Chapter One

Introduction

1.1 Background to the Study

Tuberculosis (TB) is a communicable disease that is still a public health issue globally[1]. TB is mostly manifested in the lungs and it is a result of *Mycobacterium tuberculosis*. M. tuberculosis has adapted to living by infiltrating the human immune system and remaining inside the host for decades. It is an intracellular species of bacteria with a mycolic acid coating that is quasi and generates cells once every 18–24 h. It can be averted and remedied using therapeutic effects. TB infection is airborne from person to person, so it is an air-borne disease. Accordingly, a cough, sneeze or spit from an infected person releases the bacterium, *M. tuberculosis* into the air. Hence, this causes an infection in an individual who has come in contact with such a contaminated environment[2]. Latent tuberculosis infection (LTBI) is characterized by constant immune response to M. tuberculosis antigen stimulation in the absence of clinically manifest active TB[3]. Globally, around a quarter of the population is infected with TB[3]. With an anticipated 10 million cases and 1.5 million fatalities in 2018, TB is the leading causes of mortality from a communicable disease worldwide. It is estimated that nearly 15 million new active TB cases are reported annually, with India, Nigeria, Indonesia, South the Philippines, Africa, China, Bangladesh, and Pakistan bear the heaviest burden[4]. The African continent recorded 24 percentage of global incidences and 32 percentage of fatalities. This involved countries with few of the world's deadliest tuberculosis outbreaks, particularly those with a higher HIV prevalence in the population[5]. Correspondence to the World Health Organization, 58

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million individuals have survived tuberculosis in this century alone[3]. Like other respiratory infections, TB has a tendency to cause lasting damage or destruction of host tissues. As a result, it progresses from a curable condition to chronic morbidity in both adults and young adults. Tuberculosis incidence, illness, and unfavorable effects are becoming more generally acknowledged during adolescence and early adulthood[6]. Adolescence is widely recognized as a developmental stage that influences many elements of future health and well-being[7]. In several nations of the world, the number of (10–19 years) as well as young adults (20–24 years) are far more than any other age group; youths from the ages of 10–24 years currently account for twenty-five percentage (25%) of the globe's populace. These young men and women are more probable to contract transmittable kinds of TB and have a much better variety of communal links outside the home[6]. As a result, in addition to being sick, teenagers and young adults with TB contribute to the disease's spread. The incidence of TB grows fast throughout adolescence in severe tuberculosis endemic environments, culminating in young adulthood[8]. According to a recent estimate, one million and eight hundred thousand adolescents and young adults (ages 10–24 years) contracted tuberculosis in 2012, accounting for 17% related to every new TB illness diagnoses worldwide. The WHO African region recorded that young people had the largest number of tuberculosis occurrences (534000, UI 359 000–912 000). WHO estimates that 8.6 million events of tuberculosis were reported in 2012, with 530,000 brand-new cases of TB being youngsters under the age of 15 and 74,000 child fatalities from the condition. These statistics were significantly above those in the previous year's record, indicating that even more tuberculosis cases were being reported amongst youngsters

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worldwide[9]. In Nigeria, the prevalence of tuberculosis in young adults from the ages of 15 and older was predicted to be 318 per 100,000 populace for smear-positive cases and also 524 as bacteriologically confirmed. Young adults are risky reproductive action groups who are especially susceptible to HIV/AIDS illness and, as a result, in danger of tuberculosis in the dual pandemic[10].

In addition, teenage years includes a duration of essential modification that integrates boosting vulnerability to TB with distinct developmental and societal features to produce specific threats for TB transmission, infection, and disease[11]. TB preventive and care measures that address the requirements of young adults are consequently needed for optimal attempts to eradicate TB for everyone. Whilst also setting and enforcing standards and consolidating infection prevention and control measures, WHO assists countries in preventing tuberculosis diseases[12]. These preventative measures are particularly vital in places where there is an elevated risk of TB transmission, such as health centers, community set-ups, as well as TB-affected family units[2]. WHO likewise improves preventive measures by detecting people with latent tuberculosis (LTBI) earlier and also offering TB preventive treatment (TPT) to individuals with LTBI and active TB, addressing co-morbidities and associated dangers, as well as disease-related health inequities, and having a major impact to global health-related accessibility[13]. However, WHO strongly recommends and routes the global study community's TB vaccination advancement programs by promoting clinical consensus, giving support on vaccination appraisal, as well as evaluating the clinical proof for plan initiatives. Targeting wider antecedents of TB outbreaks can also aid in the prevention of TB infection and illness. This will necessitate expanded

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TB screening at the local scale, improved TB testing follow-up at either the community and household levels, and expanded access to shorter (1–3 month) rifamycin-based regimens[3]. TPT, or TB preventative treatment, is a well-established aspect of care for persons coping with HIV, contacts of TB patients, those on immunotherapy, and anyone at risk for contracting TB. TPT's success is based on recognizing those who would gain most from it, using established efficacy regimens, and optimizing adherence to therapy till the end. Unless these steps are regularly applied, therapy may have a detrimental impact on TB transmission and medical costs. Tuberculosis current standard of care encompasses important phases in the programmatic management of TPT (PMTPT) maintaining the flow of preventative treatment: highlighting vulnerable populaces (PLHIV as a component of the HIV treatment plan, home links, and other people), eliminating active TB, running tests with respect to LTBI, prescribing medications, and also surveillance unfavourable reactions, compliance, and conclusion of therapy. Adolescents and young adults at superior risk of establishing TB gain from preventative treatment, typically 6 months of isoniazid. Isoniazid preventive treatment (IPT) is advised for household links of contagious instance of TB and that, upon testing, are discovered not to possess active TB on their own.

TB is alleviated with a benchmark 6-month program of four antibacterial medications under the control of the health worker or a qualified and experienced person, according to the Africa CDC. Multidrug-resistant tuberculosis (MDR-TB) is a type of tuberculosis triggered by bacteria that are resistant to the two prominent first-line anti-TB medications, isoniazid and rifampicin.MDR-TB can be treated and cured with

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second-line medications. Nevertheless, second-line therapy choices are restricted and need comprehensive radiation treatment (approximately two years of therapy) utilizing costly and harmful drugs. Extensively drug-resistant tuberculosis (XDR-TB) is a more severe type of MDR-TB induced by bacteria which do not react to one of the most comprehensive second-line anti-TB medications, often leaving individuals with no other options for treatment. The FDA issued a revised drug for XDR-TB on August14, 2019. Besides, there is a TB vaccine that is minimally successful. It offers only peripheral prevention against transmission of infection. The first effective step in mitigation is to prevent the transmission. This is accomplished by recognizing and curing patients with active tuberculosis. A further attribute is profiling people with unexposed tuberculosis and also preventing the development of active infectious tuberculosis. TB infection control by preventing transmission in various settings such as hospitals is a critical step in prevention. Pasteurization of dairy likewise assists in the prevention of bovine tuberculosis in humans. Preventing TB infection and limiting disease progression are crucial to reducing TB occurrence to the rates envisioned by the End TB Strategy[2].

1.2 Statement of the Problem

When children are treated for pulmonary tuberculosis, the outcomes are favorable; however, data on end results for youngsters (0–18 years) and young people (15–24 years) are without a doubt limited[13 15]. This limitation of the study is partially caused by a lack of clear meanings of age associates (i.e., pediatric, youngster, teen, and young people) and also an absence of government and neighborhood dedication to this specific age group[16].Youth may be understudied due to obstacles in developing

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progressions, increased obligations related to work, education, and also reliance on family commitment including young adults in research study [17]. Pediatric instances (0–18 years) represent 10 percent of all new and regressive TB cases in Africa, contrasted to 6.5 percent internationally. Furthermore, the African territory has the greatest account of tuberculosis in adolescents especially in contrast to any other region. Considering the large infection rates amongst more youthful age, impediments are typically researched in adult populaces. Considering the direct consequence, the obstacles to initiation of therapy in children and adolescents are less well understood[18]. Adolescents as well as young adults that develop TB are notably prone to be instrumental to ongoing transference in the neighborhood because they frequently exhibit 'adult-type' lung TB well-known to be sputum smear-positive.

Knowledge is critical in providing perspective into a person's views and behaviors. It is a critical factor in shaping a person's actions (over behavior). s actions (over behavior). Knowledge about TB infection prevention is a pivotal factor in the development of action plans to prevent and manage pulmonary tuberculosis disease among adolescents and young adults[19]. Thus, this study is done to assess the knowledge and practice of tuberculosis preventive measures among adolescents and young adults in Ifako-Ijaiye Local Government Area of Lagos State, Nigeria.

1.3 Justification of the Study

Adolescent tuberculosis poses distinct hurdles in regards to case discovery and also management[19]. Adolescents with tuberculosis may present to perhaps pediatric or adult health services, where care might probably be inadequate. Indication from the programmatic monitoring of human immunodeficiency virus (HIV) shows that

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adolescents have unique adherence support needs[20]. These young adults are more probable to acquire contagious types of TB and possess a more substantial variety of societal links outdoors. Thus, the TB burden among adolescents, as well as issues associated with their involvement and continuum in treatment, have lately been recognized as a prerogative aspect for adolescent health and wellness research study in low-and middle-income countries[21]. Most national tuberculosis programs (NTPs) do not document information with regard to the adolescent age group because adolescents are included in the WHO's 5–14 year as well as 15–24year age groups[22]. Despite the fact that adolescents are considered as key populations for TB transmission in the community, there have been few reports on adolescent TB in endemic areas. Adult TB cases have long received attention, and monitoring records have not been separated to enable evaluation of TB in adolescents. As a result, prophylactic and treatment programs frequently ignore young adults. This present study will however describe the prevalence of TB infection in Ifako-Ijaiye Local Government (LG) among adolescents and young adults, identifying preventive strategies carried out.

1.4 Aim and Objectives of the Study

The overall aim of the study is to assess the knowledge and practice of TB preventive measures among adolescents and young adults in Ifako-Ijaiye Local Government, Lagos State, Nigeria.

Specific Objectives

The specific objectives are to:

i. assess the knowledge of TB preventive measures among adolescents and young adults in Ifako-Ijaiye LGA

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ii. assess the practice of TB preventive measures among adolescents and young adults in Ifako-Ijaiye LGA

iii. identify the factors influencing the practice of TB preventive measures among adolescents and young adults in Ifako-Ijaiye LGA

1.5 Research Questions

i. What is the knowledge of TB preventive measures among adolescents and young adults in Ifako-Ijaiye LG?

ii. Describe the practice of TB preventive measures among adolescents and young adults in Ifako-Ijaiye LG?

iii. What are the factors influencing the practice of TB preventive measures among adolescents and young adults in Ifako-Ijaiye LG?

1.6 Significance of the Study

Tuberculosis is major negative impact due to its global health impact, public health implications, and emergence of drug-resistant strains, need for vaccine development, and social and economic impact. This study will be essential for the prevention and control of TB, early detection and treatment, reduction of stigma, and improved quality of life. It is therefore important to promote TB education and awareness among adolescents. This study will be essential for the development of effective vaccines against the disease. Currently, the Bacillus Calmette-Guérin (BCG) vaccine is the only vaccine available for TB, but it is not very effective against the most common form of TB.

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1.7 Scope of the Study

The scope of the study does not extend to all Local Government in Lagos State; the researcher The scope of the study does not extend to all Local Government in Lagos State; the researcher purposively selected six (6) health facilities which include: three (3) Primary Health Care Centers (PHCs), two (2) Private facilties and Ifako General Hospital in Ifako-Ijaiye Local Government Area (LGA) of Lagos State. The three (3) Primary Health Care Centers (PHCs) are Ifako PHC, Iju PHC and Agbado Kola PHC; and the two (2) private facilities are Longe Hospital and Ahmadiyyha Hospital.

1.8 Operational Definition of Terms

It is essential to provide operational definitions for some of the study's key terminologies in order to improve conceptual coherence and clarity. This is necessary to avoid conceptual ambiguity. The next sentence:

Contact: Anyone that was introduced to an individual infected with tuberculosis Household contact of TB patient: A that is staying or that had stayed in the same house as the contagious TB individual.

High TB Transmission Setting: An establishing with a significant recurrence of people with unexposed or undiscovered active TB, or where contagious TB individuals exist and there is a great threat of TB transference. TB infected individuals are most transmittable when they are without treatment or improperly treated. Proliferation is enhanced by aerosol-producing procedures and by the existence of extremely vulnerable people.

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Household Contact: An individual who exchanged the exact encased space as the instance ratio for several evenings or for regular or extended daytime durations throughout the 3 months prior to the commencement of current therapy.

Latent Tuberculosis Infection (LTBI): A circumstance of consistent immune reaction to activation by M. tuberculosis antigens without evidence of scientifically manifest active tuberculosis. This is likewise described to as TB infection. Generally, there is no gold basic test for direct recognition of M. tuberculosis infection in human beings. Majority of the infected individuals have very little signs and symptoms of TB yet are at risk for active TB illness.

Programmatic Management of Tuberculosis Preventive Treatment (PMTPT): All collaborated events through public and private health caretakers as well as the society focused on increasing TB preventative treatment to people that require it.

TB Preventive Treatment (TPT): Treatment provided to people that are regarded susceptible to TB disease in order to decrease that risk. Additionally, described as TB infection treatment, LTBI therapy or TB preventive treatment.

Tuberculosis (TB): This is a condition caused by M. tuberculosis. In this document, it is generally described as “active” TB or TB “disease” so as to differentiate it from TB infection.

WHO African Region: This includes- Algeria, Zimbabwe, Angola, Zambia, Benin, Botswana, Eswatini, Sierra Leone, Guinea-Bissau, Mauritius, Republic of the Congo, Burkina Faso, Eritrea, Tanzania, Burundi, Cameroon, Mali, Cape Verde, Liberia,

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Equatorial Guinea, Central African Republic, Ethiopia, São Tomé and Príncipe,

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Kenya, Chad, Uganda, Namibia, Comoros, Niger, Togo, Rwanda, Ivory Coast, South Sudan, Gambia, Malawi, Democratic Republic of the Congo, Seychelles, Guinea, Madagascar, South Africa, Mauritania, Ghana, Senegal, Mozambique, Lesotho, Gabon, Nigeria.

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Chapter Two

Literature Review

2.1 Conceptual Review

Tuberculosis

Pathophysiology

Aerosolization

This account of tuberculosis pathophysiology caused by *M. tuberculosis* will start where it will end: with the spread of pathogenic bacteria. There are various steps and criteria in the TB transmission cascade[1]. The presence of a source of bacteria-the index case-is the first criterion for transmission. That source must produce infectious particles, which means it must either have, either primary or active tuberculosis. Mucous membranes, weakened dermal layers, the digestive system, and, most commonly, the respiratory tract are all places where *M. tuberculosis* can infect healthy people[2]. An individual with active tuberculosis of the lungs or larynx who may aerosolize *M. tuberculosis* is the source, as mentioned[1]. The source generates these aerosolizations via forceful expiratory actions such as coughing, sneezing, shouting, or singing (Fig. 1A)[1,3]. M. tuberculosis can then survive in the air. Individuals who are susceptible inhale aerosolized *M. tuberculosis*. When inhaled, some of these droplets smaller than 5 µm in size and containing 1–3 bacilli can reach the alveolar sacs[3,4]. The size of the infectious particles, on the other hand, ranges from 0.65 to > 7 m[5]. The bacteria settle in the alveolar sacs once they reach them.

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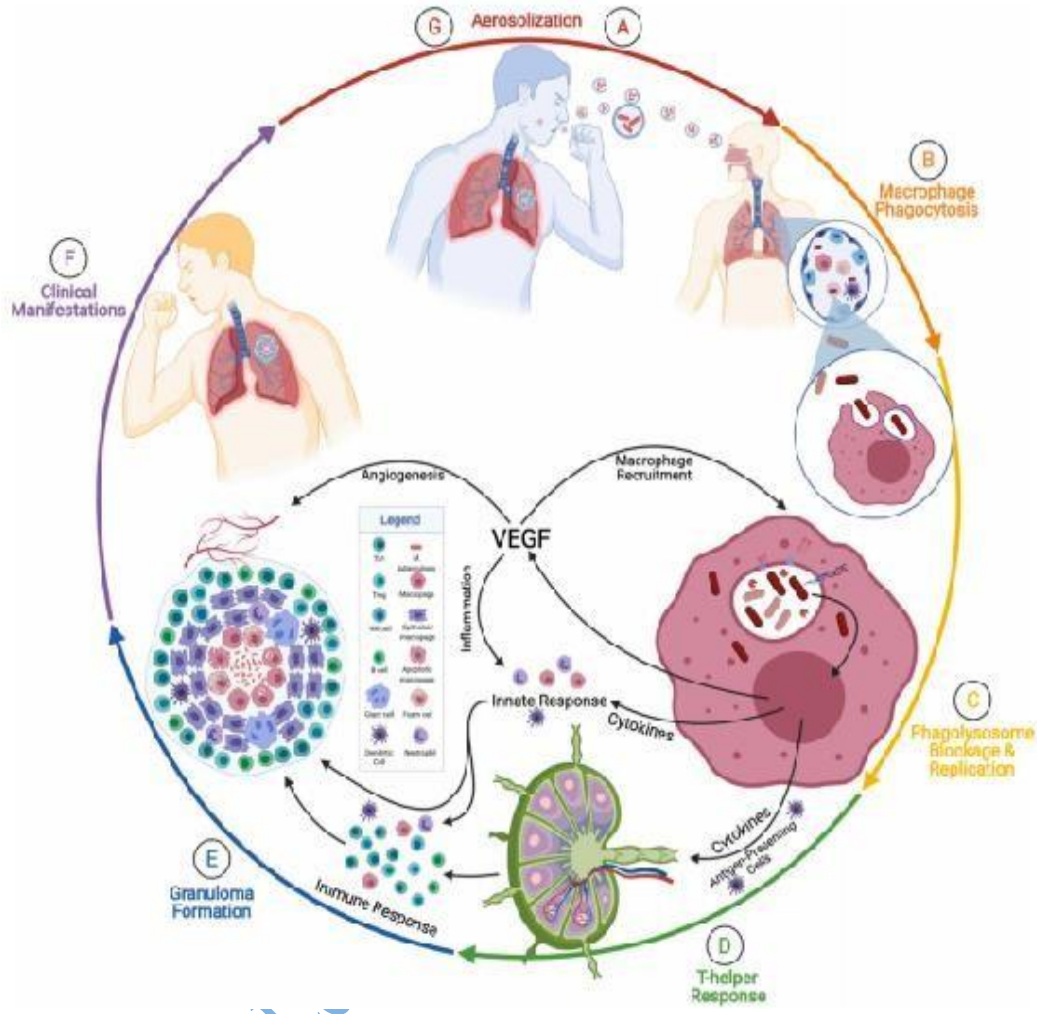

Figure 2.1: Seven Steps in the Pathophysiology of Active Tuberculosis. (Adapted from "Granuloma, 2021).

