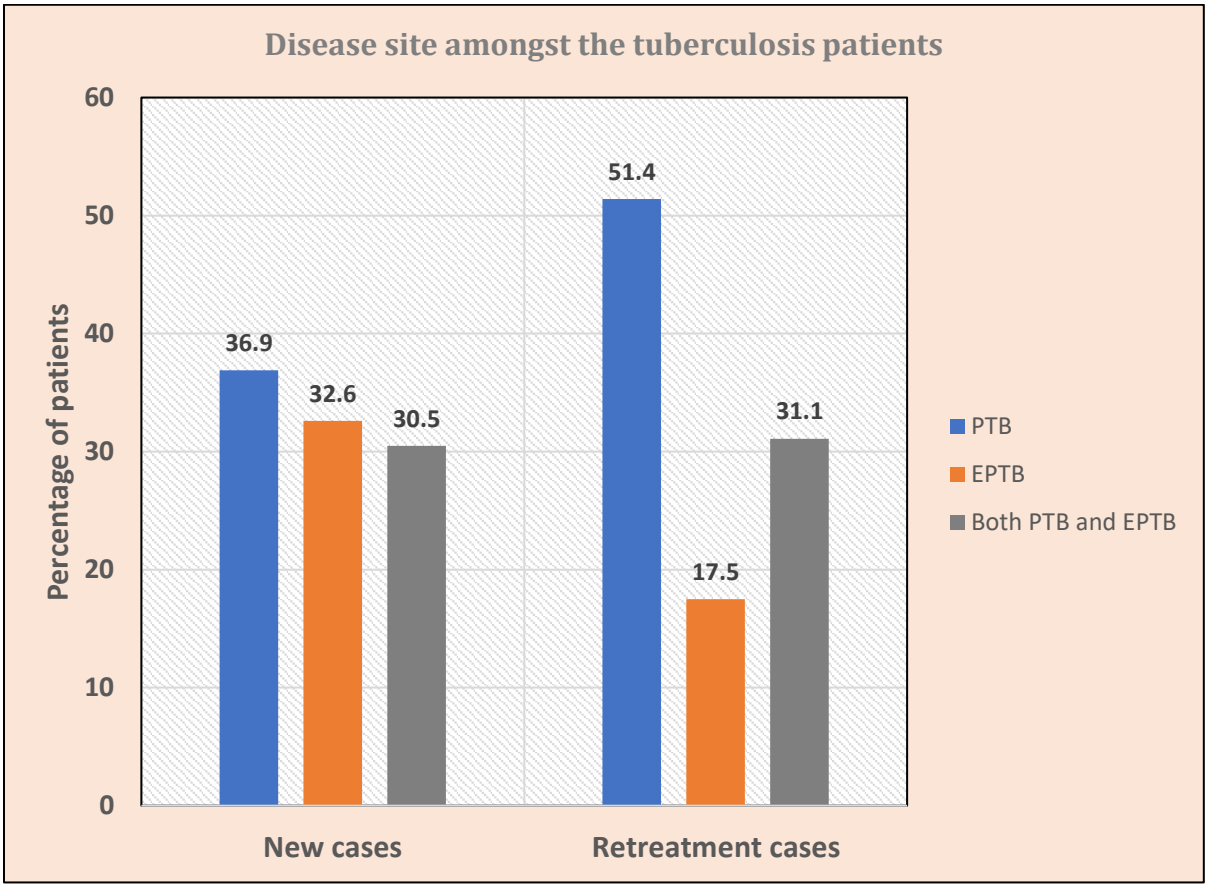

Figure 2: Disease site presentation amongst patients with tuberculosis at Laquintinie Hospital Douala, Cameroon from 2016 to 2019: new and retreatment cases

The majority (67%) of the retreatment cases were recorded to have received standard regimen instead of the correct retreatment regimen. Furthermore, with respect to comorbidities, most patients had been tested for HIV, with 33.3% of new patients and 46.5% of retreatment cases being HIV positive. Out of those with a positive status, 715 (74.4%) of the new cases were on ARVs and 99.1% on Cotrimazole preventive treatment (CPT) whereas for the retreatment cases 183 (90.6%) were on ARV and 97.5% on CPT as shown in table 3.1.

Table 3.1: Demographic and clinical characteristics of patients with TB at Laquintinie Hospital Douala, Cameroon from 2016 to 2019: new and retreatment cases

		New cases		Retreatment Cases	
Variable		**Frequency (n)**	**Percentage (%)**	**Frequency (n)**	**Percentage (%)**
Age group	0-14	247	8.6	12	2.8
	15-24	435	15.1	37	8.5
	25-34	750	26.0	98	22.6
	35-44	608	21.1	134	30.9
	45-54	409	14.2	93	21.4
	55+	438	15.2	60	13.8
	Total	2887	100.0	434	100.0
Gender	Male	1557	53.9	252	58.1
	Female	1329	46.0	182	41.9
	Total	2886	100.0	434	100.0
Year of diagnosis	2016	677	23.4	96	22.1
	2017	673	23.3	92	21.2
	2018	743	25.7	120	27.6
	2019	794	27.5	126	29.0
	Total	2887	100.0	434	100.0
Disease site	PTB	1066	36.9	223	51.4
	Both PTB and EPTB	881	30.5	135	31.1
	EPTB	940	32.6	76	17.5
	Total	2887	100.0	434	100.0
Drug regimen	Standard[1]	2884	99.9	290	66.8
	Retreatment[2]	3	0.1	144	33.2
	Total	2887	100.0	434	100.0
HIV status	Negative	1883	65.2	227	52.3
	Positive	961	33.3	202	46.5
	Not recorded	43	1.5	5	1.2
	Total	2887	100.0	434	100.0
Eligible for ART services					
	Taking ARVs	715	74.4	183	90.6
	Not taking ARVs	66	6.9	19	9.4
	Not recorded	180	18.7	0	0
	Total	961	100.0	202	100.0
Eligible for CPT[3]					
	CPT given	952	99.1	197	97.5
	CPT not recorded	9	0.9	5	2.5
	Total	961	100.0	202	100.0

NB: 1: Standard treatment: (2RHEZ/4RH), 2: Retreatment [50]3: Cotrimazole Preventive Treatment

3.2 Lab characteristic of TB patients in Laquintinie Hospital Douala, Cameroon from 2016 to 2019: new and retreatment cases

A third of the patients who tested for smear microscopy were negative, and hence diagnosed on clinically. Gene Xpert was used in a 91(31%) of the new cases and 181(41.7%) of the retreatment cases. Failure, which is a positive smear result after treatment, was seen in 0.7% of all smear positive new cases. Among retreatment cases we found only one still positive after treatment, which gives a failure rate of 0.4%, table 3.2.