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Macrophage Phagocytosis

When *M. tuberculosis* has established itself in the alveolar sacs, the bacilli will make contact with alveolar macrophages, also known as dust cells in this context, as well as monocytes and dendritic cells (Fig. 1B)[6]. Because they operate in surfactant environments, alveolar macrophages are believed to have restricted bactericidal activity in tuberculosis[7]. *M. tuberculosis* will bind with dust cells via mannose

receptors, scavenger receptors, complement receptors (CR1, CR3, CR4), Fc receptors, and surfactant protein receptors (SPR)[8,9]. The pathogen recognition receptor mannose receptor monitors trafficking, antigen presentation, macrophage differentiation, and inflammation. The most widely available receptor on human monocyte-derived macrophages is the mannose receptor. Once *M. tuberculosis* binds to the mannose receptor, the mannose receptor gathers Grb2, which stimulates the Rac/Pak/Cdc-42 pathway of *M. tuberculosis* uptake. The Rac/Pak/Cdc-42 pathway is associated with *M. tuberculosis* absorption and recruits the Src homology 2 (SH2) domain-containing protein tyrosine phosphatase 1 (SHP-1).SHP-1 reduces the activity of the trafficking phospholipid phosphatidylinositol 3-phosphate (PI3P), curtailing phagosome and lysosome fusion[9]. Secretory acid phosphatase (SapM), a lipid phosphatase produced by *Mycobacterium tuberculosis*, also removes PI3P from the phagosome. Furthermore, PI3P is a binding molecule that interacts with lysosome proteins[10]. As a result, PI3P is a regulatory lipid required for the phagosome-lysosome consolidation and is removed in phagosomes containing live *M. tuberculosis*. Thereby, the Rac/Pak/Cdc-42/SHP-1/PI3P cascade enhances *M. tuberculosis* progress within alveolar macrophages[9]. Further to that, the bacilli have a diverse set of cell wall lipids that aid in macrophage evasion. Lipoarabinomannan (LAM), phosphatidylinositol mannoside (PIM), sulfated glycoplipid (SL), trehalosedimycolate (TDM), and dimycocerosate phthiocerol (DIM) are examples of these lipids. *M. tuberculosis* infectiousness is increased by LAM and PIM.SL and TDM prevent lysosome- phagosome fusion. DIM prevents acidification and intensifies phagosome permeability[9]. Inside the macrophages, the bacilli activate toll-like receptors (TLRs)

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and discharge mycolyl-arabinogalactanpeptidoglycan (MAGP), deoxyribonucleic acid (DNA), and ribonucleic acid (RNA) into the cytosol. These processes are carried out by the early secreted antigenic target, 6 kDA (ESX-1)/Type VII secretion system, which adversely affects the phagosome membrane[11]. The host TLRs will initiate the myeloid differentiation primary response 88 (MyD88) signaling pathway, as well as the nuclear factor kappa-light-chain enhancer of activated B cells (NF-B) and cytokines. The MAGP will be recognised by nucleotide-binding oligomerization domain 2 (NOD2)/caspase recruitment domain 15 (CARD15), that will activate NF-B and cytokines such as tumour necrosis factor (TNF), interleukin 1 beta (IL-1), interleukin (IL)-6, and Type I interferon (IFN)[12]. When bacterial DNA enters the cytosol, it induces the stimulator of interferon genes STING pathway via cyclic guanosine monophosphate (GMP)-adenosine monophosphate (AMP) synthase (cGAS) and IFN-activable protein 204 (IFI204), boosting the stimulation of the NF-κB and interferon regulatory factor 3 (IRF3) cytokine expression pathways.In addition, the DNA will stimulate absent in melanoma 2 (AIM2), exacerbating inflammasome activation and maturation of IL-1 and IL-18. When bacterial RNA enters the cytosol, it induces retinoic acid inducible gene 1 (RIG-1)/melanoma differentiation-associated protein 5 (MDA5)/mitochondrial antiviral signalling (MAVS), NOD2, and protein kinase R (PKR), resulting in the activation of IRF3 and NF-κB. Furthermore, the bacterial RNA will initiate inflammasomes through the nucleotide binding and oligomerization domain (NOD)-like receptor family (NLR) pyrin domain containing 3 (NLRP3), resulting in the maturation of IL-1 and IL-18[13]. In turn, the cytokines and NF-κB will recruit immune cells and initiate the immune response against the M.

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tuberculosis intruder. Consequently, the pathophysiological immune pathway is characterized by bacterial RNA, DNA, and MAGP. Additionally, the phagosome bacilli prevent vacuolar proton adenosine triphosphate synthase (ATPase), natural resistance associated membrane protein 1 (NRAMP1), and inducible nitric oxide synthase (NOS) from interacting with the phagosome. This hinders the vesicle from dropping in pH, maintaining the bacilli and enabling cell division to occur. Besides, to further inhibit phagosome and lysosome fusion, the bacteria select coronin, a host protein that activates phosphatase calcineurin, which restricts fusion[14]. *M. tuberculosis* also causes macrophages to communicate and produce vascular endothelial growth factor (VEGF) into the extracellular space[15]. Multiple VEGF isoforms play an essential role across many granuloma processes linked to mycobacterium pathogenesis. Angiogenesis, monocyte accumulation, macrophage recruitment, and inflammation are examples of these processes. As aforementioned, VEGF is in charge of blood vessel recruitment and vascular permeability via a physiological process known as angiogenesis[16]. The reason for angiogenesis into the resultant tuberculosis granuloma is ambiguous. There are also immunological and pathological explanations. Immunologically, the subsequent blood vessels will provide a quick route for immune cells to access the granuloma and combat the infection. Pathologically, the resulting blood vessels will act as an intermediary for the bacteria to enter systemic circulation and spread to other parts of the body[15]. Whatever the purpose of angiogenesis is, the vasculature is haphazard, devoid of pericytes, has an insufficient basement membrane, and is hyperpermeable. Aside from angiogenesis, the VEGF Receptor (VEGFR) has been linked to lymph angiogenesis and mycobacterial specific T cells. Next function

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of VEGF is as a macrophage chemokine, which contributes to tuberculosis progression by selecting monocytes and macrophages in a nonangiogenic manner. This selection aids bacterial infection by offering new host cells and makes a significant contribution to cell death signal transduction connected with granuloma regeneration. The third feature of VEGF's input to mycobacterial infection and granuloma formation is inflammation. This inflammatory process is severe for safeguarding and adds value to the disease's symptomatology and lung pathology. VEGF suppression has been shown to reduce granulomatous inflammation, and co-treatment with corticosteroids reduces tuberculosis patient mortality by 17%[16]. When these processes of angiogenesis, macrophage recruiting and selection, and inflammation are combined, VEGF becomes one of the most significant contributors to tuberculosis pathophysiology. Pathophysiologically, the aforementioned stages depict the formation of bacteria, and thus the start of bacteremia and the intrinsic inflammatory reaction[14]. Dust cells' chemokines will attract natural killer cells, gamma delta (ɣδ)-T cells, neutrophils, and monocytes[17].

Blockage of Phagolysosomes and Replication

M. tuberculosis reproduces intracellularly inside macrophages after blocking phagosome-lysosome fusion (Fig. 1C). Asymmetric cell division is a very specific type of cell division found in *M. tuberculosis.* Asymmetric cell division occurs when bacilli grow predominantly from one pole, resulting in the formation of a fast-growing daughter cell and a slow-growing daughter cell. The slow-growing daughter cell varies significantly from the fast-growing daughter in that it must establish a growth pole from scratch. These distinctions are most noticeable in that the distinctions between

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the daughter cells affect both growth rate and antibiotic resistance, which could explain why this bacterium is so proficient and tenacious in humans. During this stage of the latent infection, the macrophage and *M. tuberculosis* will move from the alveolar space into the lung parenchyma, either together or separately. Once in the lung parenchyma/interstitium, the immune cells will combine to develop a granuloma around the intruder, which is also known as a tuberculoma in this case. The bacteria infect the logarithmic phase of growth and must be incorporated as the granuloma forms with the synchronous selection of monocytes and immune cells. Pathologically, anatomical translocation to the lung parenchyma is attributed with pulmonary inflammation. As previously indicated, the bacilli recreate intracellularly, resulting in macrophage obliteration such as through apoptosis, pyroptosis, necroptosis, ferroptosis, and extracellular trap-associated damage[12]. Apoptosis is the first layer of protection against harmful bacteria, and highly virulent strains suppress the apoptotic process[8]. Apoptosis and pyroptosis, on the other hand, limit *M.tuberculosis* growth, whilst necroptosis and ferroptosis help the bacteria survive and thrive[12].

T-helper Response

The dendritic cells and monocytes from beforehand in the narrative will have transitioned to local and regional lymph nodes to stimulate T-cells via major histocompatibility complex MHC class II proteins and IL12 (Fig. 1D)[3,18]. This group of differentiation 4 (CD4+) reaction happens after the first three weeks of infection, but during that time M. tuberculosis has greatly multiplied and may have spread to other organs[7]. Because HIV patients have a lower CD4+ T-cell count, they are more vulnerable to being unable to regulate their tuberculosis infection. These antigen-

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specific T cells will prompt the TH1 response, which, as previously stated, begins three weeks after infection[8]. The cell-mediated immune response is controlled by TH1 cells. This response includes stimulating endothelium, metastasizing effector T cell populations, and, most importantly for granulomas, stimulating macrophages with interferon gamma (IFN) and group of differentiation 40 (CD40) ligand. IFNɣ will be distributed by natural killer cells that have been selected to the lesion[19]. The primary effects of cell-mediated immunity are as follows: The first is a type IV hypersensitivity reaction, which is the pathophysiological cause of the positive Mendel-Mantoux test with purified protein derivative tuberculin glycerol extract. The second primary effect is the discharge of IFNɣ. i.e., the further stimulation of macrophages with accelerated bactericidal features with a purpose to fight the intruder. The third effect will be the progression of the granuloma, attributable to a huge range of macrophages selected to the preliminary lesion[7]. TH2 cells play a minor perceived function in tuberculosis, and are liable for upgrading humoral immunity via secretion of IL-4, IL-five, IL-10, and IL13[7].

Granuloma Formation

A granuloma, as an analogy, is a bacterial prison that intends to confine a bacterium within a wall of immune cells. The IFNɣ from the TH1 response will permit the development of the phagolysosome inside the macrophages, cause the macrophage to supply nitric oxide through nitric oxide synthase, and catalyze autophagy. TNF alpha (TNFα) will be distributed by activated macrophages as a result of their inability to exclude the pathogen. TNFα causes monocytes to differentiate into epithelioid histiocyte cells, which form caseating granulomas containing M. tuberculosis. Some

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these epithelioid histiocyte cells collectively form massive cells. The TNFα maintains a feedback mechanism by selecting additional monocytes to replace newly formed differentiated monocytes[8]. The granuloma is made up of macrophages and lymphocytes that envelops and constitute *M. tuberculosis*.TH1, regulatory T cells (Treg), natural killer (NK) cells, B cells, Giant cells, dendritic cells, neutrophils, macrophage, foam cells, and epithelioid macrophage are all engaged in granuloma formation (Fig. 1E). The hypoxic environment inside the granuloma momentarily limits *M. tuberculosis* development, but it may also upgrade angiogenesis into the tuberculoma[13]. Admittedly, the necrotic pool within the granuloma helps as both a source of nutrient and an integrity protection for this pathogen. Furthermore, the resultant vasculature increases the availability of nutrients to the bacteria[17].

TB/HIV Coinfection

HIV coinfection presents distinct clinical problems in patients with active tuberculosis. The likelihood of active tuberculosis rises quickly following HIV infection, and the symptoms of pulmonary tuberculosis at this phase are identical to those seen in HIV-negative people[20]. At CD4 counts of less than 200 cells per cubic millimetre, tuberculosis may appear atypically, with mild infiltrates, pleural effusions, hilar lymphadenopathy, and other signs of extrapulmonary tuberculosis in up to 50% of patients. When CD4 counts fall below 75 per cubic millimetre, pulmonary signs may be missing, and dispersed tuberculosis, characterised as vague, chronic febrile sickness with broad organ involvement and mycobateremia, is more common, with significant early mortality; polyclonal disease. Such occurrences are frequently misdiagnosed as other infectious diseases and are only discovered after an autopsy. Asymptomatic,

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subclinical tuberculosis with false sputum smear and chest radiography signs and positive culture results is a typical hallmark of HIV-associated tuberculosis and may contribute for 10% of cases in tuberculosis-endemic areas. In such areas, up to 25% of patients seeking HIV treatment had undetected active tuberculosis. As a result, testing for tuberculosis is suggested for all HIV-infected patients in order to detect patients with active tuberculosis before initiating isoniazid preventative therapy in the remaining patients[20].

Even in resource-constrained areas, the existence of any one of four symptoms (cough, fever, night sweats, or weight loss) has been demonstrated to have responsiveness in the range of 80% for detecting individuals who require further definitive examination. Assertive tuberculosis screening and testing is offered in areas where the illness is substantially endemic, because subclinical tuberculosis in individuals with HIV infection or noncommunicable diseases (e.g., diabetes mellitus and tobacco-related chronic lung disease) may be neglected otherwise.

Global TB Report

Since 1997, the World Health Organization (WHO) has published a Global Tuberculosis (TB) report that offers an up-to-date estimation of the global TB condition and summarises advances and initiatives in disease prevention, diagnosis, and treatment at the national, regional, and global levels. The 2020 Global TB report was published on October14, 2020, and was consolidated in the framework of global TB control strategies and United Nations (UN) objectives set in the political declaration at the UN General Assembly high-level meeting on TB held in New York

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in September 2018. The data accounted for over 99% of the world's population and reported data from 198 countries. The 2020 Global TB Report has two noteworthy highlights: it integrates and expands on the United Nations (UN) Secretary-2020 General's progress report on tuberculosis (TB), which was demanded in the political declaration at the high-level meeting on TB. The report also includes preliminary estimates of how the astounding corona virus disease-2019 (COVID-19) pandemic will affect TB health services, treatment, and prevention efforts. Notwithstanding, even before the COVID-19 pandemic, global TB intervention strategies were off track, and the statistical gap between the approximate number of people with TB globally and the figures given to public health authorities remains large. If all unsolved cases with tuberculosis, including those from the private industry, could be discovered, the structural deficit in meeting all targets would be greater; thus, failure to meet objectives cannot be attributed to the discrepancies between reported and predicted numbers of people with tuberculosis[21].

In 2019, tuberculosis remained the biggest cause of mortality caused by a single infectious pathogen. In 2019, an estimated 10.0 million people developed tuberculosis (TB), including 5.6 million men, 3.3 million women, and 1.1 million children. Tuberculosis (TB) affects all countries and age groups. There were also an estimated 1.2 million TB deaths among HIV-negative people and an additional 208, 000 deaths among HIV-positive people. Adult's accounts for about 80 percent of all TB patients, with children aged 15 years accounting for 12 percent. The majority of people who developed tuberculosis in 2019 lived in the WHO regions of South-East Asia (44%), Africa (25%), and the Western Pacific (18%), with relatively small percentages in the

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Eastern Mediterranean (8.2%), the Americas (2.9%), and Europe (2.5%). The 30 high TB burden countries accounts for over 80 percent of new TB cases in 2020. India (26 percent), Indonesia (8.5%), China (8.4%), the Philippines (6%), Pakistan (5.7%), Nigeria (4.4%), Bangladesh (3.6%), and South Africa (3.6%) attributed for two-thirds of the global total[21].

While progress is being made, it is expected that the world will not eliminate tuberculosis as a global public health threat by2035, as outlined in the End TB Strategy. For example, while the aim was to reduce TB infection rate by 20% between 2015 and 2020, the 2020 global TB report indicates a decline of only 9% in Incidence rate during this time frame, with a yearly decline of only about 2%. Accordingly, the 35% death reduction target was not met, with only a 14% change in mortality rates achieved between 2015 and 2020. Adolescent tuberculosis is frequently overlooked by medical practitioners and can be difficult to diagnose and treat. The major limitations are related to shortcomings in TB identification, for all TB and drug resistant TB in particular, TB prevention, and TB response funding, including integral TB research[21].

Impact of COVID-19 on TB Services

Tuberculosis is a disease which disproportionately affects individuals who are socially and economically vulnerable. Prior to COVID- 19, tuberculosis (TB) was the leading infectious disease killer globally[22]. Modeling studies have suggested that COVID-19 will probably threaten tuberculosis control programmes, particularly in low-income and middle-income settings, affecting tuberculosis prevention, case detection, and

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management[23]. Prior to the onset of the COVID-19 pandemic the global fight against TB received a much-needed boost with the 2018 United Nations High Level Meeting (UNHLM) which resulted in a political declaration with bold commitments and targets for TB to be achieved by the end of 20224[24,25]. The 2018 UN General Assembly (UNGA) Political Declaration on Tuberculosis was truly a pivotal turning point in global efforts to end the TB epidemic. Ambitious targets were set for diagnosing and treating an additional 40 million people with TB by 2022, mobilizing US$13 billion annually for TB care and prevention and $2 billion per year for research and development. Before the COVID-19 pandemic, WHO estimated that less than 70% of all new tuberculosis cases were notified to surveillance systems and this proportion was likely to be even lower among young people aged 10–24 years (hereafter referred to as young people)[26]. In 2019 alone, there were approximately 10.0 million new TB infections and 1.5 million TB deaths globally.

In 2020, as the COVID-19 pandemic spread across high TB burden countries, their TB health services were disrupted[26]. Recognizing that both TB and COVID-19 were airborne respiratory infections several countries used their TB programmes as a launch pad for mounting a response against COVID-19, diverting some cadres of staff, certain specialized health facilities and laboratories from TB to COVID-19. While this was good for addressing COVID-19 it adversely impacted TB prevention and care delivery. At the same time people faced barriers in accessing TB care and diagnostic services due to restrictions in mobility, fear and stigma. The biggest impact was on TB diagnosis and enrolment on treatment which plummeted down in most high TB burden countries. Impacts were also seen on other areas of TB prevention and care and also

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on TB research and development. A study done by civil society highlighted the array of disruptions in the global fight against TB. A modelling study shows that due to the COVID-19 pandemic-related lockdowns and restrictions, between 2020 to 2025 the global TB incidence could increase by 6.3 million and mortality up by 1.5 million[26,27]. This would mean a setback of 5-8 years in the global response to TB.