Table 3.2: Laboratory results of patients with tuberculosis at Laquintinie Hospital Douala, Cameroon from 2016 to 2019

	New cases		Retreatment cases	
Variable	**Frequency**	**Percentage**	**Frequency**	**Percentage**
Initial smear results				
Negative	506	32.3	84	27.6
+	518	33.1	114	37.5
++	530	33.8	104	34.2
+++	13	0.8	2	0.7
Sub total	1567	100.0	304	100.0
Not recorded***	1320	-	130	-
Total	2887		434	
GeneXpert[1]				
MTB Not Detected	9	9.9	0	0.0
MTB Detected, R(+)	3	3.3	3	1.7
MTB Detected, R(-)	78	85.7	175	96.7
MTB Detected, R(?)	1	1.1	3	1.7
Sub total	91	100.0	181	100.0
Not recorded***	2796	-	253	-
Total	2887		434	
Smear results after 5 months				
Negative	917	98.8	104	99.2
+	11	1.2	2	1.9
Sub total	928	100.0	106	100.0
Not recorded***	1959	-	249	-
Total	2887		434	
Smear results after Tx[2]				
Negative	615	98.7	122	99.2
+	8	1.3	1	0.8
Sub total	623	100.0	123	100.0
Not recorded***	2264	-	311	-
Total	2887		434	

NB: Not recorded indicates not applicable for people with EPTB, not requested or missing***
1. GeneXpert results: R(+) is rif resistance, R(-) is rif sensitive, R(?) is indeterminate. 2.Tx: Treatment

3.3 Description of treatment outcomes of registered tuberculosis patients at Laquintinie Hospital Douala, Cameroon from 2016 to 2019: new and retreatment Cases

Six mutually exclusive outcomes were recorded after treatment of the TB patients: “cured”, “completed”, “failed”, “died”, “lost-to-follow-up”, or “transferred out”.

In this study, patients who completed their treatment and/or were cured were considered to have as a successful treatment outcome, while those who had outcomes such as failure, died, defaulted, or transferred out were categorised as unsuccessful treatment outcome.

Thus overall, new cases recorded a treatment success of 84.4% and retreatment cases 74.4%, table 3.3. Although in both the new and retreatment cases, the success rates seem to decrease from 2016-2019, new cases recorded a greater treatment success of at least 80% while retreatment cases had at least 68% from the period of 2016 to 2019, **Figure 3** in the next page.

Table 3.3: Treatment outcomes of patients with tuberculosis at Laquintinie Hospital Douala, Cameroon from 2016 to 2019

Main category	Treatment Outcomes	New Cases	Retreatment Cases
		Frequency (%)	Frequency (%)
Successful outcome	Cured	645 (22.3)	125 (28.8)
	Completed	1791 (62.0)	198 (45.6)
	Sub total	**2436 (84.4)**	**323 (74.4)**
Unsuccessful outcome	Failure	16 (0.6)	6 (1.4)
	Died	153 (5.3)	30 (6.9)
	Defaulted	137 (4.8)	27 (6.2)
	Transfer out	145 (5.0)	48 (11.1)
	Sub total	**451 (15.6)**	**111 (25.6)**
	Total	**2887 (100.0)**	**434 (100.0)**

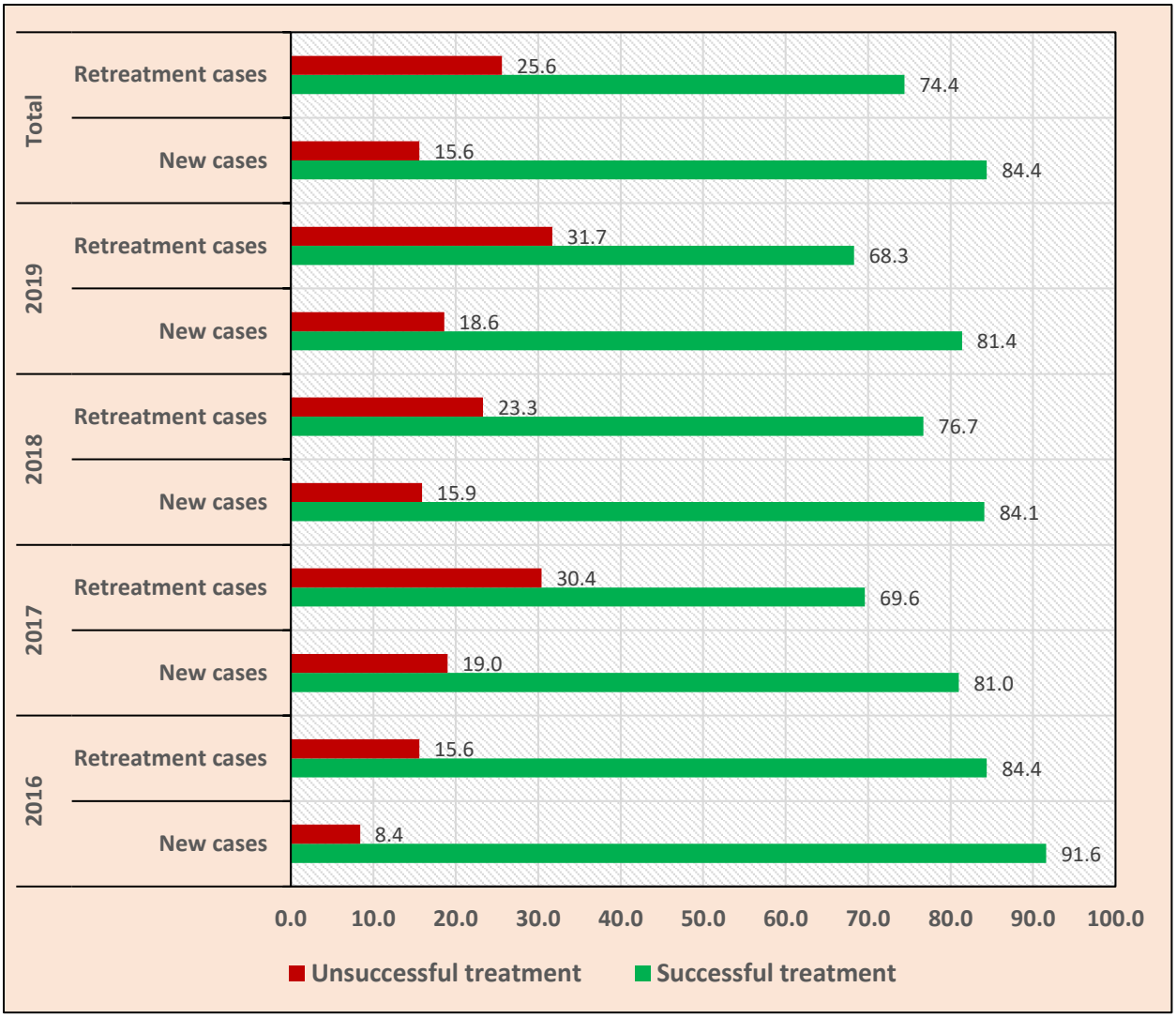

Figure 3: Successful and unsuccessful TB treatment outcomes of patients with tuberculosis at Laquintinie Hospital Douala, Cameroon from 2016 to 2019: new and retreatment Cases

Cross tabulations of treatment outcomes per baseline characteristics revealed that for the new cases, cured and completed combined (successful outcome) was above 80% in all age groups, and highest in the youngest (93%). Proportion deaths increased with age from 1.2% to 5%, lost to follow-up ranged from 2.4% to 5% in all age groups, and failures below 1% in all age groups, see table 3.4.