Unlike COVID-19, TB notification data of most countries are not available publicly on a real-time daily basis, but on annual and quarterly frequency. India is an exception, with real-time TB notification system which is publicly available. This real- time TB data was extremely useful in India to rapidly detect the problem in 2020, take corrective measures and monitor progress. TB notification in India fell dramatically immediately after announcement of the lockdown on 23rd March 2020[28]. Recovery from this dramatic drop did not happen by default, but because of a massive effort by the TB programme in India which included active TB screening and testing in the community, expansion of rapid molecular testing sites in the country, bidirectional COVID-19 and TB testing, vulnerability mapping of communities, restarting of private clinics and launch of a people's movement against TB called "Jan Andolan". These efforts were possible because of existing high level of political commitment by the Prime Minister and the Health Minister of India, and funding made available to the TB programme. TB diagnosis and enrolment increased in the later part of 2020 but overall annual TB notification in 2020 fell short by 25% when compared to 2019. Since the 'clock is ticking' more efforts will be required for achieving UNGA TB targets. Sharp declines in TB notification rates were also seen in other high TB burden countries in 2020[29]. In general, countries in Asia had a higher decline in TB

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notification when compared to Africa and other parts of the world. TB patients coinfected with SARS-CoV-2 appear to have three times the mortality of patients who have TB alone[8]. The extent of overlap between TB and COVID-19 and impact on mortality and long-term functional recovery, needs to be further researched. The socio-economic consequences of the COVID-19 pandemic are unfolding. The COVID-19 pandemic increased some of the important risk factors for TB such as malnutrition, poverty and social inequities. WHO had estimated that 22% of the global TB burden in 2019 could be attributed to undernutrition[29]. TB thrives in impoverished and socio-economically marginalized settings. How quickly world leaders can address and reverse these socio-economic consequences of the COVID-19 pandemic will determine to what extent they will impact incidence and mortality due to TB. The widespread use of masking and social distancing is anticipated to reduce transmission of TB, particularly transmission occurring outside the household. South Africa's national COVID-19 response has generated unprecedented mobilization of resources and has focused the political agenda on health and underlying social determinants that increase vulnerability and mortality. The resulting political and public participation for COVID-19 must also now include HIV and tuberculosis[30]. The COVID-19 pandemic has had multiple effects on all aspects of TB: increased rates of disease and risk for key populations; disruption of diagnosis, access to preventive treatment for those infected with the mycobacterium, and therapy for those with active disease; and unchecked medical, social and economic consequences of the disease for patients, families and communities. The strain on health policies and services due to the pandemic interfere with all the three dimensions of the comprehensive approach to

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combat TB: active case finding, treatment of all types of TB and preventive therapy. These approaches depend on well-organized and funded systems, with strong ties into the communities and including mechanisms for providing therapeutic support and social support that can help the sick complete their treatment.

TB in Nigeria

According to the World Health Organization's 2018 Global Tuberculosis Report, Nigeria has a TB prevalence rate of 219 per 100,000 population, with an estimated incidence of Multidrug-resistance TB (MDR-TB) of 12 per 100,000[31]. Nigeria was named one of the top 20 countries with the highest number of incident TB cases among HIV-positive people and the general population. The national government through the Federal Ministry of Health responded to this challenge by defining three major TB control targets in the country:

> *"to detect at least 70% of all TB cases by2020, attain a treatment success rate of at least 90% for all new bacteriologically confirmed TB cases by 2020, and completely eradicate TB as a national epidemic (= 1/1,000,000 population) by 2050"*[32].

Globally, the WHO recommended the End TB Strategy, which details tuberculosis prevention and control interventions, objectives, and targets. The DOTS Strategy has been adopted with different levels of success around the world, though most countries in Sub-Saharan Africa, including Nigeria, have not improved considerably toward meeting the global targets[33]. Factors contributing to this entail national governments' limited effect and financial constraints for TB prevention and control. This is

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demonstrated in the poor healthcare systems, which have inadequate TB

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infrastructure, insufficient human resources, as well as poor diagnostic and laboratory services[30]. The potential of the general health systems within which TB services are offered, which is aptly captured as "service readiness," is critical to the successful implementation of the End TB strategy and sustainable interventions for TB control. The term "readiness" refers to a health facility's level of capability and competence to provide multidisciplinary approach, effectiveness, and thorough care to patients. The provision of trained personnel, regulations, infrastructural facilities, medical commodities, essential drugs, and diagnostic tools capacity are strong determinants of readiness. The WHO developed the Service Availability and Readiness Assessment (SARA) tool, which includes standards for TB service readiness, and countries are intended to use it to evaluate performance in improving quality of care. Several research have been performed in Nigeria to evaluate the health-care system, as well as the efficiency of TB diagnosis and clinical management[34].

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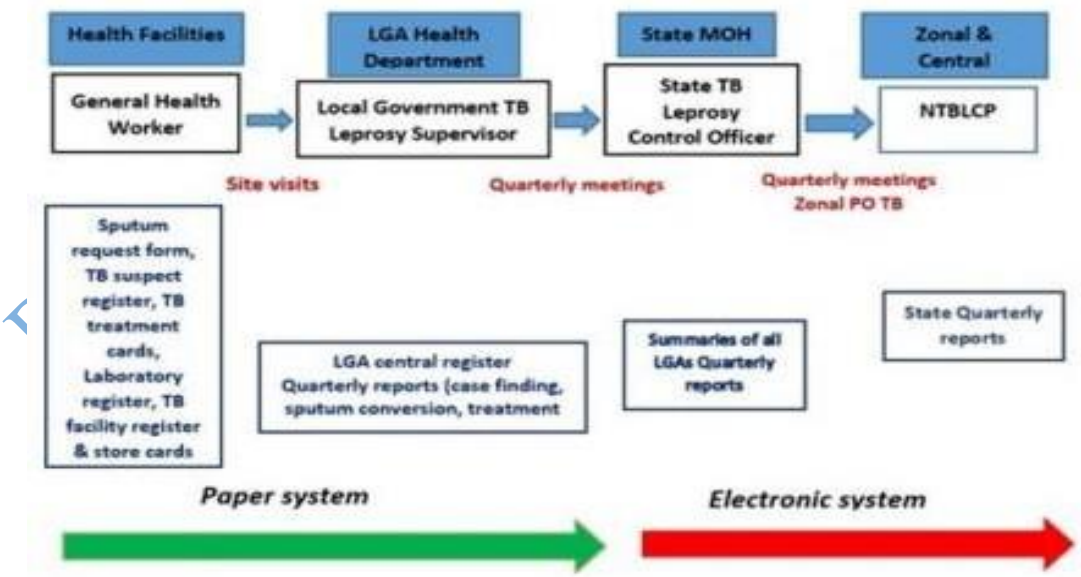

Figure 2.4: *Current Transmission Path of TB Data in Nigeria*

Nigeria is a high prevalence country for tuberculosis (TB), multidrug resistant tuberculosis (MDR-TB), and TB-HIV, with 440,000 cases in 2019.With 117,320 (27%) of reported cases being notified in 2019, the country has some of the minimum case diagnostic accuracy among high TB burden countries, which both restricts infection control measures and delays treatment initiation[29]. Furthermore, a recent national evaluation of TB services for confirmed TB patients discovered that health facilities do not have steady access to adequate equipment and drug supplies, and health workers do not receive mandatory training trainings or regular supervision[35]. These findings suggest that Nigeria's current health system faces numerous challenges in the management of presumptive and confirmed tuberculosis[36]. Historically, Nigeria's national TB screening and treatment programme was restricted to the public sector. Since the majority of Nigerians report seeking health care from the private sector, and the WHO's STOP TB strategy advises referencing private facilities to the national TB programme, Nigeria's National TB and Leprosy Control Programme (NTBLCP) and its beneficiary partners have lately sought to increase participation of the private sector in Nigeria's TB response[36,37]. Outside of Nigeria, most research investigated private sector TB service delivery in LMICs such as Ethiopia, India, Kenya, the Philippines, and Thailand have found significant flaws in the potency of tuberculosis case management by private clinicians and pharmacists[38,39,40]. Several studies in Nigeria have reviewed treatment success rates (TSR) in clinical facilities involved in small-scale PPM pilots in Anambra, Imo, Kaduna, Lagos, Ogun, and Plateau states. Although these research findings discovered that observed TSR for private industry patients was relatively low than Nigeria's national treatment success

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target of 90%, these rates were frequently significant compared to TSR reported for public sector patients in those states, indicating that PPM should be scaled up in Nigeria to enhance access to care[37,41,42]. The United States Agency for International Development (USAID)-funded Sustaining Health Outcomes through the Private Sector (SHOPS) Plus programme, which began introducing a public-private mix (PPM) approach in 2018 to strengthen private industry TB case screening and treatment in the urban areas of Lagos and Kano states, is one of the largest efforts to scale up PPM in Nigeria to date. The PPM approach used by SHOPS Plus is based on models used in India, and it is the first effort in Nigeria to build, teach, and empower large networks of private, multi-cadre facilities to check, diagnose, and treat tuberculosis[43,35]. The ability of the SHOPS Plus network model to provide quality services is yet to be tested, and it is unclear whether improving multiple cadres of private providers' TB knowledge and management capacity contributes to overall improvements in TB quality of care in Nigeria. Existing PPM care quality studies in Nigeria have focused mainly on treatment outcomes rather than testing and treatment commencement, and have also only included clinical providers[35].

Adolescents and Young Adults with TB

The concept of adolescence, which refers to the stage of life that occurs between childhood and adulthood, has been the subject of a lot of discussion over the years. It encompasses both biological development and significant alterations in social roles, all of which have occurred over the course of the previous ten years. The onset of puberty has been sped up in almost all societies as a result of the practice of early puberty; however, increased awareness of ongoing development has pushed the terminal age

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well into the 20s. Concurrently, the prolonged sequence of transition periods, such as finishing school, getting married, and having children, is changing common notions of when maturity starts to set in. It is possible to say that the period of time spanning from childhood to adulthood now accounts for a greater proportion of the life cycle than it ever has before. This comes at a time when new societal influences, such as advertising and digital media, are having an effect on the health and wellbeing of individuals during these years. For the purpose of formulating laws, social policies, and service delivery systems that are developmentally appropriate, it is necessary to have a definition of adolescence that is both broader and more exhaustive. There haven't been many studies done that specifically look at the TB burden in adolescents. In the United States, adolescents accounted for approximately one-third of all paediatric cases that were reported between the years of 1994 and 2010. Despite this, people aged 10 to 19 years old show a different spectrum of disease manifestations, including adult-type illness, from which respiratory samples can be collected more easily. The Stop TB Partnership has a number of goals, two of which are to reduce the global burden of TB (prevalence and mortality) by fifty percent by the year 2015 in comparison to levels in 1990 and to eliminate TB as a public health problem by the year 2050. In order to accomplish this objective, adolescents, despite the fact that they make up a significant portion of the paediatric age group but exhibit striking differences from younger children, ought to be regarded in a distinct manner. This is due to the fact that preventative measures for tuberculosis differ for children and adults. A definition of adolescence that is 10–24 years old, rather than 10–19 years old, fits more closely to adolescent growth and a general understanding of this life

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stage. Furthermore, such a definition would permit longer participation in a greater variety of contexts[24]. Approximately 850,000 adolescents (ages 10–19) and 1 million young adults (ages 20–24) become infected with tuberculosis (TB) each year[44,45]. A significant transitional period in terms of both physiologic maturation and social function takes place between the ages of ten and twenty-four[46]. During this period of time, people build conditions that will serve as a foundation for their future well-being. These conditions can be broken down into five categories: the biological, mental, psychological, relational, and financial conditions[47]. According to a group of adolescent health specialists whose work was coordinated by David Ross, the following five aspects of one's well-being are essential for making the passage from childhood to adulthood as painless as possible: Initiative and adaptability; Wellbeing; Affiliation and community participation; Stability and a good environment; & Training, expertise, literacy, abilities, and vocation (Table 1)[48]. The TB disease and the therapeutic interventions used to treat it can have a negative influence on several aspects of health, derailing the growth and changes that are typically associated with this phase of transition. It is imperative for health care professionals, community representatives, and lawmakers to fully comprehend exactly how TB disease and care affect AYAs' health[48]. This is due to the sheer number of AYAs who are affected by tuberculosis (TB) and the impact of this stage in development in establishing a framework for a healthy, beneficial old age. Despite the enormous population of teenagers and young adults (ages 10–24). The rate of infection with Mycobacterium tuberculosis is said to be particularly high during adolescence and young adulthood, and there may be a momentarily elevated risk of disease progression after infestation

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between the ages of 12 and 24 years when compared to children and elderly elders. These findings are based on statistical information. In spite of this, several complications related to tuberculosis manifest themselves for the first time or worsen during the adolescent years[49]. These complications include HIV infection, diabetes, hazardous drug use (including cigarette use), and mental health disorders. In addition, a significant number of preteen girls and young women struggle with the physical challenges of pregnancy and childbirth, which can increase the risk of tuberculosis in these individuals as well as have other unfavourable effects. When transitioning from child to adult health services, adolescents face unique age-related obstacles that prevent them from receiving adequate treatment. This is especially true in tuberculosis-endemic regions, which typically have a dearth of specialised adolescent health care services[50]. According to the findings of a study conducted on young people in Kenya between the ages of 12 and 18, the prevalence of tuberculosis was found to be six times higher than what was suggested by case notifications. A previous study conducted in Botswana found that young adults between the ages of 10 and 19 who were receiving treatment for tuberculosis had higher rates of dropping out of follow-up than adults. It is well known that adolescents and young adults are a particularly vulnerable age group when it comes to the global HIV pandemic. Despite the fact that mortality rates are falling across the board for all other age groups, the number of HIV-related deaths among adolescents continues to rise. Despite the growing awareness of the significance of the teenage age range in HIV prevention efforts, tuberculosis is still underrepresented in young people[30].

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The Difficulty in Locating Individuals Infected with Tuberculosis

Only 7.1 million (71 percent) of the 10 million people who are estimated to have developed tuberculosis in 2019 have been identified and reported to the various national TB programmes around the world. This leaves a gap of 2.9 million people (29%). These missing people with tuberculosis include both those who were diagnosed with the disease but did not report it to public health authorities (including those who were not reported from the private sector), as well as those who were not diagnosed and were therefore not treated for the disease. According to the most recent definitions, this pool also includes patients who have drug-susceptible or drug-resistant tuberculosis. Only 206,030 (41 percent) of the estimated 500,000 people with rifampicin resistant or multidrug-resistant tuberculosis (RR/MDR-TB) were identified, as a result of inadequate testing for drug susceptibility especially among new people with tuberculosis. However, a greater proportion of people with drug resistant TB are missing. Only 61 percent of people who were bacteriologically confirmed to have pulmonary TB were tested for RR/MDR-TB in 2019. This includes 59 percent of people who had not previously been treated for TB and 81 percent of those who had previously been treated for the disease. In 2019, only 57 percent of people who were identified to have pulmonary TB had their diagnosis bacteriologically confirmed. Only 177,099 people were enrolled in treatment, which is only 38 percent of the estimated number of people who developed RR/MDR-TB in 2019. This is despite the fact that 206, 030 people were found to have MDR/RR-TB and were notified of their condition in 2019, which is a 10 percent increase from the number of 186, 883 people in 2018. The search for and treatment of people with tuberculosis who have gone missing

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requires an ongoing, concerted effort and a focus on the entire world. According to the World Health Organization (WHO), a decrease of 50 percent in the number of people with TB who are detected could result in up to 400,000 additional deaths from TB each year. To ensure that no one with tuberculosis is missed, the governments of countries with a high TB endemicity need to ensure that diagnostic testing for TB can be performed quickly and is available in every health facility. It has been reported that many countries are using GeneXpert machines for COVID-19 testing because COVID-19 is causing disruption of health services. Other countries have reassigned TB programme staff to COVID-19, causing further shortages of the already limited resources for TB diagnostics and treatment. In the wake of the COVID-19 pandemic, novel plans are required in order to keep tuberculosis diagnostic services operational[51]. It is essential and urgently required that innovations be developed to adapt TB diagnostic platforms to screen for both TB and COVID-19, that additional machines be rolled out, and that investments be made in the development of low-cost rapid diagnostic tests for both infections. The World Health Organization (WHO) estimates the global burden of tuberculosis using a variety of methodologies, some of which are as follows: the use of data from national prevalence surveys; notification data adjusted by a standard factor to account for under -reporting, over - and under diagnosis; inventory studies that measure under-reporting; and expert opinion on TB detection gaps. Among these methodologies, the use of data from national prevalence surveys is the most widely used. The results of prevalence surveys have, more often than not, demonstrated that country estimates of prevalence have been lower than what was observed; consequently, the incidence estimates upon which the global estimates are

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based may be lower than what actually exists. The methods that are used to estimate the burden of tuberculosis are continually being improved; however, imperfections still exist, which may explain the relatively wide uncertainty intervals, particularly with respect to estimates at the country level. According to Garcia-Basteiro. 2018, in the past there have been significant discrepancies between the estimates of the global burden of TB provided by the WHO and the Institute for Health Metrics and Evaluation, which is responsible for carrying out the Global Burden of Disease project. These discrepancies were caused by differences in the methodological approaches that were used to estimate the burden of TB. These methodological challenges in estimating the global burden of tuberculosis may have significant repercussions at the level of programmatic implementation in individual nations. If national targets for tuberculosis are based on trends of TB notifications, as has been proposed by some industry experts, then national TB programmes may set targets that are either unreasonably high or appear to be setting unambitious targets. We urge the global TB community, which is currently being led by the WHO Global Task Force on TB Impact measurement, to continue addressing this challenge and to harmonise approaches for the estimation of the burden of TB[52]. This will ensure that disease burden estimates become more robust by providing a more precise estimate of the size of the TB incidence -detection gap. It is also very important to develop reliable methods and tools for estimating the burden of tuberculosis at the sub-national level, which is where the majority of the work to find people who have TB is being done. This is something that has been proposed by a few countries, including Indonesia. Several interventions, many of which have already been implemented, albeit to

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varying degrees, in a variety of settings, are in place to narrow the gap between TB incidence and detection, and excellent reviews have been published on the topic[32]. At the national and sub-national level in countries, some of the most important steps that need to be taken to address the challenge of missing people with tuberculosis include the identification of TB at risk populations to be targeted to actively find people with TB, the use of highly sensitive methods for TB screening and specific TB diagnostic tests (such as Xpert MTB/RIF), linkage to care and treatment of all people who are identified to have active TB, and measures to ensure retention in care and a Cascade analysis is an effective method for identifying bottlenecks in the pathway to care, treatment, and cure for tuberculosis, and it should be used at all levels of the national TB programme[35]. It's possible that a significant barrier to finding people who have tuberculosis is the lack of coordination between TB services and the locations where people go to get health care. It would be beneficial to align the various health services, not only for tuberculosis but also for the more effective delivery of health care services in general. It has been demonstrated that lowering the prevalence of tuberculosis in a variety of settings can be accomplished by ensuring that a sizable portion of the targeted population is provided with tuberculosis screening and diagnostic testing services on an ongoing basis[53]. In order to accelerate tuberculosis detection efforts and close the gap between tuberculosis incidence and notification rates, such strategies need to be adopted and expanded across the globe.