Table 3.4: Treatment outcomes by baseline characteristics of patients registered with new tuberculosis at Laquintinie Hospital Douala - Cameroon, from 2016 to 2019

	Frequency (%)						
Category	**Total**	**Cured**	**Completed**	**Failed**	**Died**	**Lost**	**Transferred out**
Total	**2887 (100.0)**	**645 (22.3)**	**1791 (62.0)**	**16 (0.6)**	**153 (5.3)**	**137 (4.7)**	**145 (5.0)**
Age							
0-14	247 (100.0)	21 (8.5)	209 (84.6)	1 (0.4)	3 (1.2)	6 (2.4)	7 (2.8)
15-24	435 (100.0)	133 (30.6)	242 (55.6)	1 (0.2)	9 (2.1)	23 (5.3)	27 (6.2)
25-34	750 (100.0)	213 (28.4)	417 (55.6)	7 (0.9)	35 (4.7)	38 (5.1)	40 (5.3)
35-44	608 (100.0)	134 (22.0)	375 (61.7)	2 (0.3)	39 (6.4)	27 (4.4)	31 (5.1)
45-54	409 (100.0)	78 (19.1)	260 (63.6)	2 (0.5)	29 (7.1)	21 (5.1)	19 (4.6)
55+	438 (100.0)	66 (15.1)	288 (65.8)	3 (0.7)	38 (8.7)	22 (5.0)	21 (4.8)
Total	**2887 (100.0)**	**645 (22.3)**	**1781 (62.0)**	**16 (0.6)**	**153 (5.3)**	**137 (4.7)**	**145 (5.0)**
Gender							
Male	1557 (100.0)	333 (21.4)	972 (62.4)	5 (0.3)	87 (5.6)	80 (5.1)	80 (5.1)
Female	1329 (100.0)	312 (23.5)	818 (61.6)	11 (0.8)	66 (5.0)	57 (4.3)	65 (4.9)
Total	**2886 (100.0)**	**645 (22.3)**	**1790 (62.0)**	**16 (0.6)**	**153 (5.3)**	**137 (4.7)**	**145 (5.0)**
Year							
2016	677 (100.0)	182 (26.9)	438 (64.7)	3 (0.4)	23 (3.4)	15 (2.2)	16 (2.4)
2017	673 (100.0)	109 (16.2)	436 (64.8)	2 (0.3)	40 (5.9)	70 (10.4)	16 (2.4)
2018	743 (100.0)	182 (24.5)	443 (59.6)	6 (0.8)	51 (6.9)	18 (2.4)	43 (5.8)
2019	794 (100.0)	172 (21.7)	474 (59.7)	5 (0.6)	39 (4.9)	34 (4.3)	70 (8.8)
Total	**2887 (100.0)**	**645 (22.3)**	**1791 (62.0)**	**16 (0.6)**	**153 (5.3)**	**137 (4.7)**	**145 (5.0)**
Disease type							
PTB	1947 (100.0)	637 (32.7)	947 (48.6)	13 (0.7)	122 (6.3)	111 (5.7)	117 (6.0)
EPTB	940 (100.0)	8 (0.9)	884 (89.8)	3 (0.3)	31 (3.3)	26 (2.8)	28 (3.0)
Total	**2887 (100.0)**	**645 (22.3)**	**1791 (62.0)**	**16 (0.6)**	**152 (5.3)**	**137 (4.7)**	**145 (5.0)**
Drug regimen[1]							
Standard[1]	2884 (100.0)	644 (22.3)	1789 (62.0)	16 (0.6)	153 (5.3)	137 (4.8)	145 (5.0)
Retreatment[1]	3 (100.0)	1 (33.3)	2 (66.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Total	**2887 (100.0)**	**645 (22.3)**	**1791 (62.0)**	**16 (0.6)**	**152 (5.3)**	**137 (4.7)**	**145 (5.0)**
HIV status							
Negative	1883 (100.0)	513 (27.2)	1125 (59.7)	8 (0.4)	58 (3.1)	87 (4.6)	92 (4.9)
Positive	961 (100.0)	128 (13.3)	633 (65.9)	8 (0.8)	94 (9.8)	48 (5.0)	50 (5.2)
Total	**2844 (100.0)**	**641 (22.5)**	**1758 (61.8)**	**16 (0.6)**	**152 (5.3)**	**135 (4.7)**	**142 (5.0)**
HIV/ART Services							
Not taking ARVs	66 (100.0)	8 (12.1)	36 (54.5)	0 (0.0)	11 (16.7)	1 (1.5)	10 (15.2)
Taking ARVs	715 (100.0)	97 (13.6)	483 (67.6)	5 (0.7)	64 (9.0)	34 (4.8)	32 (4.5)
Not Applicable	1882 (100.0)	513 (27.3)	1124 (59.7)	8 (0.4)	58 (3.1)	87 (4.6)	92 (4.9)
Total	**2663 (100.0)**	**618 (23.2)**	**1643 (61.7)**	**13 (0.5)**	**133 (5.0)**	**122 (4.6)**	**134 (5.0)**

NB: 1) Standard regimen (2RHEZ/4RH); Retreatment (2HREZS/1RHEZ/5RHE)

For the retreatment cases, approximately 74% success was recorded in all the age groups with the lowest (65%) recorded in the age group of 15-24 years. Unlike the new cases, more deaths were recorded, ranging from 4.1% to 6.8% in the various age groups. Also, 10.1% deaths were recorded among the HIV positives than their negative counterparts (3.1%). Lost-to-follow-up and transferred out were 6.2% and 11.1% respectively, table 3.5.

Table 3.5: Treatment outcomes by baseline characteristics of patients registered with tuberculosis for retreatment TB at Laquintinie Hospital Douala – Cameroon, from 2016 to 2019