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2.2 Theoretical Review Clinical Manifestations

In terms of clinical significance, there are two types of tuberculosis (Fig. 1F): primary tuberculosis and secondary tuberculosis.

Primary tuberculosis is a new infection; that is, this was the first time someone has been infected with *M. tuberculosis*[8]. This (primary) infection occurs when the immune system is unable to regulate the initial infection, which is common in immunodeficient people. The primary infection is one of the story's climaxes. At this phase, the infected person can produce infectious *M. tuberculosis* aerosol and contaminate the next susceptible individual (Fig. 1G). Assume that the immune system and granuloma contain *M. tuberculosis* but that the bacteria are not removed. The disease is said to be latent in this case and can advance to secondary tuberculosis at a later phase. Bacteria produce protective biofilms inside necrotic tissue during the underlying stage of tuberculosis[7]. Eventual immunosuppression enables M. tuberculosis to reactivate within the granuloma, resulting in pulmonary disease, extra-pulmonary disease, or miliary tuberculosis. The most likely consequence following LTBI is pulmonary disease, which consists the ghon complex radiographic finding and cough, hemolysis, weight loss, night sweats, anorexia, and fever. Extrapulmonary disease spreads to lymph, the genitourinary system, the gastrointestinal system, the pleura, and the skeletal system (with the later developing in tuberculosis spondylitis). Miliary tuberculosis is a disease in which the granuloma has spread throughout the body and tuberculomas are present.

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Secondary tuberculosis can also be the end of the story because the tuberculoma can solubilize and discharge after bacterial reactivation (cavitation), and the bacilli are vaporised through the air passages. To summarise, infection with *M. tuberculosis*, as well as the pathophysiology of the disease known as tuberculosis, can result in primary or secondary clinical manifestations[17].

Clinical Features

Chronic cough, sputum production, appetite loss, weight loss, fever, night sweats, and haemoptysis are the classic clinical characteristics of pulmonary tuberculosis. Extrapulmonary tuberculosis affects 10% to 42% of patients, based on race or ethnic background, age, existence or lack of underlying disease, *M. tuberculosis* strain genotype, and immune status. Extrapulmonary tuberculosis can impair any organ in the body and has a wide range of clinical manifestations, necessitating a high level of clinical speculation[54].

A suspected pulmonary TB case is described as anyone who has coughed for two weeks or more, with or without symptoms of weight reduction, fatigue, fever, night sweats, heart palpitations, lightheadedness, appetite loss, and vomiting blood, whereas an extra-pulmonary TB case is defined as anyone who has symptoms based on the affected organ, vertebral spine (back pain, bloating on spine); bone (deeply entrenched pain and swelling of the bone); Joints (excruciating joint distension, typically involving one joint); renal and urinary tract (distressing urination, blood in urine, increased urination, lower back ache/loin ache); upper respiratory tract (hoarseness of voice, physical discomfort on swallowing); pleural membrane of lungs (chest pain,

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shortness of breath, fever); meninges of the brain (headache, recurrent fever, stiff neck, vomiting, restlessness, seizures, disorientation); lymph node (painless enlargement of the node, may leak pus); skin (recurring ulcer following antibiotic therapy, discharging pus) and certain general symptoms (weight loss, persistent fever, night sweats)[55].

Screening and Diagnosis

There are two key components to effective tuberculosis screening and diagnosis. People with TB symptoms must recognise that they are sick and seek accurate and effective care, and health-care providers must respond fast and effectively. Regrettably, it can take 3 months or more for symptomatic individuals to convey to the health sector, and another 1 month for the health system to diagnose tuberculosis[56,57]. As a result, significant delays between the onset of symptoms and the diagnosis are frequently the standard. Huge majority of symptomatic patients who presented to health centers may also neglect to be adequately tested or analysed with relevant microbiological or radiological tests, resulting in TB diagnosis being overlooked[58,59]. For decades, so-called "passive case finding" issues have burdened TB Control Programs, and programmes frequently underestimate the proportion of patients affected from pre-diagnostic setback to follow-up. Active case finding, in which people who do not intentionally seek health care are quickly and effectively sought out and tested for tuberculosis irrespective of symptoms, has the capability to alleviate some of these restrictions. As recently demonstrated in Vietnam, community-wide testing for active tuberculosis can help decrease TB incidence and infection[60]. An evaluation of many active case finding projects in 16 countries, on the other hand,

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found no effect on national case notifications, owing to costs and a lack of human resources[61]. Several different active case finding undertakings have reported reduced sensing yields of tuberculosis, and programmatic barriers include insufficient health care worker training, understaffing, community wariness, poor education, and a lack of community knowledge and understanding about tuberculosis[62,63].

A confirmed TB case must be diagnosed in a laboratory. Case detection is accomplished through assessment for TB symptoms as well as sputum microscopy for AFB. Two positive smears out of three confirm TB positivity. Sputum smear-negative instances are diagnosed after three negatives, as well as an X-ray and medical officer attestation[55].

Lastly, an examination of 21 national TB epidemiological surveys conducted in Asia between 1990 and 2012 revealed that between 40% and 79% of patients with bacteriologically-positive TB did not acknowledge TB symptoms and were only discovered through chest X-ray screening of all survey participants. With such a disproportionate amount of asymptomatic TB patients, conventional testing and analytic algorithms experience difficulties, addressing the question of whether community need for chest X-ray should be increased in the commonly performed setting.

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Latent Tuberculosis Infection (LTBI)

Latent tuberculosis infection (LTBI) affects nearly two million people across the globe and is a driving force behind the global tuberculosis (TB) pandemic[64]. This symptomless situation caused by *Mycobacterium tuberculosis* increases the likelihood of advancement to tuberculosis disease (TB) which is more probable to appear shortly

after infection or with immune suppression[65,66]. Testing and therapeutic interventions for latent *M. tuberculosis* infection are recommended for communities with an increased proportion of latent infection (e.g., foreignborn persons from tuberculosis-endemic regions), as well as those with an increased likelihood of reactivated disease (e.g., patients with HIV infection or diabetes, and patients undergoing immunosuppressive therapy), as well as those have both factors (e.g., recent history of patients with tuberculosis). A tuberculin skin test or an interferon-gamma release assay can be used to detect latent infection. The Centers for Disease Control and Prevention in the United States, the National Institute for Health and Clinical Excellence in the United Kingdom, and the European Centre for Disease Prevention and Control all recommend using the interferon-gamma release assay and tuberculin test to screen for latent M. tuberculosis infection in different age and vulnerable individuals. The tuberculin skin test is less costly and is therefore recommended in low-income regions. It is as delicate but less specific as the interferon-gamma release assay[67].

Test for LTBI

The Mantoux tuberculin skin test is frequently used to screen people who are at elevated danger for tuberculosis. Those who have received prior immunization of the BacilleCalmette-Guerin vaccine may experience a false-positive test result. In people with sarcoidosis, Hodgkin's lymphoma, malnutrition, and, most remarkably, active tuberculosis, the test may be falsely/negatively positive. In those who screened positive for the Mantoux test, interferon gamma release assays (IGRA) on a blood sample are preferred. Since they are not affected by immunisation or the majority of

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environmental mycobacteria, they produce fewer false-positive results. They are, however, harmed by *M. szulgai, M. marinum,* and *M. kansasii.* When used in conjunction with the skin test, IGRAs could enhance responsiveness, but when used solely, they may be less delicate than the skin test[68].

Treatment of LTBI

For decades, the treatment of LTBI – also known as tuberculosis preventive treatment (TPT)–has been a critical tool for TB control in many moderate settings. Current WHO recommendations highlight the significance of tailored LTBI screening and TPT in high-prevalence countries[64]. However, only a small percentage of people with LTBI are recognised, assessed, and treated in most countries. According to a recent meta-analysis, only 18.8 percent of those qualified for testing completed TPT.

The 'Cascade-of-Care' Structure to Improve LTBI Treatment

A person's journey from *M. tuberculosis* infection to treatment completion can be depicted as a 'cascade-of-care' (Figure 2.3). A structure like this allows health care providers to measure where defection occurs and track the progress of approaches to improve each step. While relatively safe and shortened rifamycin-based routines have improved TPT success rates, decline occurring prior to treatment initiation constitute the most significant fall-out (occurring in up to 70% of contacts) and portray the most significant impediment. The maximum loss occurs during the preliminary stages of contact identification, LTBI testing, and medical assessment. The causes of pre-treatment drop-out in the care cascade are numerous and context-dependent. TPT extended range must identify and resolve the factors that impact advancement through

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this cascade. An analysis of variance trial executed in five low- and high-prevalence countries centred on geared strategies to minimize fall-out period leading up to treatment initiation[69]. The areas received a three-phase health promotion program that bolstered primary healthcare capacity and inspected the LTBI treatment cascade. The initiatives considerably improved TPT commencement at intervention sites. The benefits were seen predominantly in low-and middle-income countries, and they provide the proofs required to validate scaling up in equivalent settings. Notwithstanding examples of impactful TPT scale-up, international recommendations are not widely adopted. In 2019, below 20% of interactions received TPT over a five-year period worldwide, highlighting ongoing scaling challenges and widespread scepticism about preventive care[64]. Resolving this inertia will necessitate TB preventative measures gaining the sufficient expertise to sustain scale-up. TPT is primarily introduced into TB control programmes through intimate contacts of TB patients. This high-risk group is easily identified and may be persuaded to partake in testing due to their recognisable exposure and expected self - interest. Contacts gain from the recentness of their exposure as well, improving the probability of interrupting progression of the disease shortly after infection. Nevertheless, considerable constraints to involvement must be removed[70]. Once programmes have gained expertise offering TPT to close contacts, they can broaden medication to additional large populations.

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Active Tuberculosis

Evaluation of active tuberculosis based exclusively on clinical manifestations is challenging, as is detecting the disease in those with compromised immune systems. A TB diagnosis should be recommended for patients who have evidence of pulmonary disease or constitutional symptoms that continue more than two weeks. The formative evaluation usually includes a chest X-ray and repeated sputum cultures for acid-fast bacilli (AFB). *M. tuberculosis* in a specimen is used to provide a conclusive diagnosis of tuberculosis (e.g., sputum, pus, or a tissue biopsy). The challenging culture method for this slow-growing bacterium, on the other hand, can take two to six weeks for blood or sputum culture. As a result, treatment is frequently initiated before cultures are validated[71].

Sputum microscopy and liquid medium culture, followed by drug susceptibility testing, are now suggested as standardized procedures for identifying active tuberculosis. In resource-constrained countries, using solid media is more cost- effective. Interferon-gamma release assays and tuberculin skin tests are ineffective in detecting active tuberculosis. Nucleic acid amplification tests, imaging, and histopathological examination of biopsy samples supplement these evaluations. These evaluations are supplemented by nucleic acid amplification testing, radiography, and histological inspection of biopsy specimens. Early identification of tuberculosis may be possible with nucleic acid amplification tests and adenosine deaminase screening. However, these examinations are not regularly indicated because they rarely change how a person is managed. Antibody blood tests are not specific or sensitive, hence

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they are not indicated. Approximately 30% of all tuberculosis patients and more than 90% of those with multidrug resistant and severely drug-resistant tuberculosis do not acquire a diagnosis in resource-constrained settings with a greater incidence of tuberculosis and HIV infection. A novel molecular diagnostic test called the Xpert MTB/RIF assay identifies *M. tuberculosis* complex in 2 hours and has a substantially higher selectivity than smear microscopy. When opposed to smear microscopy, the test had a 45 percent higher rate of case detection in HIV-infected patients. This biochemical assay, which is presently being applied in district-level laboratories in 67 countries with greater tuberculosis burden, has the ability to enhance the effectiveness of national tuberculosis programmes[71].

Drug-Resistant Tuberculosis

The recent gold standard for first-line drug susceptibility testing is an automated liquid culture method, which produces results in 4 to 13 days. When tested against automated liquid culture, commercial molecular line-probe assays can produce findings in 24 hours. The Xpert MTB/RIF assay provides data on rifampin tolerance within 2 hours, which is a marker for multidrug-resistant tuberculosis in regions with a high incidence of drug resistance, because rifampin resistance in the absence of isoniazid is rare. To prevent false positive rifampin resistance outcomes, assay adjustments have been implemented. The World Health Organization (WHO) proposes that routine drug susceptibility testing be undertaken concurrently with the Xpert MTB/RIF assay to validate rifampin resistance and the susceptibility of the *M. tuberculosis* isolate to other medications. The microscopic-observation drug-susceptibility (MODS) assay, the nitrate reductase assay, and colorimetric reductase techniques are some more drug

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resistance diagnostic procedures. On the premise of coding formation, the MODS assay detects *M. tuberculosis* bacilli as well as isoniazid and rifampin resistance. This is because most of these procedures are not now accessible in tuberculosis-endemic areas, it is predicted that only 10% of individuals of multidrug-resistant tuberculosis are presently detected worldwide, with only half receiving proper treatment[72].

Improving Sub-Optimal Tuberculosis Prevention

Recent estimates of the global burden of latently infected persons with Mycobacterium tuberculosis suggest that 23 percent of the global population, or approximately 1.7 billion people, harbour this infection. The confidence interval for these estimates ranges from 20-4 percent to 26.4 percent. This large pool of people who are latently infected is the seedbed for future cases of tuberculosis. It has been estimated that this pool of people who are latently infected will generate 16.3 people with active TB per 100,000 population by the year 2030, and 8.3 people with active TB by the year 2050. However, with the diagnostic and treatment tools that are available now and those that will hopefully become available in the future, the majority of these TB cases, if not all of them, can be avoided. There are currently no readily available tools that can identify the subset of latently infected individuals who are likely to develop active tuberculosis. This presents a significant obstacle for those working in the field of tuberculosis prevention. Although certain bio-signatures have the potential to offer this benefit, none of them have been developed to the point where they can be used to support programmes that aim to deliver targeted TB preventive therapy[73]. As the programmatic management of TB preventive therapy moves forward, we believe it is imperative that this area of research also receives the appropriate attention,

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particularly funding, in order to assist in the refinement of the targeting of TB preventive therapy. Even though the global goal of eliminating tuberculosis through preventive therapy would not be met until 2019, it is encouraging to see that progress is being made in this area. Despite this, it is necessary to rejoice in even the smallest of victories that have been achieved. For instance, preventive therapy for tuberculosis was administered to 4.1 million people in 2019, which is nearly double the number of patients who were given this treatment in 2018. It is commendable that among people infected with HIV, 85 percent of those who were eligible to receive TB preventive therapy actually did receive it. There was an increase in the number of household contacts who were provided with TB preventive therapy in 2019 compared to 2018; however, the provision of TB preventive therapy to household contacts of people with active TB remained low. This is evidenced by the fact that there was an increase in the number of household contacts who were provided with TB preventive therapy in 2019; however, there was a decrease in the number of household contacts who were provided with TB preventive therapy in 2018. It would appear that the development of new regimens that are both shorter and equally effective, such as a weekly dose of rifapentine and isoniazid for three months (3HP), a daily dose of rifampicin plus isoniazid for three months (3HR), a daily dose of rifapentine plus isoniazid for one month (1HP), and a daily dose of rifampicin for four months (4R). We believe that combination therapies such as 3HP, 3HR, and 1HP have been a truly major advance in the sense that they may have allayed the fears held by some TB programme managers and opinion leaders at the national level. These managers and leaders were concerned that TB preventive therapy, using isoniazid preventive therapy, could promote the

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development of resistance, paving the way for acceleration of TB preventive therapy. These fears were allayed by combination therapies such as 3HP, 3HR, and 1HP. In our opinion, this present opportunity ought to be seized in order to make certain that tuberculosis preventive therapy services are rapidly scaled up. The implementation of this TB preventive therapy will make a contribution to the overarching goal of hastening the rate at which TB cases are falling around the world. In order to effectively prevent future cases of tuberculosis (TB), it is not enough to simply locate and treat those who already have the disease; rather, efforts should also be made to address social and other factors that contribute to the disease. While efforts are being made to actively find people with tuberculosis and to provide TB preventive therapy, governments need to ensure that the expansion of economies continues in this COVID-19 era, and that it percolates to all segments of the population in every nation[33]. If the world hopes to eliminate tuberculosis as a threat to public health by the year 2035, it is imperative that measures be taken to combat the primary risk factors for the disease, including malnutrition, poverty, diabetes, tobacco use, and air pollution in the home[74]. Furthermore, since the year 2000, the World Health Organization (WHO) has projected that 54 million people have survived tuberculosis (including a large proportion of children and adolescents)[75]. However, these people are more likely to develop residual lung damage and recurrent tuberculosis, and they are at an increased risk for all cause-mortality (standardised mortality ratios: 2.91 (95 percent)[76]. We urge national TB programmes to incorporate post-tuberculosis health and wellbeing interventions in the package of services provided to people with TB. Additionally, we encourage the research community to undertake research that is

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intended to unravel the biomedical and social determinants impacting TB survivors' long-term prognosis[76]. Since the global leaders who signed the declaration at the UN general assembly high level meeting on tuberculosis more than two years have passed. The fact that we are not currently on track to meet the testing and treatment goals is both disappointing and disheartening. Even though global political and public health systems have been severely shaken by the COVID-19 pandemic, which has undoubtedly displaced TB from the number one slot in the year 2020, the expectation is that with the rollout of COVID-19 vaccines and public health measures, COVID-19 may be brought under control. This is despite the fact that the pandemic has severely shook global political and public health systems. The COVID-19 pandemic will have long-term socioeconomic effects that will further drive poverty, malnutrition, and poor living conditions, all of which are risk factors associated with the prevalence of tuberculosis (TB). As a result, tuberculosis is likely to quickly reclaim its position as the leading infectious cause of death across the globe. Within eleven months of the initial discovery of COVID-19 as a new human pathogen, global coordination and political will, along with enormous financial investments, led to the development of effective vaccines against SARS-CoV2 infection. The global community is at a point where it needs to concentrate similarly on the development of new vaccines for tuberculosis using new technological methods. We urge the World Health Organization (WHO), other UN agencies, and partners to develop mechanisms that strongly push countries to ensure that multisectoral accountability frameworks for tuberculosis are not just developed, but are pursued with vigour as well. It is necessary to create holistic programmes for human development, and leaders must be held

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accountable for seeing that these programmes are put into action. Inequalities in global health that contribute to the epidemiology of tuberculosis should also be addressed by multiple approaches and sectors. These inequalities include the environment and climate control, gender, age, socioeconomic status, and wealth, as well as the distribution of resources. It is not yet too late to do this, and on World Tuberculosis Day in 2021, we expect that every influential leader and influential person will get the message that it is time to reduce inequities as we work towards a world free of tuberculosis. Although there is a continuing need to develop new tools for the prevention and treatment of tuberculosis (TB), our firm belief is that the application of existing tools in a way that is both effective and efficient can significantly reduce the burden of TB and advance efforts to eliminate TB as a threat to public health on a global scale. Now is the time to get started on this project. In the past two to three years, tuberculosis (TB) control programmes all over the world have fallen short of their ambitious goals, primarily as a result of flaws in the underlying system. The pandemic caused by COVID-19 and its rapid spread around the world has brought to light the inherent flaws in existing health care systems. The most important overarching problem that applies to all communicable diseases that are of significance to public health is that of establishing a stable healthcare infrastructure on which to construct disease-specific programmes like the one for tuberculosis[76].