	Frequency (%)						
Category	**Total**	**Cured**	**Completed**	**Failed**	**Died**	**Lost**	**Transferred out**
Total	**434 (100.0)**	**125 (28.8)**	**198 (45.6)**	**6 (1.4)**	**30 (6.9)**	**27 (6.2)**	**48 (11.1)**
Age							
0-14	12 (100.0)	2 (16.7)	7 (58.3)	0 (0.0)	1 (8.3)	0 (0.0)	2 (16.7)
15-24	37 (100.0)	11 (29.7)	13 (35.1)	1 (2.7)	3 (8.1)	2 (5.4)	7 (18.9)
25-34	98 (100.0)	25 (25.5)	42 (42.9)	1 (1.0)	4 (4.1)	7 (7.1)	19 (19.4)
35-44	134 (100.0)	42 (31.3)	63 (47.0)	1 (0.7)	8 (6.0)	7 (5.2)	13 (9.7)
45-54	93 (100.0)	29 (31.2)	42 (45.2)	2 (2.2)	10 (10.8)	6 (6.5)	4 (4.3)
55+	60 (100.0)	16 (26.7)	31 (51.7)	1 (1.7)	4 (6.7)	5 (8.3)	3 (5.0)
Total	**434 (100.0)**	**125 (28.8)**	**198 (45.6)**	**6 (1.4)**	**30 (6.9)**	**27 (6.2)**	**48 (11.1)**
Gender							
Male	252 (100.0)	68 (27.0)	113 (44.8)	4 (1.6)	14 (5.6)	20 (7.9)	33 (13.1)
Female	182 (100.0)	57 (31.3)	85 (46.7)	2 (1.1)	16 (8.8)	7 (3.8)	15 (8.2)
Total	**434 (100.0)**	**125 (28.8)**	**198 (45.6)**	**6 (1.4)**	**30 (6.9)**	**27 (6.2)**	**48 (11.1)**
Year							
2016	96 (100.0)	35 (36.5)	46 (47.9)	0 (0.0)	7 (7.3)	2 (2.1)	6 (6.3)
2017	92 (100.0)	12 (13.0)	52 (56.5)	0 (0.0)	10 (10.9)	11 (12.0)	7 (7.6)
2018	120 (100.0)	46 (38.3)	46 (38.3)	4 (3.3)	7 (5.8)	3 (2.5)	14 (11.7)
2019	126 (100.0)	32 (25.4)	54 (42.9)	2 (1.6)	6 (4.8)	11 (8.7)	21 (16.7)
Total	**434 (100.0)**	**125 (28.8)**	**198 (45.6)**	**6 (1.4)**	**30 (6.9)**	**27 (6.2)**	**48 (11.1)**
Disease type							
PTB	358 (100.0)	123 (34.4)	140 (39.1)	6 (1.7)	27 (7.5)	23 (6.4)	39 (10.9)
EPTB	76 (100.0)	2 (2.6)	58 (76.3)	0 (0.0)	3 (3.9)	4 (5.3)	9 (11.8)
Total	**434 (100.0)**	**125 (28.8)**	**198 (45.6)**	**6 (1.4)**	**30 (6.9)**	**27 (6.2)**	**48 (11.1)**
Drug regimen[1]							
Standard[1]	290 (100.0)	90 (31.0)	130 (44.8)	4 (1.4)	15 (5.2)	20 (6.9)	31 (10.7)
Retreatment[1]	144 (100.0)	35 (24.3)	68 (47.2)	2 (1.4)	15 (10.4)	7 (4.9)	17 (11.8)
Total	**434 (100.0)**	**125 (28.8)**	**198 (45.6)**	**6 (1.4)**	**30 (6.9)**	**27 (6.2)**	**28 (11.1)**
HIV status							
Negative	227 (100.0)	79 (34.8)	91 (40.1)	4 (1.8)	7 (3.1)	17 (7.5)	29 (12.8)
Positive	202 (100.0)	46 (22.8)	105 (52.0)	2 (1.0)	22 (10.9)	9 (4.5)	18 (8.9)
Total	**429 (100.0)**	**125 (29.1)**	**196 (45.7)**	**6 (1.4)**	**29 (6.8)**	**26 (6.1)**	**47 (11.0)**
HIV/ART services							
Not taking ARVs	3 (100.0)	1 (33.3)	0 (0.0)	0 (0.0)	2 (66.7)	0 (0.0)	0 (0.0)
Taking ARVs	183 (100.0)	41 (22.4)	96 (52.5)	2 (1.1)	17 (9.3)	9 (4.9)	18 (9.8)
Not Applicable	226 (100.0)	79 (35.0)	90 (39.8)	4 (1.8)	7 (3.1)	17 (7.5)	29 (12.8)
Total	**412 (100.0)**	**121 (29.4)**	**186 (45.1)**	**6 (1.5)**	**26 (6.3)**	**26 (6.3)**	**47 (11.4)**

NB: 1) Standard regimen (2RHEZ/4RH); Retreatment (2HREZS/1RHEZ/5RHE)

3.4 Factors associated with unsuccessful treatment outcomes of patients with tuberculosis at Laquintinie Hospital Douala – Cameroon, from 2016 to 2019: new and retreatment cases

3.4.1 New treatment cases

Tables 3.6 provides detailed accounts of the results of the binary regression analysis (bivariate and multivariate analysis) of selected factors associated with unsuccessful TB treatment outcomes for the new cases.

During the bivariate analysis, TB patients in the age group 0-14 years (OR 0.39, 95% CI: 0.23 - 0.66), having extrapulmonary TB (OR 0.45, 95% CI: 0.35 – 0.58), and those for whom smear results were not applicable at diagnosis (OR 0.58, 95% CI: 0.42 - 0.80) had less risk of unsuccessful treatment outcome. However, being HIV positive (OR 1.76, 95% CI: 1.43 - 2.16), heavy smear (OR 1.69, 95% CI: 1.24 - 2.32), being diagnosed and having treatment in the years 2017 (OR 2.56, 95% C.I: 1.83 - 3.56), 2018 (OR 2.05, 95% C.I: 1.47 – 2.87), 2019 (OR 2.49, 95% C.I: 1.80 – 3.45) showed increased risk of unsuccessful outcome (table 5).

In the multivariate analysis model, we adjusted for all the variables in the table: age, gender, year of diagnosis, disease type, HIV status and smear results before treatment. TB patients aged 55years and above had about 50% increased risk of unsuccessful treatment outcomes (aOR 1.53, 95% CI: 1.07 - 2.18) compared to those 25-34 years. Furthermore, compared to HIV-negatives, being HIV positive had more than double risk of unsuccessful treatment outcomes (aOR 2.26, 95% CI: 1.75 - 2.92). Patients with initial smear results (+) (aOR 1.57, 95% CI: 1.10 - 2.22) and initial smear results (++) (aOR 2.01, 95% CI: 1.43 - 2.83) had higher risk of unsuccessful treatment outcome than those who has negative smear results. The risk of unsuccessful treatment was almost double if being diagnosed and treated in 2017 (aOR 1.85, 95% C.I: 1.25 – 2.73) and 2019 (aOR 2.13, 95% C.I: 1.48 – 3.06) compared to their counterparts in 2016 (table 3.6).

Table 3.6: Association between unsuccessful treatment outcomes and selected determinants among new tuberculosis patients registered at Laquintinie Hospital Douala – Cameroon, 2016 to 2019

Variable	Total	Frequency (%)		OR	95% C.I	aOR	95% C.I
		Success	Unsuccess				
Age	2887	2436 (84.4)	451 (15.6)				
25-34	750	630 (84.0)	120 (16.0)	-		-	
0-14	247	230 (93.1)	17 (6.9)	**0.39**	**0.23 - 0.66**	0.66	0.35 - 1.22
15-24	435	375 (86.2)	60 (13.8)	0.84	0.60 - 1.18	0.94	0.65 - 1.37
35-44	608	509 (83.7)	99 (16.3)	1.02	0.76 - 1.37	0.91	0.65 - 1.26
45-55	409	338 (82.6)	71 (17.4)	1.10	0.80 - 1.52	1.06	0.74 - 1.52
55+	438	354 (80.8)	84 (19.2)	1.25	0.92 - 1.70	**1.53**	**1.07 - 2.18**
Gender	2886	2435 (84.4)	451 (15.6)				
Male	1557	1305 (83.8)	252 (16.2)	1.10	0.89 - 1.34	1.17	0.93 - 1.48
Female	1329	1130 (85.0)	199 (15.0)	-		-	
Year of diagnosis	2887	2436 (84.4)	451 (15.6)				
2016	677	620 (91.6)	57 (8.4)	-		-	
2017	673	545 (81.0)	128 (19.0)	**2.56**	**1.83 - 3.56**	**1.85**	**1.25 – 2.73**
2018	743	625 (84.1)	118 (15.9)	**2.05**	**1.47 – 2.87**	1.47	0.99 – 2.17
2019	794	646 (81.4)	148 (18.6)	**2.49**	**1.80 – 3.45**	**2.13**	**1.48 – 3.06**
Disease type	2887	2436 (84.4)	451 (15.6)				
PTB	1947	1584 (81.4)	363 (18.6)	-		-	
EPTB	940	852 (90.6)	88 (9.4)	**0.45**	**0.35 0.58**	0.48	0.05 4.92
HIV Status	2844	2399 (84.4)	445 (15.6)				
Negative	1883	1638 (87.0)	245 (13.0)	-		-	
Positive	961	761 (79.2)	200 (20.8)	**1.76**	**1.43 - 2.16**	**2.26**	**1.75 - 2.92**
Initial smear results	2493	2106 (84.5)	387 (15.5)				
Negative	506	428 (84.6)	78 (15.4)	-		-	
Positive +	518	423 (81.7)	95 (18.3)	1.23	0.89 - 1.71	**1.57**	**1.10 - 2.22**
Positive ++	530	405 (76.4)	125 (23.6)	**1.69**	**1.24 - 2.32**	**2.01**	**1.43 - 2.83**
Positive +++	13	12 (92.3)	1 (7.7)	0.46	0.06 - 3.57	0.47	0.06 - 3.72
Non Applicable	926	838 (90.5)	88 (9.5)	**0.58**	**0.42 - 0.79**	1.37	0.13 - 14.14

3.4.2 Retreatment cases

Table 3.7 shows the crude odds and adjusted odds of the selected factors associated with unsuccessful TB treatment outcomes for the retreatment cases.

In the binary analysis, being diagnosed and receiving treatment in years 2017 (OR 2.26, 95% C.I: 1.16 – 4.79), 2019 (OR 2.51, 95% C.I: 1.29 – 4.89) showed increased risk of unsuccessful treatment outcome than those in 2016.

In the multivariate analysis, we adjusted for age, gender, year of diagnosis, disease type, HIV status and smear results before treatment.

The risk of unsuccessful treatment outcome was more than double among those diagnosed and treated in 2017 (aOR 0.53, 95%CI: 1.05 - 6.10), about three times in 2019 (aOR 2.93, 95% C.I: 1.34 – 6.43) compared with those in 2016. However, the risk of unsuccessful treatment outcome was lower in the age groups of 35-44 years (aOR 0.50, 95% CI: 0.25 - 0.98), 55 years and above (aOR 0.36, 95% CI: 0.14 - 0.93) compared to those 25-34 years, table 3.6.

Table 3.7: Association between unsuccessful treatment outcomes and selected determinants among tuberculosis patients getting retreatment registered at Laquintinie Hospital Douala – Cameroon, 2016 to 2019

Variable	Total	Frequency (%)		OR	95% C.I	aOR	95% C.I
		Success	Unsuccess				
Age	434	323 (74.4)	111 (25.6)				
25-34	98	67 (68.4)	31 (31.6)	-		-	
0-14	12	9 (75.0)	3 (25.0)	0.72	0.18 - 2.85	1.16	0.25 - 5.43
15-24	37	24 (64.9)	13 (35.1)	1.17	0.53 - 2.60	1.03	0.41 - 2.60
35-44	134	105 (78.4)	29 (21.6)	0.60	0.33 - 1.08	**0.50**	**0.25 - 0.98**
45-55	93	71 (76.3)	22 (23.7)	0.67	0.35 - 1.27	0.58	0.25 - 1.20
55+	60	47 (78.3)	13 (21.7)	0.60	0.28 - 1.26	**0.36**	**0.14 - 0.93**
Gender	434	323 (74.4)	111 (25.6)				
Male	252	181 (71.8)	71 (28.2)	1.39	0.89 - 2.17	1.24	0.72 - 2.14
Female	182	142 (78.0)	40 (22.0)	-			
Year of diagnosis	434	323 (74.4)	111 (25.6)				
2016	96	81 (84.4)	15 (15.6)	-		-	
2017	92	64 (69.6)	28 (30.4)	**2.36**	**1.16 – 4.79**	**2.53**	**1.05 – 6.10**
2018	120	92 (76.7)	28 (23.3)	1.64	0.82 - 3.29	1.80	0.77 – 4.23
2019	126	86 (68.3)	40 (31.7)	**2.51**	**1.29 – 4.89**	**2.93**	**1.34 – 6.43**
Disease type	434	323 (74.4)	111 (25.6)				
PTB	358	263 (73.5)	95 (26.5)	-		-	
EPTB	76	60 (78.9)	16 (21.1)	0.74	0.41 - 1.34	0.58	0.02 - 18.02
HIV Status	429	321 (74.8)	108 (25.2)				
Negative	227	170 (74.9)	57 (25.1)	-		-	
Positive	202	151 (74.8)	51 (25.2)	1.01	0.65 - 1.56	1.21	0.69 - 2.14
Initial smear results	377	287 (76.1)	90 (23.9)				
Negative	84	67 (79.8)	17 (20.2)	-		-	
Positive +	114	83 (72.8)	31 (27.2)	1.47	0.75 - 2.89	1.74	0.85 - 3.57
Positive ++	104	77 (74.0)	27 (26.0)	1.38	0.69 - 2.75	1.28	0.61 - 2.70
Positive +++	2	2 (100)	0 (0)	0.00	0.00	0.00	0.00
Non Applicable	73	58 (79.5)	15 (20.5)	1.02	0.47 - 2.22	1.70	0.06 - 51.35

CHAPTER FOUR

4.0 DISCUSSIONS, CONCLUSION AND RECOMMENDATIONS

4.1 Discussion

This study describes the treatment outcomes of registered TB patients, new and retreatment cases in Laquintinie Hospital of Douala, thus provides information on the epidemiology of TB in Douala, one of the main cities in Cameroon. TB was slightly more common in young adult males in both the new and retreatment groups. The HIV seropositivity rate was 33.3% and 46.5% in the new and retreatment cases, respectively. The overall treatment success rates were 84.4% in the new cases, and 74.4% in the retreatment cases. Aged 55 years and above, having HIV test positive, having initial smear results of (+) and (++), and being treated in 2017 and 2019 were associated with a higher proportion of treatment unsuccess among the new cases. Poor treatment in the retreatment cases was determined by being diagnosed and treated in the years 2017 and 2019.