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Risks and Difficulties Posed by the COVID-19 Pandemic for Multidrug-Resistant Tuberculosis Care and Management

The pandemic caused by COVID-19 represents a one-of-a-kind risk to the provision of healthcare to patients suffering from multidrug-resistant tuberculosis (MDRTB), and it

poses a risk to the success of global control efforts. According to the World Health Organization's global tuberculosis report for 2020, the reallocation of human, financial, and other resources away from tuberculosis treatment and prevention and toward the COVID-19 response has resulted in fewer TB case notifications in more than 200 countries[64]. As a result of disruptions in health services brought on by the COVID-19 pandemic, the number of TB notifications in three of the countries with the highest TB burden—India, Indonesia, and the Philippines—fell by as much as 30 percent from the beginning of 2020 until the middle of the year, when compared with the same period in 2019. The effects of COVID-19 on tuberculosis services have been felt all over the world[77]. It is important to note the decline in notifications because; if the number of tuberculosis patients who are identified decreases by 25%–50%, the number of deaths caused by TB could rise by as much as 400,000 in 2020[77]. As a result of the reassignment of personnel and budgetary resources from national TB programmes to COVID-19–related duties in many high TB endemic countries, there is less staff available for TB healthcare services, a decline in data collection, and TB laboratories are being re-assigned for COVID-19 testing[78,79]. Over the course of the past year, China and South Africa have shifted their attention to COVID-19, which has resulted in a diversion of both financial and staff resources away from the management of tuberculosis and drug-resistant tuberculosis (DR-TB). This is the situation in many of the countries that have a high TB incidence rate[78,80]. In countries with a high TB endemicity, a decrease in the provision of direct services to TB patients has been observed. The fact that frontline TB staff have also become ill with COVID-19, just like the communities they serve, has an additional negative impact on

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already understaffed services. Interference from COVID-19 with the process of implementing new MDR-TB regimens. In the past ten years, three new anti-tuberculosis drugs, bedaquiline, delamanid, and pretomanid, have been approved for use. Combinations of these new, as well as previously approved and repurposed drugs, are leading to increased rates of successful treatment[50,77,78]. Recent developments in the drug development pipeline for tuberculosis (TB), including several ongoing clinical trials, provide much-needed hope for improved treatment outcomes. These developments are aimed at shortening TB treatment, improving treatment outcomes in MDR-TB, and treating people with latent TB infection (LTBI). The all-oral WHO regimen for treating MDR-TB for a period of six months is easier to tolerate, has higher treatment success rates, and lower mortality rates[81]. As a result of the disruption caused by COVID-19 to TB services, it is anticipated that the number of MDR-TB cases will increase in the years 2021 and 2022, which will have a further negative impact on the treatment outcomes[82]. There is an immediate need to ring fence current investments in tuberculosis services, maintain gains made in tuberculosis control, accelerate roll out of TB diagnostic and treatment services, and invest more in the development of new drugs and treatment regimens for tuberculosis in anticipation of the emergence of drug resistance to new TB drug regimens. All of these things are urgently needed. The intensive phase of drug therapy for the treatment of MDR-TB requires the use of five different drugs, and patients with MDR-TB need to be followed up at a TB clinic so that they can receive their medications, have their adherence monitored, be checked for toxicity, and have their progress monitored. Despite the rollout of mobile technologies to familiarise patients on their MDR-TB

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regimens, the lockdowns have disrupted plans to implement a shorter, all-oral TB treatment for MDR-TB patients. This is despite the fact that the treatment would be administered orally[82]. Treatment regimens for multidrug-resistant tuberculosis that are recommended by the WHO include bedaquiline, linezolid, and fluoroquinolone, with either clofazimine or cycloserine added[80]. The patients, their families, and the TB services have all suffered as a result of the disruptions that have been caused to the best practise models of community-based ambulatory MDR-TB care. Because they are not designed to isolate such a large number of patients with COVID-19 while also protecting MDR-TB patients who are particularly vulnerable, TB hospitals and other healthcare facilities face significant challenges. As a result, the lockdown of COVID-19 and other mitigation efforts are having a significant impact on tuberculosis services and will further delay the achievement of WHO END TB targets for elimination[83]. To accelerate the recovery process for all types of tuberculosis, there is an immediate demand for novel anti-TB medications that are risk-free, highly effective, long-lasting, and have a low potential for adverse drug interactions. Inadequately treated, undiagnosed, and untreated cases of tuberculosis create the conditions for the development of increased drug resistance, the continuing spread of multidrug-resistant tuberculosis (MDR-TB), and the creation of lung co-morbidities, all of which led to poor COVID-19 treatment outcomes. In addition, patients with MDR-TB have a greater risk of experiencing sequelae at the conclusion of their treatment, and COVID-19 has the potential to make this risk even greater. It is essential to determine at an early stage which patients might gain advantages from participating in pulmonary

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rehabilitation[74,81]. Patients suffering from tuberculosis appear to be more susceptible than the general population and should be given vaccination priority for COVID-19.

The Responsibilities of Community Health Workers (CHW) in Tuberculosis Prevention

Community health workers are an essential part of human resources for health (HRH) strategies to combat and control the tuberculosis (TB) epidemic. These workers are essential for engaging and involving affected persons and communities, as well as for integrating prevention and care services for the disease with relevant community-based health and development activities[80]. When included as a component of a national tuberculosis control programme, community-based care is an approach that can be considered acceptable, effective, and cost-effective for the delivery of TB services. Community health worker interventions can contribute to finding missing people with tuberculosis and to improving TB treatment outcomes, and eventually contribute to decreasing TB incidence, burden, and costs[82]. These contributions can be made through: stigma reduction, awareness rising of TB signs and symptoms, and psychosocial support; improving early case finding and notifications, and treatment support; household contact tracing, preventing transmission, and facilitating access to TB services; including referral of presumptive TB cases[84]. Community health worker programmes should take into account human rights factors that influence a person's susceptibility to tuberculosis, as well as their ability to detect the disease and receive treatment for it. Tuberculosis is a disease that is associated with poverty: living conditions that are unsanitary, overcrowding, inadequate ventilation and poor nutrition all increase the risk of transmission. Outreach, peer and community support for treatment adherence, and training on human rights issues are some of the ways in

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which community health worker programmes can assist in addressing and resolving issues relating to stigma, discrimination, and exclusion. Due to occupational working conditions, as well as lower detection and reporting rates, men have a higher risk of contracting tuberculosis (TB) and dying from the disease. As respected members of the community, CHWs are in a position to make an impact and contribute to efforts to address these barriers and imbalances[80].

TB should be treated not only as a disease but also as a more comprehensive socioeconomic and community problem, keeping in mind that poverty and a lack of food and nutrition provide ideal conditions for this infectious disease. TB is a disease that affects the lungs. When it is feasible, community health worker (CHW) programmes should integrate tuberculosis (TB) services with community-based work and with programmes for other diseases, such as HIV. TB is the most common opportunistic infection for people living with HIV, and it is responsible for one out of every three deaths that are related to HIV. Despite the fact that CHWs do not always provide the full scope of services, task-sharing strategies are becoming increasingly popular. Health policy and system support within interdisciplinary primary healthcare teams can be considered in order to optimize community health worker programmes for HIV, TB, and malaria services. An evidence guide can be used for this purpose. It is essential for community health workers to receive adequate training based on their competencies, supportive supervision, and management.

The ENGAGE-TB approach highlights areas where Community Health Workers who are employed in HIV programmes can play a role in strengthening approaches to the identification, diagnosis, and referral of people who have symptoms of tuberculosis.

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TB Services that CHWs Provide

A) Community Outreach

- Fight against prejudice and stigma while working to eliminate discrimination.
- Investigate and track down household contacts as part of your search.
- People diagnosed with tuberculosis and multidrug-resistant tuberculosis should receive psychosocial support.
- Carry out communication initiatives geared toward behaviour modification and community mobilisation.
- People who have symptoms consistent with tuberculosis should be referred to a doctor for a diagnosis of TB and any related diseases.
- Lead local advocacy activities

B) Services Related to Testing, Support for Treatment, and Support for Patients

- Screen for tuberculosis and TB-related morbidity, including through home visits and HIV counselling and testing, diabetes screening, and other similar procedures.
- Make it easier for people to get access to diagnostic services (such as collecting sputum and specimens and transporting them, or accompanying people who may have tuberculosis to diagnostic services.

C) Assistance with Treatment

- Achieve better results from treatment (increasing numbers cured; reduced loss to follow up).

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- Begin and continue to provide tuberculosis prevention measures (TB preventative therapy, TB infection control).
- Patients who are undergoing treatment for tuberculosis and co-morbidities should be offered treatment and support. Services of assistance
- Offer treatment adherence support in the form of peer support, educational opportunities, and individual follow-up.
- Coordination of support for social services and means of subsistence (e.g. food supplementation, income-generation activities).
- Palliative care should be offered in the patient's home for tuberculosis and diseases related to it.

D) Within Hiv Programmes

- Determine whether the symptoms, such as coughing, fever, or weight loss, are related to tuberculosis.
- Co-treatment for tuberculosis and antiretroviral therapy should be offered to people who suffer from both HIV and TB.
- Treatment for tuberculosis prevention must be provided.
- Keeping an eye on how the TB treatment is going (clinical and laboratory).
- Recognize the potential adverse effects of anti-tuberculosis and/or anti-HIV medications, and if necessary, encourage or assist with clinic visits or consultations.
- When patients attend HIV care services, it is important to educate them about TB.

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- Utilize community engagement strategies that are specific to tuberculosis and HIV in order to combat the stigma associated with these diseases and to increase awareness of cough hygiene, TB preventive treatment, HIV prevention, as well as the availability of testing and treatment services.
- Assist in the process of referring HIV/TB patients to health clinics that are equipped to accept patients and provide treatment for them, including ensuring
- that patients have access to transportation between ART facilities and TB treatment centres.
- TB treatment adherence support should be provided in HIV settings, including home-based care settings.
- Efforts should be made to combat stigma, to encourage people to seek care, and to locate other appropriate support mechanisms.
- Data on TB and HIV-referred patients should be cross-checked between the HIV services and the TB services.

As a result, it is essential that the people living in the community have a fundamental understanding of tuberculosis (TB) and the treatment options that are available for it. Regarding tuberculosis (TB), the appropriate mentality and behaviours of the general population are of equal importance.

TB Treatment Strategies

Despite the frequently reported high morbidity rates associated with tuberculosis infection as well as significant advances in the development of effective anti-tuberculosis drugs, tuberculosis continued to be a major public health problem all over

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the world. Incorrect diagnosis and treatment, inadequate adherence to medication, increased travel and migration, the presence of multi-resistant tuberculosis, and, more recently, the pandemic of HIV/AIDS are some of the factors that have contributed to this alarming rise in the prevalence of tuberculosis. The World Health Organization encouraged the use of the Directly Observed Treatment Short Course (DOTS) strategy in an effort to lower the number of people who have tuberculosis. In 1995, the World Health Organization (WHO) began implementing their plan to combat tuberculosis (TB). It was developed with the intention of ensuring that a trained health worker or supervisor administers the prescribed TB drugs and watches the patient as they swallow each dose.

The Components of DOTS

DOTS are comprised of five essential components, which are as follows:

i. A political commitment with increased and sustained financing;
ii. Case detection through quality-assured bacteriology;
iii. Standardized treatment with supervision and patient support;
iv. An efficient drug supply and management system; and
v. A monitoring and evaluation system and impact measurement.

DOTS involve giving the patient the medication that was prescribed to them, observing them as they take the medication, checking for any adverse effects, documenting the visit, providing counselling, and responding to any questions the patient may have. Despite the fact that the strategy is predicated on the administration of short-term treatment regimens for a minimum of six months, it also includes tenets

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such as political commitment, good management practices, sputum smear microscopy for diagnosis, and the direct observation of doses in order to ensure adherence. In addition, it includes the registration of each patient who is discovered, which is then followed by standardized multi-drug treatment. There is also a secure supply of high-quality anti-TB drugs for all patients who are undergoing treatment. Individual patient outcome evaluations are conducted to ensure patients are cured, and cohort evaluations are conducted to monitor the overall performance of the programme. Because patients may try to hide tablets in their mouths or avoid taking medications altogether, the person administering therapy must maintain a high level of vigilance throughout the entirety of the treatment period. A degree of cooperation from the patient is necessary because of these potential behaviours. Investments in strengthened health systems, including trained personnel, an effective procurement and drug distribution system, and an effective monitoring and surveillance system are required for appropriate DOTS implementation. These investments are required for DOTS to be implemented correctly. Following the Abuja Declaration in 2001, the DOTS strategy was approved for nationwide use in Nigeria. Since then, it has been put into practice in each and every state that makes up the federation as well as in virtually all of the local government areas. Over three thousand DOTS centres were operational in the country of Nigeria as of the year's end (2007). In 2006, the World Health Organization (WHO) developed a brand new six-point strategy to combat tuberculosis (TB), which builds on the achievements of DOTS while also addressing head-on the most significant problems associated with the disease. Its mission is to ensure that all tuberculosis patients, including those who are co-infected with HIV and those who

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have drug-resistant TB, have universal access to high-quality diagnosis and treatment that is centred on the patient by the year 2015. This will help it achieve its goal of significantly reducing the global burden of tuberculosis by the year 2015. Additionally, the strategy lends its support to the creation of innovative and efficient tools for the prevention, diagnosis, and treatment of tuberculosis. The Global Plan to Stop TB 2006-2015 is supported by the Stop TB Strategy, which was developed by the Stop TB Partnership.

Components of the Tuberculosis Elimination Strategy

The following items make up the six parts of the Tuberculosis Elimination Strategy:

i. Seeking to improve the quality of DOTS's expansion and improvements.

   DOTS needs to expand into even the most remote areas in order to fulfil its mission of making high-quality services widely available and accessible to all those who have a need for them, including the neediest and most vulnerable individuals. At least a portion of DOTS was being used in at least 183 countries around the world in 2004, including all 22 of the high-burden countries that are responsible for 80 percent of the total number of TB cases worldwide.

ii. Taking action to combat tuberculosis and HIV, as well as multidrug-resistant tuberculosis (MDR-TB) and other challenges. In order to achieve the goals that have been set for 2015, including the United Nations Millennium Development Goal that is related to tuberculosis, it is essential to address issues such as

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TB/HIV, MDRTB, and other challenges. This requires significantly more action and input than the implementation of DOTS.

iii. Making a contribution to the fortification of health systems. The national TB control programmes need to make a contribution to the overall strategies that are being developed to advance financing, planning, management, information and supply systems, as well as scale-up innovative service delivery.

iv. Involving all of the caregivers in the process Patients diagnosed with tuberculosis typically seek treatment from a diverse range of public, private, corporate, and volunteer health care providers. All of the different kinds of health care providers need to be involved in order to guarantee that all patients can be reached and that the care they receive is of a sufficient standard.

v. Giving people who have tuberculosis and communities more agency. Projects that focus on community tuberculosis care have demonstrated to people and communities how they can perform essential TB control tasks. These networks have the potential to not only mobilise civil societies but also guarantee political support and long-term sustainability for TB control programmes.

vi. Facilitating and encouraging research to be done. Although the tools that are available can control tuberculosis, improved practises and eventual elimination will be dependent on the development of new diagnostics, drugs, and vaccines. The DOTS programme will continue to play a central role in the Stop TB Strategy.

According to the Global Plan to Stop TB, 2006-2015, the implementation of the strategy is to take place over the course of the next decade. The Global Plan is an all-

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encompassing evaluation of the steps to be taken and the resources that are required to put into action the Stop TB Strategy and to accomplish the goals listed below:

1.1 By the year 2015, bring the TB death rate and prevalence down to half of what they were in 1990 levels.

1.2 By the year 2050, eradicate tuberculosis as a threat to public health (1 case per million population).

The full recovery requires continuous treatment for a full six months with a number of different medications, which can be difficult for both patients and those working in the medical field. Inadequate treatment of tuberculosis leads to an increased risk of the development of TB strains that are resistant to drugs as well as a prolonged transmission of the disease. The WHO/IUATLD strategy known as DOTS has acknowledged and emphasised the importance of the necessity of permanent adherence to TB treatment. Nigeria has adopted a strategy for the prevention of tuberculosis (TB) that includes activities of progressive control in order to meet the goal set by the World Health Organization (WHO) to end TB by the year 2035. DOTS has been in operation within the country since 1996; however, it had been estimated that in 2016, only 35 percent of the estimated total number of sputum acid-fast bacilli positive patients in Indonesia were notified, while the cure rate was 86 percent. Indonesia has the second-highest TB burden in the world, with an estimated one million TB cases per year, which translates to 391 incident TB patients per 100,000 population per year. This places Indonesia in the global setting as the second country with the highest TB burden. It is estimated that 2.8 percent of newly diagnosed cases of tuberculosis and 16 percent of cases that have been treated in the past have

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multidrug-resistant tuberculosis (MDR TB). It is estimated that there is a prevalence of 0.4 percent of HIV among TB patients in Indonesia[85].