4.1.1 Gender description of the study population

Similar to other studies done in the same hospital in Douala [31], Ethiopia [55], India [60], Uzbekistan [61], Nepal [62] we observed a higher number of TB in males than females. Also the WHO reports that globally, more males being infected with TB than females (almost 2:1 male to female ratio) [46]. However, studies in: Pakistan showed TB more in females than males; perhaps reason being the women have more restrictions to movements, and thus will commonly use the small diagnostic centres and health facilities that are closer to their houses where they can access by foot [63]; rural China where females visit lower local health facilities as compared to the men who rather seek health care in larger facilities [64]. The high proportion of TB in males in our study, could be due to social factors such as smoking and high alcohol consumption. In Cameroon, the proportion of males that consume alcohol is at least 1.5 times higher than that of females [65, 66], likewise a higher proportion of males (13.9%) who use tobacco products as compared to females (4.3%) [67]. Besides, other factor such as job-related risk could contributed to the high prevalence in males than females [46]. However, there seem to be no significant biological differences in immune response causing the different incidences [68].

4.1.2 Age description of the study population

As reported in other studies [10, 69], we also observed a high proportion of TB among the adults. Unlike children around the age of 10years, adolescence and young adults turn to be more prone to TB disease from progression of latent infection. Also, the cumulative increasing prevalence of TB infection could also explain the common trend of higher incidence of TB disease with increase age [26, 70]. Thus as reported by the WHO, like in most African other states, it is likely that the TB infection in Cameroon is more prevalent amongst young adults than in high-income countries where the disease is predominantly among the elderly who may have been infected a long time ago and may get reactivations [46], or among immigrants from high burden countries. The reduced risk of TB infections in high income countries during the last century has been due to improved health care/TB programs, improved economic, social status as compared to the low-income countries [31, 46].

4.1.3 TB type of the study population

The EPTB of the new cases and of the retreatment is high. This could probably be due to the fact that it is a tertiary hospital which receives referral cases from other health care facilities [56] and maybe also a reflection of high HIV prevalence in the country. Three new TB cases got the retreatment drugs (2HREZS/1RHEZ/5RHE), rather than the standard treatment (2RHEZ/4RH) recommended by the NCTP and WHO [50], being treated for miliary TB. Also, 66.8% of the retreatment cases got (2RHEZ/4RH). The facility did this for two reason – firstly, stock out of Streptomycin and secondly, they decided to commence with the modified treatment regimen for retreatment cases (3RHEZ/3RHEZ or 6RHEZ) as shown in table 1.2 which was to commence by 2020.

4.1.4 TB smear results of the population

In new cases, sputum microscopy found less than 1% strongly positive (+++), and almost a third each for (++), (+) and negatives. Tenue *et al.*, [59], showed less than 1% (++++), and using a different category may explain the difference, as both showed around 1% in highest bacteria load. However, El-Sony *et al.*, had among the 9.6% (514/5338) of the population who demonstrated acid fast bacilli 8.8% (+), 32.5% (++), and 58.8% (+++) [71]. Contrary to our study, this increase in percentage with grading could be because they worked with a population aged 15 – 49year old who could possibly produce good sputum.

4.1.5 HIV/AIDS status of the study population

We noticed high rate of TB patients with known HIV status (98.5%). The percentage of TB patients of with documented HIV results in Cameroon stands 93% [50], 86% for the African region and 69% globally [46]. This high testing could be because all opt-out testing for HIV is done for all diagnosed TB patients and vice versa as recommended by the Centers for Disease Control and Prevention (CDC) and WHO [32]. Also, probably due to the scale-up of HIV testing to attain the 95-95-95 UNAIDS target, all people who come to the health facility are counselled and asked to do an HIV test by the physicians/psychosocial workers. One third of the new cases and almost one half of the retreatment cases tested positive to HIV on average. The co-infection rate in this study is quite high though similar to 37.6% gotten by [31] and 35.6% gotten by [59] in Cameroon, 38% in San Francisco, US [54] and higher than 19% gotten by [72] in Thailand. Though the HIV prevalence of Cameroon (15 – 59years) has been declining over the past years, from 4.8% in 2002 to 4.1% in 2012 to 3.1% in 2019 [73], the TB-HIV co-infection status has not been good with Cameroon being ranked by the WHO among the top 41 high TB-HIV burden countries in 2014 [74] to top 30 countries with high TB/HIV burden in the world and in the top 20 countries with the highest estimated number of incident TB cases among PLW HIV in 2019 [46].

4.1.6 Successful treatment outcome

The overall success rate success rate was (2436+323)/(2887+434) = 83.1% and is overall success rate obtained by Mbatchou *et al*., in a previous study at same hospital in was 75.2% [31]. This result is also better than success rates from other studies in Cameroon with 68.1% in Yaounde, [10], 78% in South West Region [59] and also other African studies, Ethiopia (60.1%) [75]; Nigeria (74%) [69], and Somalia (81.8%) [76]. The success rate of the new cases, 84.4% is closed to the target recommended by the WHO (85%) [46] and that of the Cameroon National TB Control Program (87%) [50] while that of the retreatment cases 74.4% is less. The intensification of the community-based interventions programs and treatment done as spelled out by NCTB may have improved treatment success and, also reduce those lost-to-follow-up. Moreover, the collaboration between the MOH, and the CDC implementing partners in the domain of TB, HIV and the decentralization of diagnosis and treatment centres have possibly increased the awareness of the importance of treatment adherence, ensuring early HIV testing for those diagnosed with TB, proper DOTS follow-up might have also improved on the success

rate. However, other underlining factors such as poor living conditions, undernutrition, other comorbidities might have contributed to making the success rate below the expected value.

Treatment completed was recorded as results in 62.0% and 45.6% in the new and retreatment group, respectively. In both groups, the highest rates of treatment complete was recorded in the age groups 0 – 14 years while the lowest in 15-24 years. This could be because parents will want their children to get well, thus will do their best to ensure their kids take their medications to the end. Well as puberty sets in, there is slightly lower "compliance" with respect to taking the medications to the end especially when they start feeling well.

4.1.7 Age, comorbidities, and treatment outcome

The percentage of deaths increased progressively with increasing age especially in the new treatment group. Age related changes of the immune system can enhance susceptibility of the elderly to infectious diseases, failure of some vaccines, autoimmunity and also death [77].

Moreover, this could be due to a variety of factors, including HIV and other comorbidities like diabetes. Haungu *et al.*, in a systematic review showed very high association between patients with TB-diabetes mellitus and death [12]. Again, the case fatality among those positive for HIV in the new and retreatment groups was about three times to those HIV negative. Among the new cases, being HIV positive and not taking ART accounted for twice the number of deaths compared to those HIV positive and taking ARTs. A high association of mortality and HIV infection has been reported in many studies [10, 31, 54, 55, 69]. Those co-infected with HIV/TB are more likely to experience toxic reactions to drugs than those who are not HIV-infected, increase pill burden since they will possibly have to take the HIV and TB drugs with the possible impact on adherence.

4.1.8 Lost-to-follow-up

An overall lost-to-follow-up of 4.9% was recorded. Several values of lost-to-follow-up have been reported: 4.2% in [78], 9.5% in [59], 20.1% in [10] in Cameroon; in several parts of the world: 2.9%, 3.4%, 16% and 17.4% in [79-82]. The differences noticed could be at the level of organization of the DOTS strategies adapted at the various settings. Like [59], more males were lost-to-follow-up than females in our study. The reason could be because women are more likely to follow and possibly adhere to treatment as compared to men in our settings [59] and in general [83]. Moreover, men are more mobile in this our settings for economic reasons.

4.1.9 Treatment failure

Similar to [10, 59, 78], less than 2% failures were recorded in our study. Treatment failure after the standard treatment means the cases will have to be retreated. For those who failed after the retreatment, perhaps they did not adhere to the treatment or maybe multi drug resistant (MDR) TB has developed. This is not good for public health; thus, new investigations must be done including testing for MDR TB with GeneXpert and culture.

4.1.10 Determinants of unsuccessful treatment outcome

The determinants of unsuccessful treatment outcome in the new cases detected in multiple logistic regression analysis were: 55years and above, being HIV positive, patients with initial smear results of (+) / (++) and being diagnosed and treated in 2017. For the retreatment cases, the risk of unsuccessful treatment outcome was more than double among those diagnosed and treated in 2017 about three times in 2019. The reason for those aged 55 years above having increased risk of unsuccessful treatment outcomes could have been due to increased presence of comorbidities including diabetes [12].

The year 2016 had a better treatment outcome as compared to all the other years as we move from 2017 to 2019. Year of diagnosis and treatment were strongly associated with treatment unsuccess with the years 2017 and 2019 having increases risk of treatment unsuccess. One might one to think that the socio-political crisis in the country that began in 2017 (started as the strike of teachers of the English subsystem of education and common law lawyers) might have indirectly affected the management of the patients or influence the day-to-day activities, livelihood of the general population and TB patients, making them not to come for their drugs, being lost-to-follow-up, thus treatment unsuccess. There is an influx of internally displaced persons (from the South West and North West regions of Cameroon (the UN refugee agency reports 679,393 from those two regions by March 2020 [84]), into the other parts of the country including Douala due to the ongoing crisis in those mentioned regions. Some of these people might have TB, while others might be coming to live in the home of others that have or are currently being treated for TB. This may have led to poor follow-up of the TB patients by the limited health staff resulting to the declining treatment success across these years. Moreover, these people have to deal with other issues of their lives ranging from affected livelihood and economic activities, overcrowded housing, psychological stress, poor nutrition, which might have affected their treatment adherence and also their final outcome.

4.2 Strengths and limitations

4.2.1 Strengths

This study has several strengths. It uses data from routing setting and thus reflects the reality on the field - Douala, Littoral region of Cameroon. It uses standard categories of TB and can easily be compared with other studies. Double data entry was done to have quality assured data that was a truly a copy of the registers.

4.2.2 Limitations

There are some limitations to the study. This is routine TB registers, not research registers. Therefore, the data will contain some common errors and mistakes and omissions which may have affected the results.

Secondly, variables not included in the registers are of course not available for analysis. Hence, many risk factors cannot be identified such as socio-economic status, household situation, alcohol consumption, social and behavioural factors.

Thirdly, being a reference hospital, quite number of patients were transferred to a place closer to their homes; thus, final treatment outcome could not be ascertained for them.

4.3 Conclusion

All in all, in this cohort, the success rate in the new cases was 84.4% and that of the retreatment cases 74.5%, below the target set by the National TB Control program and WHO. Overall success rate was higher than a previous study in the same area. Unsuccessful treatment was more common at the end of the study than the start, and HIV positive patients had a double risk of unsuccessful outcome. Around 10% of HIV positive TB patients died and only around 3% in HIV negatives. For new cases, unsuccessful treatment outcome was higher in patients aged >54years than those aged 25-34years, higher for patients with initial smear results of (+) and (++).

4.4 Recommendations

We therefore recommend the following:

To researchers

- Conduct further research to identify and evaluate socio-economic factors not captured in the TB registers which could be potential barriers to treatment success.

For the National TB Control Program and ministry of public health (MoH)

- To follow-up and ensure timely and proper documentation of lab results and other vital data not captured into the TB register.
- Trace the lost-to-follow-up cases as they might still be positive and spreading the TB in the community.
- Follow up of the failed retreatment cases to identify if drugs were not taken, testing for MDR TB with GeneXpert and culture.

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APPENDICES

Appendix 1: Administrative authorization from the director of Laquintinie Hospital of Douala, Cameroon

REPUBLIQUE DU CAMEROUN
PAIX – TRAVAIL – PATRIE

MINISTERE DE LA SANTE PUBLIQUE

DIRECTION HOPITAL LAQUINTINIE

BP 4035 – DOUALA CAMEROUN
TEL/FAX. : (237) 33 42 15 40
Email : hopital_laquintinie@yahoo.fr

REPUBLIC OF CAMEROON
PEACE – WORK – FATHERLAND

MINISTRY OF PUBLIC HEALTH

HEAD OFFICE OF THE
LAQUINTINIE HOSPITAL

BOX 4035 – DOUALA CAMEROON
TEL/FAX. : (237) 33 42 15 40
Email : hopital_laquintinie@yahoo.fr

N°____/AR/MINSANTE/DHL/CM

AUTORISATION DE RECHERCHE

Monsieur FONCHA Robert NUIFONDIENG, Etudiant au Centre International de Santé – Université de Bergen, est autorisée à effectuer une recherche de trois (03) mois pour la période allant de **novembre 2020 à janvier 2021** au sein de l'Hôpital Laquintinie de Douala, sur le thème : **«Evaluation des résultats du traitement des patients atteints de tuberculose enregistrés à l'Hôpital Laquintinie de Douala-Cameroun : Une étude rétrospective de cohorte».**

Les travaux s'effectueront sous la supervision du **Dr ESSOLA Josiane épse ETAMBA**, Médecin Biologiste, dans le respect du code d'éthique et de déontologie en vigueur à l'Hôpital Laquintinie de Douala.

Toute publication de ce travail devra préserver les intérêts de l'Hôpital et des personnels y ayant participé. Une copie sera transmise au Centre de Documentation pour archivage.

En foi de quoi la présente Autorisation de Recherche est délivrée pour servir et valoir ce que de droit.