TB Prevention Guideline

In health care services and other settings where there is a high risk of Mycobacterium tuberculosis transmission, there is a need for prevention across all approaches, including infection prevention and control (IPC). IPC practices are essential to reduce the risk of M. tuberculosis transmission. This is accomplished by lowering the concentration of infectious droplet nuclei in the air as well as the number of susceptible individuals who are exposed to aerosols containing such pathogens. The initial recommendations made by the WHO regarding TB IPC were primarily focused on reducing the risk of transmission in health care facilities located in settings with limited resources. These initial recommendations were then expanded in 2009 to provide further guidance on the use of specific measures for health care facilities, congregate settings, and households. This expansion came about as a result of a need identified in 2009. After the 2009 guidelines had been in effect for almost ten years, it was anticipated that they would require an update in order to provide a revised evidence assessment, as well as to reinforce earlier recommendations and link to core components of effective IPC programmes in general[33]. The most recent revision of the guidelines highlights the significance of carrying out the implementation of IPC measures in a manner that is methodical and objective, giving priority to taking into account the hierarchy of IPC controls. Therefore, the interventions that have been described should not be implemented individually or in a manner that dissociates them from other administrative and environmental controls, as well as personal protection;

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rather, they should be regarded as part of an integrated package of IPC interventions in order to stop the spread of *M. tuberculosis*. These guidelines do not attempt to create a parallel programme that is solely dedicated to TB IPC; rather, they emphasise the importance of building an integrated, well-coordinated, multisectoral action towards TB infection control across all levels of care, as well as in non-health care settings with a high risk of *M. tuberculosis* transmission. This is because these guidelines do not attempt to create a parallel programme that is exclusively dedicated to TB IPC. In order to accomplish this, as a first stage, these guidelines will lay out general recommendations and activities that are considered to be good practices. Both of these aspects are essential for the establishment and efficient operation of all IPC programmes. These core components of IPC programmes are an important part of WHO strategies to prevent current and future threats, strengthen the resilience of health service providers, contribute to the prevention of conditions such as health care-associated infections, such as tuberculosis, and fight antimicrobial resistance. Therefore, it is necessary to put into action interventions that rapidly identify source cases and impede person-to-person transmission by lowering the concentration of infectious particles in the air and the amount of time susceptible individuals are exposed to those particles. These guiding principles constitute the foundation for efficient infection prevention and control (IPC). IPC practices are not routinely or systematically implemented, despite their potential benefit and impact, particularly in settings with limited resources. This is despite the fact that the implementation of IPC measures can reduce the risk of *M. tuberculosis* transmission[86].

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Administrative Controls

Any IPC strategy should begin with establishing a set of administrative controls as its first and most important component. These key measures include specific interventions that have the goal of lowering the amount of exposure to *M. tuberculosis* and, as a result, lowering the amount of transmission of the disease. They consist of prompt initiation of effective treatment as well as respiratory hygiene, triage and patient separation systems (i.e., management of patient flows to promptly identify and separate presumptive TB cases), and triage and patient separation systems. In addition, community health workers are essential to the process of promptly identifying presumptive TB cases at the community level and making use of referral systems. This helps to expedite the TB diagnosis process and makes it easier to implement other interventions. Community health workers have the potential to assist in the improvement of early TB case detection and the reduction of the risk of TB transmission throughout the community as a whole. The efficient operation of a triage system requires significantly more than the bare minimum of infrastructure (e.g., conditions for fast tracking of patients with presumed TB, rapid diagnosis, respiratory separation, use of data-recording tools for documentation, and analysis of data for developing or changing evidence-based policies). The availability, education, and sensitization of health care providers and others, who work in settings with a high risk of *M. tuberculosis* transmission, as well as continuous training for these individuals, should be given priority during the implementation. In accordance with the most recent recommendations regarding the screening for active tuberculosis disease, people who are living with HIV should be routinely screened for active TB at each and

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every visit to a health care facility. In a similar vein, routine HIV testing should be offered to all patients with presumed or diagnosed tuberculosis, in particular in settings with a high HIV burden. It is possible for triage systems to be included in collaborative activities established to prevent and detect tuberculosis as part of other disease programmes (e.g., diabetes and conditions that increase the risk of LTBI or TB disease). Below are the recommendations for administrative control:

- It is recommended that people who have signs and symptoms of tuberculosis or who have tuberculosis disease undergo triage in order to reduce the risk of M. tuberculosis transmission to health care workers (including community health workers), individuals who attend health care facilities, or other individuals who are in environments where there is a high risk of transmission.
- It is recommended that people who are suspected of having infectious tuberculosis or who have evidence of having infectious tuberculosis should undergo respiratory separation or isolation in order to reduce the risk of M. tuberculosis transmission to health care workers or other individuals who visit health care facilities.
- It is recommended that people who have TB disease begin effective treatment as soon as possible in order to reduce the risk of M. tuberculosis transmission to health care workers, individuals who attend health care facilities, or other individuals who are in environments where there is a high risk of transmission.
- It is recommended that individuals with presumed or confirmed TB practice good respiratory hygiene, which includes proper cough etiquette. This will help reduce the risk of M. tuberculosis transmission to health care workers,

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individuals who attend health care facilities, and other individuals who are in environments where there is a high risk of transmission[86].

Environmental Controls

The following are recommendations for environmental control:

- It is recommended that upper-room germicidal ultraviolet (GUV) systems be utilised in order to lessen the likelihood of *Mycobacterium tuberculosis* (*M. tuberculosis*) transmission to health care workers, patients, or other individuals who are in environments where there is a high probability of transmission.
- Ventilation systems (including natural, mixed-mode, and mechanical ventilation as well as recirculated air through high-efficiency particulate air [HEPA] filters) are recommended to reduce the risk of *M. tuberculosis* transmission to health workers, individuals who attend health care facilities, or other individuals in settings where there is a high probability of transmission[86].

Respiratory Control

The recommendation for respiratory control includes:

- Within the framework of a respiratory protection programme, the use of particulate respirators is recommended in order to reduce the risk of *M. tuberculosis* transmission to health care workers, individuals who attend health care facilities, or other individuals who are in environments where there is a high risk of transmission[86].

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Pharmacognosis

There are currently ten drugs that have been approved by the FDA to treat active drug-susceptible tuberculosis (as shown in Fig. 1)[87]. Isoniazid, rifampin, ethambutol, and pyrazinamide are the essential medications that must be taken for a period of six to nine months in order to effectively treat tuberculosis[87,88]. Chemoprophylaxis with six to nine months of isoniazid or rifampin is currently the only treatment available for LBTI at this time. During the course of these treatments, the drugs isoniazid and rifampin are given on a daily basis. Isoniazid, on the other hand, may be administered at higher dosages on a biweekly schedule. Isoniazid and rifapentine are two additional drugs that can be given to patients in order to lessen the hepatotoxicity caused by isoniazid treatment on its own[7]. Both a one-month treatment for LTBI using isoniazid-rifapentine and a four-month treatment using rifampin have recently been given the green light by the World Health Organization (WHO). In addition, a treatment called isoniazid-rifapentine for latent tuberculosis infection (LTBI) that only takes one month has only recently become available for use in the prevention of tuberculosis caused by HIV. Oral bedaquiline treatment is the standard of care for patients with multidrug-resistant tuberculosis[18]. In all other respects, drug-resistant active tuberculosis makes use of the same medications as drug-susceptible active tuberculosis, albeit at different intervals and in varying doses[86]. Isoniazid is a small molecule antibacterial drug that attacks M. tuberculosis by focusing on two of its proteins. An enzyme known as catalase-peroxidase, which shields bacteria from harmful reactive oxygen species, is the first target of this strategy. Enoyl-[acyl-carrier-protein] reductase is the second target, and it is an enzyme that plays a role in the production of mycolic acid. An

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antibiotic called rifampin is produced by the bacterium Streptomyces mediterranei. Rifampin is able to prevent transcription because it binds to DNA-dependent RNA polymerase and blocks its activity. Ethambutol is bacteriostatic because it targets probable arabinosyltransferases A, B, and C, which in turn inhibits the production of cell walls by Mycobacterium tuberculosis. Pyrazinamide is a small molecule antituberculosis agent that disrupts plasma membranes and causes intracellular acidification in M. tuberculosis bacteria. It does this by targeting M. tuberculosis's fatty acid synthetase[89]. Antibiotic rifapentine inhibits DNA-dependent RNA polymerase in addition to its antibiotic properties. Bedaquiline is a drug that is used to treat mycobacterial infections, and it works by inhibiting ATP synthase subunit[90]. The potential involvement of the numerous anti-VEGF inhibitors and combination therapies that are currently in use for the treatment of cancer needs to be investigated further for use in future tuberculosis treatments[91]. There are a variety of small molecules and antibodies that have been granted approval by the Food and Drug Administration (FDA) as anti-VEGF and anti-VEGFR treatments. These treatments for tuberculosis are supported by the understanding that VEGF concentrations are elevated in the serum of patients with active tuberculosis, that VEGF selects macrophage and blood and lymphatic vasculature, and that VEGF contributes to inflammation[6,16]. This understanding lends credence to the logic behind these treatments, which can be used to treat tuberculosis. It has been demonstrated that administering treatments that are anti-VEGF and anti-VEGF Receptor (VEGFR) can be helpful in the treatment of tuberculosis. The clinical regression of granuloma was successfully treated with intravitreal administration of bevacizumab, as shown by a

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case study that provides demonstrative evidence of the efficacy of anti-VEGF drugs in human patients[92]. Bevacizumab is an anti-VEGF-A IgG antibody that has been humanised and monoclonal[93]. Bevacizumab has also been shown to normalise vasculature in rabbits and to increase the delivery of small molecules. The enhancement of small molecule delivery seen in anti-VEGF treatment may make it possible for the antibacterial medications that are currently being prescribed to be more effective. There are at least five different isoforms of VEGF, but the only ones that can be targeted by drugs that have been approved by the FDA are A and B. In addition, there are at least three different isoforms of VEGFR, and there are drugs that are approved by the FDA to target all of them. Inhibitors of tyrosine kinase, also known as small molecules that target VEGFR, monoclonal antibodies, and fusion proteins are some of the drugs that have been given FDA approval[93]. Anti-VEGF therapy, when administered in vivo, prevents the spread of mycobacteria from the site of infection, lessens the formation of granulomas, enhances the delivery of small molecules, and has the potential to lead to the clinical regression of granulomas[13,92]. When assessing the efficacy of anti-VEGF/VEGFR antibodies and small molecules that have been approved by the FDA in the treatment of tuberculosis, clinicians and pharmaceutical companies may take a number of factors into consideration. Concerns include anti-VEGF resistance, adverse effects, changes in the function of T-helper cells, and hypoxia.

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Initiating Treatment for Tuberculosis (TB)

In theory, beginning treatment for anyone who has been diagnosed with tuberculosis should not be difficult; however, in practice, this is a much more challenging task than

it may appear. In low- and middle-income countries in Africa, Asia, and the Western Pacific, the percentage of patients with sputum smear-positive or culture-positive TB who do not begin treatment ranges from 4 percent to 38 percent. It would appear that the utilisation of rapid molecular technology does not result in any improvement to this pre-treatment loss to follow-up. Individual care can be compromised, and the risk of *M. tuberculosis* transmission within families and communities can increase even among those who do receive treatment. Turnaround times can be long between a confirmed diagnosis and the start of treatment for those who do receive treatment[71].

Preventive Measures for Tuberculosis

The spread of drug-resistant strains of *Mycobacterium tuberculosis* is becoming an increasingly difficult obstacle for public health and the prevention of tuberculosis. Initial evidence suggested reduced transmissibility of resistant strains; however, it is now clear that primary transmission of drug-resistant bacteria (as opposed to acquired resistance) is the dominant mechanism sustaining the global transmission of drug-resistant TB (DRTB) cases. DRTB stands for drug-resistant tuberculosis cases. To succeed in reaching global goals to put an end to the tuberculosis epidemic, it is essential to break the cycle of *M. tuberculosis* transmission[64].

Monotherapy with isoniazid for at least six months, also known as isoniazid preventive therapy (IPT), and treatment with regimens containing rifamycin are the two primary forms of tuberculosis preventive treatment for infections with strains that are thought to be drug-susceptible (rifampicin or rifapentine). IPT has historically been the type of tuberculosis preventive treatment that has seen the most adoption;

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however, the shorter duration of rifamycin regimens presents a clear advantage. A different approach, using a fluoroquinolone or other second-line agents, is required for the preventative treatment of multidrug-resistant tuberculosis (MDR-TB)[64].

Regardless of a patient's HIV status, the following treatment options are recommended for the treatment of LTBI:

- A 1-month regimen of daily rifapentine plus isoniazid or 4 months of daily rifampicin alone may also be offered as alternatives. • 6 or 9 months of daily isoniazid, or a 3-month regimen of weekly rifapentine plus isoniazid, or a 3-month regimen of daily isoniazid plus rifampicin.
- Young adults and adolescents living with HIV who have an unknown or a positive LTBI test and are unlikely to have active TB disease should receive at least 36 months of daily isoniazid preventive treatment in environments with high rates of TB transmission. This treatment should be continued for at least 36 months (IPT).
- In locations that are regarded as having a high rate of tuberculosis transmission as determined by national authorities, it is recommended that individuals receive daily IPT for a period of thirty-six months, regardless of whether or not they are receiving antiretroviral therapy (ART) and regardless of the degree of immunosuppression, history of previous TB treatment, or pregnancy status of the individual.

The Global Drug Review (GDG) revised the original text of this recommendation in 2019 to include two new conditional recommendations: one for daily rifapentine plus

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isoniazid for one month (1HP) and one for daily rifampicin monotherapy for four months (4R) in all treatment settings. These changes were made to accommodate the new information. These new recommendations are founded, respectively, on a low to moderate level of certainty in the aforementioned effect estimates. In addition, the GDG now recommends a duration of 3 months for daily isoniazid plus rifampicin (3HR) and of 4 months for daily rifampicin alone (4R) to reflect the usual length of time for which these regimens are currently employed. Previously, the GDG recommended a range of 3–4 months. Additionally, three previous recommendations on the use of 6H, 3HR in people 17 years, the difference in rate of confirmed TB between 4R and 9H (4R arm minus 9H arm) was 15 years of age outweigh the harm, given its safety profile, the higher rate of completion when compared with isoniazid monotherapy, and the availability of child-friendly, fixed-dose combinations of rifampicin and isoniazid. In light of this, the GDG came up with a strong recommendation in spite of the poor quality of the evidence. Regarding the efficacy and pharmacology of rifapentine in children younger than two years, there are either no data or very limited data. It is only recommended to use the 3HP regimen in children who are at least 2 years old, while the 1HP regimen should only be used in individuals who are at least 13 years old. The 2019 Global Drug Review (GDG) considered that there was a moderate level of certainty that 4R is not inferior to 9H. Furthermore, when taking into consideration the good safety profile of the 4R regimen as well as its reduced length, the GDG recommended that this regimen may also be used in settings with a high TB burden. The GDG took into account the fact that the vast majority of people would prefer a shorter regimen when making their decision to

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issue a conditional recommendation. Despite this, they voiced their concerns regarding the variability in acceptability, the uncertainty in resource requirements given its higher cost, and the potential for reducing equity should it deflect resources and decrease treatment coverage for those who are more vulnerable. The GDG came to the conclusion that the implementation of 4R must be accompanied by the mobilisation of appropriate resources from the very beginning in order to prevent shortages in the fulfilment of other programmatic requirements. Concerning 1HP, the 2019 GDG came vto the conclusion that there was a low level of certainty that its effectiveness would be non-inferior to that of 9H when utilised in programmatic settings in a variety of populations at risk. The Global Drugs Governance Board (GDG) recommended that this regimen may also be used in settings with a high TB-burden as well as in people who do not have HIV infection. This recommendation was made after taking into consideration the positive safety profile of 1HP as well as its significantly shorter duration in comparison to other LTBI regimens that have been approved. The Global Development Group (GDG) considered that most people would value its much shorter duration than other options, and that its implementation would be feasible. The Global Drugs Governance Group (GDG) came to the conclusion in this most recent update that any regimen could be used in any setting, regardless of the prevalence of tuberculosis (TB), provided that the health infrastructure can guarantee that the treatment is administered correctly without causing inequities and that active TB can be reliably excluded prior to the beginning of treatment. The GDG made the observation that all of the treatment options can be carried out by the patient themselves. Although a randomised controlled trial demonstrated that self-

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administered treatment of the 3HP is not inferior to treatment in which the patient is directly observed, there is very little additional evidence on self-administration of this regimen. The GDG pointed out that the necessity of a direct observation might present a sizeable obstacle to the implementation of the plan. People who are receiving preventative treatment for tuberculosis should also be supported by having access to advice on the treatment and management of adverse events during their interactions with health services. The GDG also found that patients undergoing treatment, clinicians who are providing treatment, and programme managers would all prefer shorter regimens to longer ones.

Interactions between Different Drugs

Rifamycins are antibiotics that stimulate the production of certain cytochrome P-450 enzymes. As a result, these antibiotics have the potential to inhibit the metabolism of medicines that are dependent on the same pathway. These include antiretroviral therapy (ART) in addition to a wide variety of other medications, including anticonvulsants, antiarrhythmics, quinine, oral anticoagulants, antifungals, oral or injectable contraceptives, corticosteroids, cyclosporine, fluoroquinolones and other antimicrobials, oral hypoglycemic agents, methadone, and tricyclic antidepressants. When rifampicin or rifapentine-containing regimens are administered, it is possible that such medicines will need to be avoided, or the dosages of those medicines will need to be adjusted. Patients living with HIV who are currently receiving antiretroviral therapy (ART) should be prescribed rifamycin-containing regimens with extreme caution due to the possibility of adverse drug interactions. It is not recommended to give these regimens to people who are currently taking protease inhibitors or

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nevirapine. This includes HIV-exposed infants who are undergoing preventive treatment. Other antiviral agents, such as atazanavir, darunavir, fosamprenavir, lopinavir, saquinavir, and tipranavir, can have their concentrations lowered by rifampicin. It must not be taken at the same time as saquinavir or ritonavir. When rifampicin is given at the same time as efavirenz, there is no need to make any adjustments to the dosage. When given in combination with rifampicin, the dose of dolutegravir must be increased to 50 milligrammes twice daily; this is a dose that is typically well tolerated and provides an efficacy that is comparable to that of efavirenz with regard to the suppression of viral replication and the recovery of CD4 cell count. According to the findings of a pharmacokinetics study, the 3HP regimen does not require any adjustments to the dosage when it is given to patients who are already taking antiretroviral regimens that contain efavirenz. It was found that the combination of rifapentine and raltegravir could be safely administered and was well tolerated by the patients. A drug interaction study involving healthy volunteers that compared dolutegravir to HP once weekly found that two out of four participants experienced toxic effects. On the other hand, results that were released more recently from a Phase 1/2 trial of 3HP and dolutegravir in adults with HIV reported good tolerance and viral load suppression. Additionally, there were no adverse events of Grade >3 related to the HP, and the results did not indicate that rifapentine reduced dolutegravir levels sufficiently to require a dose adjustment. However, the GDG emphasised the ongoing need for studies of the pharmacokinetics of 3HP when taken concurrently with other medications, particularly ART. Alcohol consumption should be avoided at all costs in conjunction with tuberculosis preventive treatment[94].

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The Challenge of Sub-optimal TB Treatment Outcomes

Data on the treatment outcomes of people who were treated for drug susceptible TB in 2018 and those who initiated treatment for drug resistant TB in 2017 can be found in the global TB report that will be published by the WHO in 2020. 85 percent of those diagnosed with new or relapsed tuberculosis, 76 percent of those diagnosed with HIV-associated tuberculosis, and 57 percent of those diagnosed with RR or MDR-TB were successfully treated globally. These numbers indicate a performance that is not quite up to par. The lack of evaluation, inadequate linkage to treatment, high rates of death, and high rates of loss to follow-up are the primary contributors to the poor treatment outcomes. The underlying causes of poor treatment outcomes include unidentified or additional drug resistance, inadequate support provided to people with tuberculosis to ensure a high level of adherence, weak recording and reporting systems, and inadequate prevention and management of advanced HIV disease including the provision of anti-retroviral treatment. Concerning children in particular, challenges include under-identification, inadequate recording and reporting, inadequate drug formulation options, inadequate caregiver availability and capacity for treatment, and persistent issues with stock outs of the few drug options that are appropriate for this population of patients. In 2019, only 30 percent of the five-year target of 3.5 million children treated for tuberculosis had been achieved. Additionally, only 8 percent of the 115,000 targets for treatment of children with RR/MDR TB had been achieved. Failures in data collection and proper and consistent disaggregation continue to have a negative impact on the ability to identify and treat patients, as well as on the development of appropriate programming and the distribution of resources for children under the age of 15 and adolescents between the ages of 10 and 19. WHO

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now recommends that the shorter 9-month MDR-TB regimens be preferred because it achieves treatment success in roughly 80 percent of participants. This recommendation is based on observational studies that were conducted in Bangladesh and sub-Saharan Africa. The results of these studies were confirmed by the results of the standardised treatment regimen of anti-TB drugs for people with MDR-TB (STREAM) Stage 1 trial. In addition, second-line injectable drugs should, if at all possible, be replaced by a bedaquiline (BDQ)-containing regimen that can be taken entirely orally. Bedaquiline is one of the new potent MDR-TB drugs, along with delamanid and pretomanid, that are now being increasingly prescribed around the world. In addition to point-of-care molecular drug susceptibility testing of second line MDR-TB drugs, the use of such regimens should be scaled up as quickly as possible in order to improve treatment outcomes, minimise adverse effects, and increase patient adherence. Furthermore, in the recent past, efforts have been made to shorten the duration of treatment for drug-resistant tuberculosis by concentrating on the use of fluoroquinolones. However, the large clinical trials that were conducted for the purpose of demonstrating efficacy for relapse-free cure were unsuccessful[95].

Directly observed treatment (DOT) has been a cornerstone of tuberculosis (TB) care and prevention for decades, despite the fact that its efficacy in comparison to self-administered treatment has been called into question. The goal of DOT is to ensure that TB treatment is taken exactly as directed. However, direct observation of the ingestion of TB treatment may be disempowering for the individual who is being treated, in addition to imposing demands on the individual being treated as well as the health care system that may be difficult to manage. It is more likely that people who

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have tuberculosis and their families will accept a strategy that is based on providing comprehensive and individualised support to people who are being treated for TB. This strategy has also been associated with higher rates of successful treatment completion. In addition, in the modern digital world, new methods of supporting people who are undergoing treatment, such as interactive two-way mobile phone text message reminders and video assisted DOT, have also been associated with high levels of treatment adherence while simultaneously providing psychological support through remote counselling[95].

2.3 Review of Empirical Studies Concept of Tuberculosis

Mycobacterium tuberculosis (MTB), as well as *Mycobacterium bovis* and *Mycobacterium africanium,* are the microorganisms that transmit tuberculosis (TB)[96]. *M. tuberculosis* is a gram-positive, acid-fast rod with a thin, flat shape. The organism is a stringent aerobe that prefers to live in organs with an increased oxygen tension. As a result, metastatic foci such as the apices of the lungs, renal parenchyma, and the developing end of bones are prevalent. In most situations, the infection is caused by the pathogenic organisms. *M. bovis*, on the other hand, is a pathogen in the same bacterial complex as *M. tuberculosis*, and its clinical features are nearly identical to *M. tuberculosis* in most cases. The bacteria that cause TB (*M. tuberculosis and M-bovis, M-africanai*) create tubercle lesions in TB patients, so the organisms are called tubercle bacilli. Acid-fast bacilli are another name for them (AFB). Inhalation of infective droplets from individuals with open pulmonary tuberculosis through coughing, sneezing, talking, or spitting is the only way the pathogenic organism is

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spread. Some of the elements that affect an individual's risk of exposure include the proportion of droplet nuclei in polluted air, the duration of time the person takes in air, and their immunity status (susceptibility to infections). Once infiltrated with tuberculosis-causing bacteria, a person can remain asymptomatic for the rest of their lives without developing the disease[97]. However, in this healthy, asymptomatic but infected individual, disease advancement can be influenced by a multitude of factors, the most pertinent of which is a weakened immune system, particularly HIV infection. Overpopulation, poor living conditions, malnutrition, and associations with other diseases all contribute to the risk of TB infection, which contributes to increased rates of re-infection and severe morbidity and mortality in patients. Tuberculosis patients are frequently drawn from the most vulnerable groups in society. Those living in poverty, in prisons, and in poor working circumstances are among them. Stress reduction, exposure to pollutants, overpopulation, poverty reduction, improved nutrition, and engagement with health care providers all lessen the risk of infection and illness development. After 5 years without therapy, 50% of primary TB patients may often die, 25% will develop chronic infectious TB, and the other 25% will be reduced gradually by strong immune defenses without treatment[98]. It has influenced and coevolved with man over millennia[99]. The pathogen's effectiveness is due in part to its ability to remain in an undetected state of dormancy within its host and, in a small percentage of cases, activate to pulmonary tuberculosis (TB) sickness months or even years later.

Tuberculosis is still the most common cause of mortality worldwide, with the majority of new cases occurring in low- and middle-income nations. Despite achievements, the

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WHO Global Tuberculosis Report 2019 emphasizes major and persistent gaps in detection and treatment, including human rights and gender hurdles[97]. The age at the time of infection, as well as the presence of any other medical condition linked to TB progression, define a human's long-term likelihood of reactivation TB from latent TB infection (LTBI). Smear-positive, pulmonary TB is a continuous infection that kills 70% of people within 10 years if left untreated[98]. Individuals with radiological evidence of previous TB (e.g., stable upper lobe fibrondular lesion with normal bronchial cultures) had a 6-to 19-fold greater risk of developing active TB from LTBI. Immunocompromised people (e.g., people living with HIV (PLWH), stable and haematological heart or lung disease, people taking tumor necrosis factor (TNF)-alpha-blockers, very young children (5 years old), and those with specific conditions (e.g., end-stage kidney failure on haemodialysis, pneumoconiosis, head and neck cancers, and, to a limited extent, type 2 diabetes and cigarettes) have a significantly higher risk of TB. Because the majority of active TB is caused by LTBI reactivation, it is possibly reversible. Adequate preventative strategies necessitate a solid grasp of both LTBI and clinical TB epidemiology[98].

When compared to the treatment of other extremely prevalent infectious diseases, such as HIV/AIDS and hepatitis C virus infection, it is evident that the treatment response for tuberculosis disease demands innovative thinking, as it is still premised on methods with limited efficacy (e.g. therapies of multidrug-resistant tuberculosis; MDR-TB), and is defined by the scale factor "long duration": customary bacteriological diagnosis, drug-susceptible diseases (i.e. 6 months) and MDR-TB (i.e. >20 months)[99,100]. Above limitations in terms of diagnosis and treatment technologies

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account for some of the modest decline in annual global TB incidence rate (~2%). The introduction and spread of MDR-TB, as well as the outbreak of co-infected TB/HIV cases, are determinants of the existing epidemiological state. Not only in the remote healthcare centers in low-income and high-TB-incidence nations, but also at TB referral centers in high-income countries, the cascade of care reveals various flaws and problems. There are still a lot of unknowns about the infectiousness of pulmonary *M. tuberculosis* patients. Mycobacterial variants can be transmitted by patients with culture-confirmed lung disease to immunocompromised individuals, resulting in secondary infection and, inevitably, the disease. The retention of the pool of people with the disease who potentially develop the disease is mostly due to improper management of contagious TB cases' contacts and poor infection prevention and control performed in healthcare facilities and communities. The risk of infection and exposure to infectious cases are determined by various factors related to the host, mycobacterial features, and the environment, which may interact to enhance or reduce the risk of infection. However, those threat variables are only partially understood, therefore therapies targeted at mitigating the effects of exposure are limited. Numerous model simulations have shown that if nations want to completely eradicate the economic and health burden of tuberculosis (i.e., annual TB incidence rate <1 case per million), disease control policies must include efficient treatment assessment and management of the patients and their contacts; however, disease control measures may not be sufficient. Further efforts are required to minimize exposure (e.g., improved and well-implemented infection control policies), guard vulnerable population (e.g., primary prevention focused on a safe and efficacious new vaccine administered to

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newborns and at major risk population groups in high and low TB incidence nations, respectively), and trace and treat individuals with a latent TB infection (LTBI). By adding above public health measures in the End TB Strategy, which was endorsed by the World Health Assembly in May 2014, the World Health Organization (WHO) emphasizes their prospective essential role. The global healthcare community has identified systematic management of LTBI as one of the most important public health measures for reducing tuberculosis[101].

Knowledge about Tuberculosis among Youth and Young Adults

Shamu 2019 analysed young men and women (18–24 years)'s TB knowledge including TB/HIV co infections, testing rates and factors associated with them. A cross sectional cluster-based household survey was conducted in two provinces. Participants completed computer-assisted self-interviews on TB knowledge, testing history and TB/HIV co infections. A participant was regarded as knowledgeable of TB if s/he correctly answered the WHO-adopted TB knowledge questions. A total of 72% had knowledge of TB, 21% underwent screening

tests for TB and 14.7% knew and tested for TB. Participants who received a social grant were more likely to be knowledgeable of TB than those who did not receive a social grant ($p<0.0001$). Participants who completed matriculation were more likely to be knowledgeable of TB than participants who did not complete matriculation ($p<0.0001$). Regarding accommodation type participants living in substandard housing were more likely to report higher knowledge of TB than those living in standard housing. In terms of basic household possessions, participants who possessed at least five basic commodities were more likely to be knowledgeable of TB than

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those who had less than five commodities (p<0.0001). Participants whose income came from family/partners and social grants were more likely to be knowledgeable of TB compared to those who were employed (p<0.0001). Participants using the print media, with higher levels of HIV knowledge, engaging in transactional sex and those who had positive attitudes towards PLWH were more likely to be knowledgeable of TB than those not using the print media, with less HIV knowledge, not transacting in sex or with negative attitudes towards PLWH.

Kalu 2015 Simple and systematic random sampling techniques were employed in the selection of schools and students who consented to participate in the study. The result of this study showed that, respondents were predominantly within the age bracket of 15-19 years 224 (61.0%), Christians 382 (95.5%), males 227 (56.7%) and reside with both parents 139 (34.8%). Most respondents (97.0%) claimed to be aware of TB with the media (34.1%) as their major source of information. Respondents exhibited a high knowledge of TB transmission but knowledge of TB causes; treatment and prevention were reported low in this study. Attitude of respondents towards TB was positive but 30.5% were not aware that TB treatment is free. Prevention practices of school adolescent toward TB is reported high because 79.5% felt that prompt diagnosis and treatment and avoiding crowded environment (36.0%) are effective strategies to prevent the spread of TB.

Pontual 2016 Medical records were reviewed for all adolescents aged 12 to 18 years hospitalized with the diagnosis of TB in Avicenne/ Jean Verdier Teaching hospital (Seine-Saint-Denis, suburb of Paris) between September 2000 and December 2004.

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Of the 52 patients identified, 52% were female. Median age at diagnosis was 15 years (range, 12–18 years). The proportion of adolescents known to be born abroad was 90%. Diagnoses resulted from the examination of a sick child in 79% of cases, a case contact investigation of an adult suspected of having TB in 19% and routine tuberculin skin test in 2%. Twenty-seven of 52 patients (52%) had isolated pulmonary disease. Sixteen patients (31%) had pulmonary and extrapulmonary TB and 8 cases (17%) had exclusively extrapulmonary disease. The site of extrapulmonary TB included pleural, meningitis, lymph node, peritoneal, osteoarticular and genitourinary. TB was confirmed by the isolation of *Mycobacterium tuberculosis* from sputum, gastric aspirate, bone or cerebrospinal fluid. No case had a relapse or recurrence of disease in median 3.2 years of follow up.

Idris 2020 *conducted a* school-based, non-randomised controlled study was conducted among secondary school students with a total of 236 respondents. The KAPS score were assessed before and 1 month after using self-administered validated KAPS questionnaire on TB. Analysis was done using repeated measures ANOVA.

The mean percentage score (SD) for baseline knowledge, attitude, practice and stigma score for the respondents were 54.0 (4.48), 65.6 (1.74), 70.0 (1.43) and 66.0 (6.88), respectively. There was a significant difference ($P < 0.001$) in the knowledge and stigma score for intervention group compared to control group, adjusted for gender, ethnicity and smoking status 4 weeks post-TB educational programme. However, with regards to attitude and practice score, there was no significant difference ($P = 0.210$ and $P = 0.243$, respectively).

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Shamu 2019 found adolescents to have average levels of knowledge and preventive practices with regards to TB. Overall, they had positive attitudes towards prevention; however, the level of stigma towards the disease was high. This high level of stigma could pose an obstacle to treatment and contact tracing in this group. Lack of knowledge regarding TB symptoms and disease transmission resulted in delay seeking for treatment and increased TB contact, confirming the results of an intervention study conducted in Alexandria, the participants in the TB education programme exhibited a significant increase in knowledge.

Shatat 2015 in an intervention study in a health education programme consisted of 90 min lecture-discussion session followed by 30 min questions and answers and, aided by slides and posters provided to 467 secondary school students in 12 schools, the knowledge about modes of transmission, TB symptoms and preventive practice of TB improved significantly. Panaligan 2012 conducted a cross-sectional study at a Philippines high school with a total population of 1,906 students. A 20-min lecture about TB was presented to the students. The high school students' knowledge of TB, which was 65.22% at baseline, increased to 86.83% after a health education intervention. These findings were similar to those of an intervention study conducted in India. The knowledge levels were significantly improved after a 30-min audiovisual health education session.

Kalu 2015 most respondents reported that prolong cough 152 (37.7%) was the major sign and symptoms of tuberculosis. Others said chest pain 82 (20.3%), weight loss 48 (11.9%), weakness 46 (11.4%) and loss of appetite 33 (8.2%) were related signs and

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symptoms of tuberculosis. About 28 (6.9%) reported lack of knowledge of tuberculosis signs and symptoms. While one hundred and twenty-two respondents felt smokers were more at risk of contracting tuberculosis, 90 (22.5%) felt people who drink alcohol are more at risk. Sixty-six in their opinion felt everyone is substantially at risk of contracting tuberculosis. However, 66 (16.5%) said they have no idea of who is at risk or not. Knowledge of causes of tuberculosis was duly exhibited as a larger proportion of the respondents said drinking of alcohol 134 (33.5%) causes tuberculosis. Others said that bacteria 103 (25.8%), virus 45 (11.2%), dirty water 7 (1.8%) and eating certain food 5 (1.2%) are causes of tuberculosis. About 104 (26.0%) reported that they have do not know what causes tuberculosis. More than two-third of the respondents381 (95.2%) are aware that tuberculosis can be transmitted from one person to another.

Practice of Tuberculosis Preventive Measures among Adolescent and Young Adult

While several studies showed level of knowledge and awareness was not associated with attitudes and practices, there was no significant change in attitudes and practices over the course of the present educational intervention study. Hashim et al 2013 conducted cross-sectional study involving 250 primary health care centres in Iraq among 500 patients, found that almost half of the patients had unfavourable attitudes and practices towards TB while 64.4% of them had good levels of knowledge. In a multi-centre community cross-sectional study conducted by Aseeri et al 2017 in a population of Saudi Arabia found that most of the respondents had general awareness but not adequate knowledge regarding TB. Majority of them also had negative attitudes towards TB and people with TB. The negative attitude was reported as

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majority thought they will not suffer from TB, feel fears towards TB and less than half would search for treatment. Of the respondents, 42.3% would avoid people with TB and 29.9% of respondents actually have fear towards them. An interventional study done by Mohammadi 2012 in Iran regarding the effectiveness of TB health education suggested that interventions should focus on the culture and beliefs of a population in order to improve and to maintain positive attitudes. The intervention programme can be led by a trained group or individual consultations concerning their learning and hometown educators with similar beliefs. The intervention programme included culturally competent interactive discussion presented through case scenarios that focused on Malay's perspectives, attitudes and preventive practices towards TB. A majority of our respondents were Malay (94.5%) since the study was conducted in Kelantan, which is located in the northeast of Peninsular Malaysia where the majority of the population is Malay (95.9%). However, the session was held without involvement of their trusted educators to influence their beliefs and culture in a single intervention programme. This element could be the reason for the lack of change in these domains.

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Factors that Influences the Practice of Tuberculosis Prevention among Adolescents and Young Adults

Kalu 2015 also found an 8% prevalence of cigarette smoking and a 20.3% prevalence of vaping. However, the number of cigarette smokers was comparatively lower than that (11.7%) reported in a 2016 survey of Malaysian adolescents. A similar survey also reported that 9.1% of Malaysian adolescents and 7.8% of adolescents in Kelantan were current e-cigarette user. Hafizuddin 2018 retrospective cross-sectional study of children and adolescents in Kelantan found that cigarette smokers were three times

more likely than non-smokers to develop TB infection. Steven 2014 conducted a case-control study of older children in Brazil also found a relationship between cigarette smoking and TB infection. In our education intervention programme, we were able to address this issue to the secondary school students and encourage them to quit smoking during the lecture and small group discussion.