Fait à Douala, le 03 NOV 2020

Le Directeur de l'Hôpital Laquintinie de Douala Par Intérim,

Pr ESSOMBA Noël Emmanuel

AMPLIATIONS :
- CM
- SG/Coordo Secteur
- CSP
- SUPERVISEUR(S)
- INTERESSE(E)
- CHRONO/ARCHIVE

Appendix 2: Ethical approval from Faculty of Health Sciences – Institutional Review Board (FHS – IRB), Cameroon

UNIVERSITY OF BUEA
P.O BOX 63
Buea, CAMEROON
Tel:(237) 332 21 34/332 28 13
Fax: (237) 332 22 72

REPUBLIC OF CAMEROON
PEACE- WORK- FATHERLAND

FACULTY OF HEALTH SCIENCES- INSTITUTIONAL REVIEW BOARD
IRB00008917-US Office for Human Research Protection (OHRP)IORG007426

Secretary : **Professor. Halle-Ekane Edie Gregory**

Your Ref _____

Our Ref: **2021/ 1256-12/UB/SG/IRB/FHS** Date: 13 JAN 2021

Notice of Ethical Approval

Application number: **1256-12**

Principal Investigator: **Foncha Robert Nuifindieng**

Study Title: **Assessment of treatment outcomes of registered tuberculosis patients in the Laquintinie Hospital of Douala, Cameroon: A retrospective cohort study**

Application Type: **Initial**
Sponsor: **Student**
Review Type: **Normal**
Date of Approval: **13th January 2021**
Expiration Date: **One year**

Principal Investigator's responsibilities:

1. The study must be conducted in strict accordance with the protocol approved by the Board
2. Changes to the protocol or its related consent documents must be approved by the Board before implementation
3. Adverse events or unanticipated problems must be reported promptly to the Board
4. Participants must receive a copy of the consent document, if appropriate
5. The Principal Investigator is responsible for the on-going conduct of the study. The study must be implemented according to national and international guidelines for the ethical conduct of research on humans. He must collaborate with the IRB's monitoring of the study's implementation.
6. Any future correspondence must include the application number, and the PI's name in the subject line.
7. A renewal application or project closure report must be submitted at least one month prior to the expiration date indicated above. These must be done using the FHSIRB's secretariat AND an electronic copy sent to: irbfhs@gmail.com, making sure to reference the application number indicated above. This form is available at http://www.healthresearchweb.org/en/cameroon/institution2130

Prof. Halle Ekane Edie Gregory
Secretary; Institutional Review Board
Faculty of Health Sciences University of Buea

Appendix 3: Response from ethical committee, REK vest – Norway

REK
REGIONALE KOMITEER FOR MEDISINSK OG HELSEFAGLIG FORSKNINGSETIKK

Region:	Saksbehandler:	Telefon:	Vår dato:	Vår referanse:
REK sør-øst C	Anders Strand		24.11.2020	154092
			Deres referanse:	

Sven Gudmund Hinderaker

154092 Behandlingsresultat hos tuberkulosepasienter ved et sykehus i Kamerun

Forskningsansvarlig: Universitetet i Bergen

Søker: Sven Gudmund Hinderaker

Søkers beskrivelse av formål:

Målet med studien er å undersøke behandlinsresultatene av tuberkulosebehandling. Dette gir ideer til hvordan man kan forbedre resultatene

The aim of the study is to assess the outcomes of treatment of tuberculosis, to find ways to improve the services.

REKs vurdering

Vi viser til søknad om forhåndsgodkjenning av ovennevnte forskningsprosjekt. Søknaden ble behandlet av Regional komité for medisinsk og helsefaglig forskningsetikk (REK sør-øst C) i møtet 29.10.2020. Vurderingen er gjort med hjemmel i helseforskningsloven (hfl.) § 10.

Slik komiteen har forstått søknadens innhold skal en ved bruk av helseopplysninger gjennomføre en retrospektiv registerstudie for å undersøke om helsetjenestene gitt ved en gitt virksomhet har hatt de ønskede resultatene og eventuelt peke på områder hvor tjenestene kan forbedres for å oppnå bedre behandlingsresultater.

Etter komiteens vurdering faller denne type studier utenfor helseforskningslovens saklige virkeområde og er ikke underlagt krav om forhåndsgodkjenning etter helseforskningsloven.

Prosjektet kan gjennomføres uten godkjenning av REK innenfor de ordinære ordninger for virksomheten med hensyn til for eksempel regler for taushetsplikt og personvern. Søker bør derfor ta kontakt med enten forskerstøtteavdeling eller personvernombud for å avklare hvilke retningslinjer som er gjeldende.

Vedtak

Avvist (utenfor mandat)

REK sør-øst C
Besøksadresse: Gullhaugveien 1-3, 0484 Oslo
Telefon:22 84 55 11 | **E-post**:rek-sorost@medisin.uio.no
Web:https://rekportalen.no

Etter søknaden fremstår ikke prosjektet som medisinsk og helsefaglig forskning, og faller utenfor helseforskningslovens virkeområde, jf. helseforskningsloven § 2.

Komiteens avgjørelse var enstemmig.

Med vennlig hilsen

Britt Ingjerd Nesheim
Prof. dr. med.
Leder REK sør-øst C

Øyvind Grønlie Olsen
Seniorrådgiver REK sør-øst

Dokumentet er elektronisk signert

Kopi av vedtak: Forskningsansvarlig institusjon

Klageadgang
Du kan klage på komiteens vedtak, jf. forvaltningsloven § 28 flg. Klagen sendes til REK sør-øst C. Klagefristen er tre uker fra du mottar dette brevet. Dersom vedtaket opprettholdes av REK sør-øst C, sendes klagen videre til Den nasjonale forskningsetiske komité for medisin og helsefag (NEM) for endelig vurdering.

Appendix 4: Sample pages of the TB register

Tuberculosis Programme **Tuberculosis Register (page 1/2)**

Date registered	BMU TB No.	Name	Sex M/F	Age	Address	Treatment Unit	Treatment start date	Regimen*	Disease site P/EP	Type of case†					
										New	Relapse	Treatment after failure	Treatment after default	Transfer in	Other

* **New case:** RHZE
Retreatment: S

† **New:** never previously treated for as much as 1 month
Relapse: previously treated, declared cured, returns smear-positive
Transfer in: registered and started treatment in another unit

Treatment after failure: smear-positive ≥ 5 months after starting treatment, commenced on retreatment
Treatment after default: returned smear-positive after default, commenced on retreatment

Tuberculosis Programme **Tuberculosis Register (page 2/2)** Year:_____

Results of smear examination								Result of treatment *(tick)*‡							TB-HIV				
Before treatment		2 months		5 months		End treatment													
Result	Lab no./ date	Result	Lab no./ date	Result	Lab no./ date	Result	Lab no./ date	Date of result	Cured	Completed	Failure	Died	Defaulted	Transfer out	HIV result (P,N,I,D)§	CD4 count	CPT (Date)	ART (Date)	Remarks (Specify BMU if transferred, ART clinic, etc…)

‡ **Cured:** negative smear at end of treatment and on one previous occasion
Completed: completed treatment, but sputum examination not done for proof of cure
Failure: smear-positive at 5 months or later during treatment, confirmed by a second positive smear
§ HIV test: P = Positive; N = Negative; I = Indeterminate; ND = Not done.

Died: died from any cause while on treatment
Defaulted: failed to collect drugs for 2 months or more after date last seen
Transferred: sent to another BMU for continuation of treatment; treatment result unknown