Shamu 2019 found factors associated with TB knowledge were being female, younger, a student, and social grant recipient, not transacting sex and having positive attitudes towards people living with HIV (PLWH). Factors associated with TB testing were being a student, receiving a social grant, living in OR Tambo district, HIV knowledge and having a family member with TB history. Factors associated with both TB knowledge and testing were being female, a student, using the print media, living in OR Tambo district and having a family member with a TB history.

Rabaah 2018 deduced Culture can affect behaviours through values, beliefs and traditional roles, and, according to a study related to health behaviour among Malaysian adolescents; culture had a great influence on desirable health behaviours among adolescents. Healthy behaviour includes good attitude and practices related to health and disease prevention.

2.4 Conceptual Framework

The conceptual framework of TB control and prevention were reported within four major categories: preventing transmission, early detection, appropriate treatment and programmatic management. By examining the interactions between these components, a conceptual framework for TB can help to guide the development of effective prevention and control program that aim to increase knowledge and awareness about

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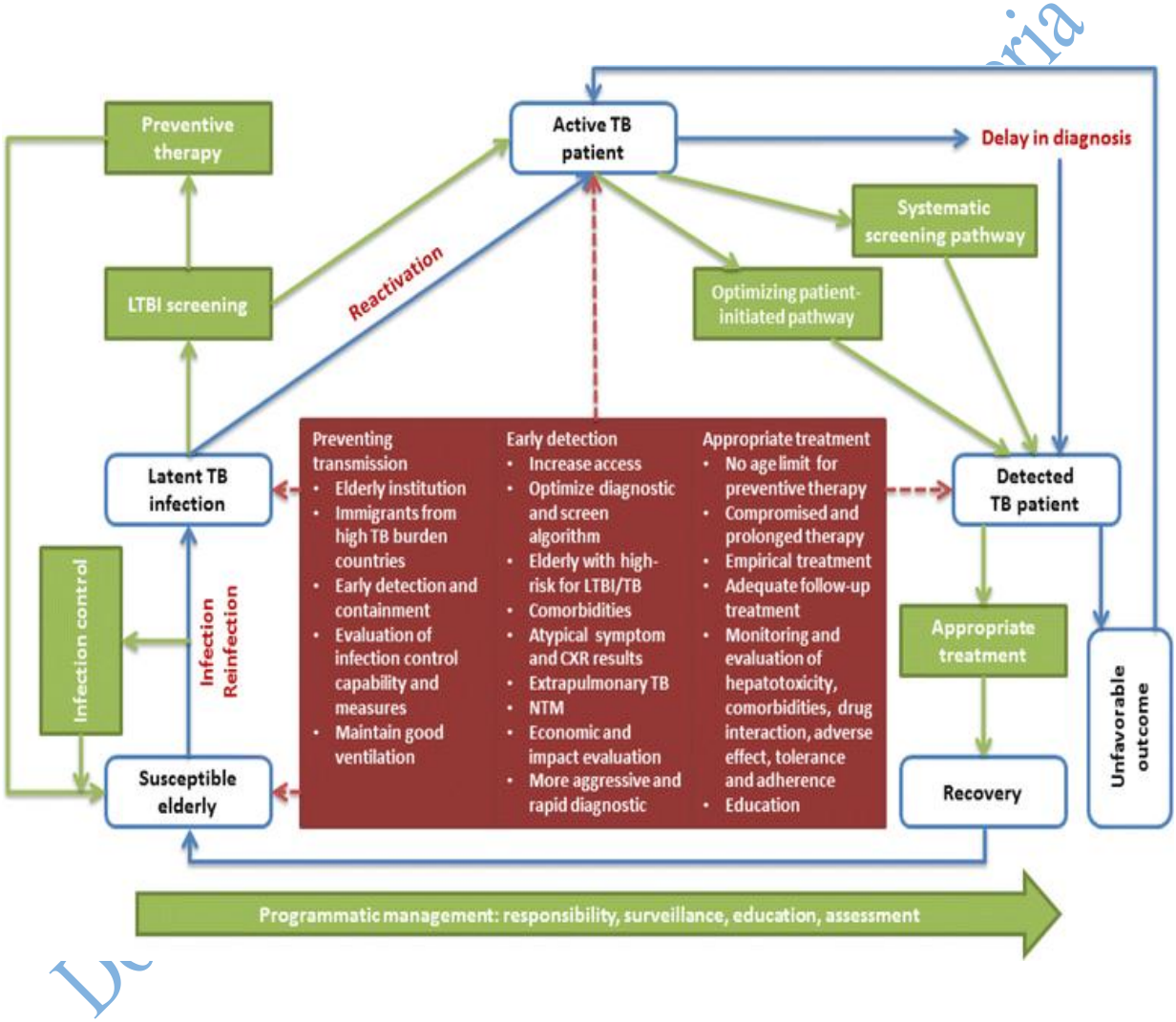
TB, address misconceptions and negative attitudes towards TB, and promote the adoption of TB preventives measures through community engagement, education and healthcare provider training. By addressing all three component the framework can help to ensure that TB prevention efforts are effective, sustainable and culturally appropriate.



Source: Researcher's Fieldwork (2023)

2.5 Summary of Gaps in Literature Reviewed

This study assesses knowledge and practice of tuberculosis preventive measures among adolescents and young adults. This study found a scarcity of research specifically focused on the knowledge and practice of TB preventive measures among adolescents and young adults. Most of the available studies primarily focused on general populations or specific high-risk groups, such as healthcare workers or people living with HIV/AIDS. This lack of research hinders a comprehensive understanding of the knowledge and practices specific to this age group. Also, this study identified significant gaps in the understanding of TB among adolescents and young adults. Many studies reported a lack of awareness about TB transmission, symptoms, and the importance of preventive measures. Moreover, there was limited knowledge about the availability and accessibility of TB services, including screening and treatment options.

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Chapter Three

Methodology

3.1 Research Design

The study design for the study was a cross-sectional design.

3.2 Population of the Study

The study population includes adolescents and young adults (AYAs) diagnosed with new sputum smear-positive tuberculosis receiving treatment at the public and private health facilities in Ifako-Ijaiye LGA, Lagos State.

Study Area

The Ifako-Ijaiye Local Government was created along with 183 other local governments on October 1, 1996 by General Sani Abacha, the then military head of state. It was carved out of Agege Local Government, with headquarters in Ifako. The 1991 census found the majority of inhabitants to be Yoruba. Ifako-Ijaiye Local Government is a border suburb town as it shares border with Ogun State. The major settlements are Ogba-Ijaiye, Ifako, Oke-Ira, Iju-Ishaga, Obawole, Iju-Ogundimu, Fagba, Agege Pen Cinema among others.

Ifako-Ijaiye is a city and local government area in Lagos, Nigeria. It has a land area of 43 square kilometres (17 sq mi) and had a population of 427,878 people in 2006.

3.3 Sample and Sampling Techniques

Cluster sampling method was used to recruit all the AYAs with smear positive TB.

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Ifako General Hospital has 49 respondents, Ifako PHC has 27 respondents, Agbado Kola PHC has 21 respondents, Iju PHC has 15 respondents, Ahmadiyyha Hospital has 13 respondents, Longe Hospital, 9 respondents and other AYAs in the community. A total number of 151 respondents were used for this study. There are six (6) facilities (4 public and 2 private) that offer DOTS free of charge in Ifako-Ijaiye LGA.

3.4 Description of the Research Instrument

The research instrument that was used in this study was an interviewed questionnaire. The questionnaire adapted included information obtained from adolescents and young adults. The questionnaire included four sections:

Section 1: Socio-Demographic Characteristics

Section 2: Knowledge of Tuberculosis

Section 3: Knowledge of Tuberculosis (TB) Preventive Measures

Section 4: Practice of Tuberculosis (TB) Preventive Measure

3.5 Validity and Reliability of the Research Instrument

To guarantee the validity and reliability of the instrument, the questionnaire for the study was adapted from previous studies and was also reviewed by an expert/supervisor for clarification, adjustments and restructuring to meet the required objectives for this study.

3.6 Data Collection

A validated questionnaire used to collect the data of this study was adapted. The questions adapted include information on socio-demographic characteristics,

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knowledge and practice regarding TB including its signs and symptoms, mode of transmission, cause, investigations and treatment, and preventive measures in Ifako-Ijaiye Local Government Area of Lagos State, Nigeria. The completed questions were collected on the spot. Data collected with the questionnaires was crosschecked for errors and cleaned. Information obtained from the questionnaire was entered into Statistical Package for Social Sciences (SPSS) version 28.0 for analysis and statistical calculation. Data analysis, frequency counts, simple percentages were used to analyse the socio-demographic characteristics. Pearson moment correlation was used for the knowledge and practice regarding TB including its signs and symptoms, mode of transmission, cause, investigations and treatment, and preventive measures. Pearson moment correlation for data analysis at 0.05 alpha levels was used to test both sides. Chi square and logistic regression was used to identify various factors influencing the practice of TB preventive measures.

3.7 Data Analysis

Statistical program for social sciences (SPSS) Version 20, was used to present socio-demographic data as descriptive statistics of percentages and frequencies. The relationship between knowledge of TB and Practice of TB preventive measures among adolescent and young adult was determined by a multivariate analysis. Chi-square was used to test the association between knowledge and selected socio demographics characteristics.

3.8 Ethical Approval

Ethical approval was obtained from

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- Lagos State University Teaching Hospital Health research ethics committee
- Lead City University Health Research and Ethics Committee.

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- Written informed consent was obtained from the respondents after details about the study would have been explained to them, and strict confidentiality of all information obtained from respondents was maintained throughout the course of the study.

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Endnotes

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Chapter Four

Results and Discussion of Findings

This chapter presents analysis of data which is divided into two sections, which includes the presentation of data and the objectives.

4.1 Demographic Data Analysis

The table below shows the percentage distribution of respondents according to their socio-demographic characteristics in Ifako-Ijaiye and the result from the study shows that out of 151 respondents, 85 (56.3%) of the respondents are Christians while 66 (43.7%) are practicing Islam. It also shows that tertiary education level has the highest percentage of 49.7% while primary level has a percentage of 11.3 and secondary level is 39.1%. Likewise, 75.5% of the respondents are single while 24.5% are not single.

The study presents that 32.5% of respondents have steady partners while 62.5% have casual partners 58.9% of the respondents in this study are student while 41.1% are shown to be non students. Furthermore, out of 151 respondents, 40.4% has someone in their household with TB, leaving 59.6% of the respondents without.

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Table 4.1; Percentage Distribution of Respondents according to their Socio-demographic Characteristics

Variable	Percent	Frequency
Age		
Less than 20	45.7	69
20 and above	54.3	82
Religion		
Christian	56.3	85
Islam	43.7	66
Educational level		
Primary level	11.2	17
Secondary level	39.1	59
Tertiary level	49.7	75
Marital Status		
Single	75.5	114
Not single	24.5	37
Type of Partner		
Steady	32.5	49
Casual	67.5	102
Occupation		
Student	58.9	89
Non student	41.1	62
Has anyone in your household ever had TB		
Yes	40.4	61
No	59.6	90

Source: Researcher's Field Work (2023)

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Figure 4.1 which illustrate a pie chart showing places used for TB testing among the respondents highlights how primary health centers has the highest frequency with a percentage of 63.3 used by respondents and traditional healer used only at a percentage of 1.3 compared to others. Other percentages include: community outreach at 10.1%, at a clinic or hospital at 11.4% and the pharmacy at 13.9%.

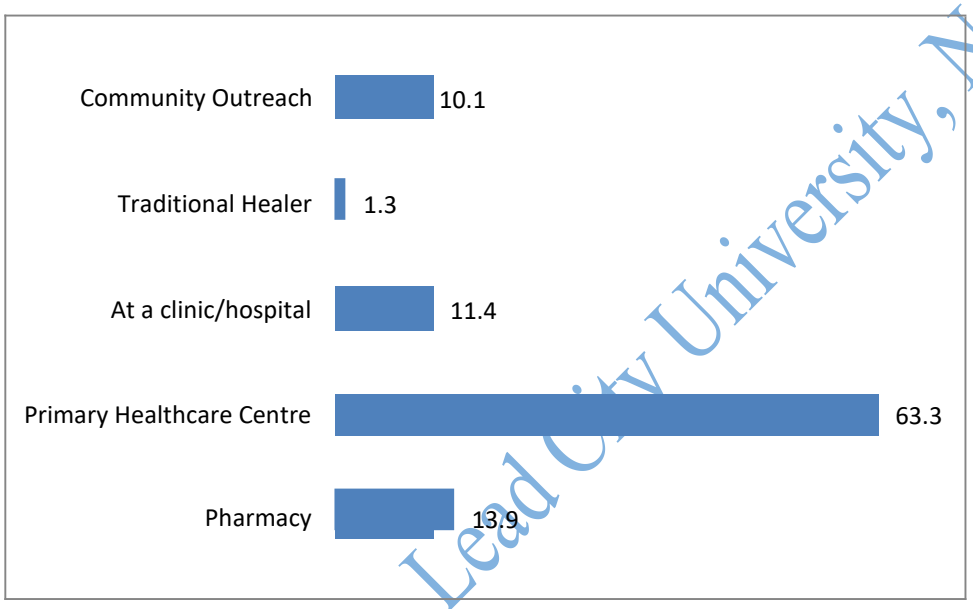

Figure: 4.1Chart Showing Places used for TB Testing among the Respondents

Source: Researcher's Field Survey (2023)

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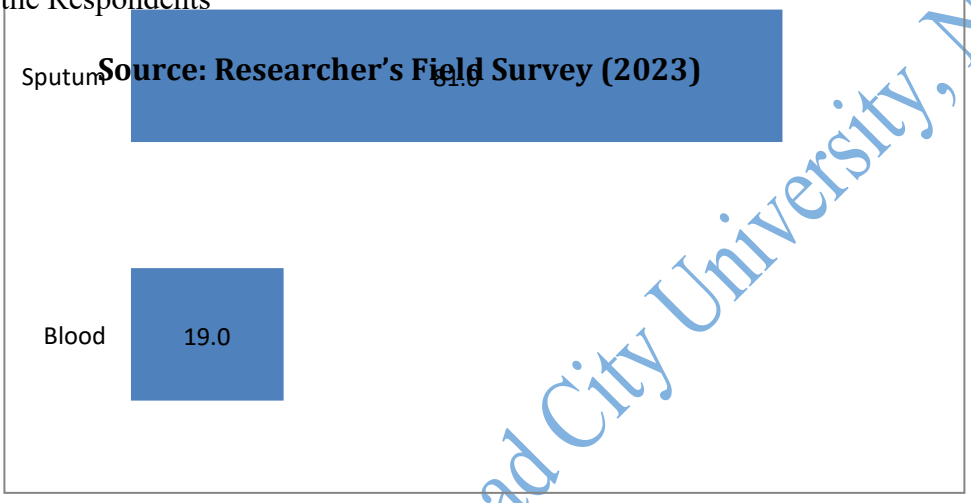
Figure 4.2 illustrating the distribution of specimens use for TB test collection among the youths and adolescents in Ifako Ijaiye LGA and it show the highest use of 81% by sputum among the respondents for TB test collection and no other use beyond blood, which has a lower 19%.

Figure: 4.2 Percentage Distribution of Specimen Use for TB Test Collection among the Respondents



Source: Researcher's Field Survey (2023)

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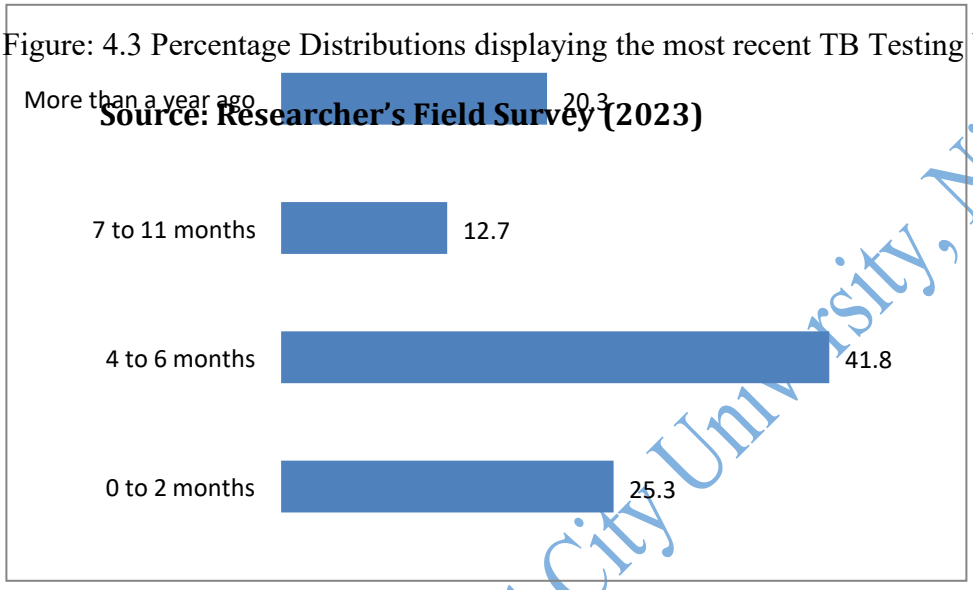
Figure 4.3 shows the most recent TB testing use which depicts how respondents had their test done 4-6 months prior at 41.8% higher than others, with the lowest percentage of 12.7 for 7-11 months. Other percentages include: more than a year ago at 20.3% and 0-2 months at 25.3%

Figure: 4.3 Percentage Distributions displaying the most recent TB Testing Use



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4.2 Presentation of Data

4.2.1 Knowledge of Tuberculosis

Table 4.2 shows the knowledge of tuberculosis among respondents in Ifako-Ijaiye LGA which illustrates that out of the 151 respondents, 94% answers correctly that anybody can get TB while 6% answered the questions incorrectly.87.4% of the respondents answered correctly that people living with HIV are more likely to get TB alongside with people that are HIV negative can get TB while a percentage of 12.6 were incorrect. It also shows that 68.9% responded correctly on the question about if a person can get TB through handshakes. 92.7% answered correctly that TB is transmitted through the air when a person with TB coughs or sneezes while 7.3% gave incorrect responses. There was a close margin of 40.4% who answered correctly on if a person can get TB through touching items in public places against a 49.6% of incorrect answers. However, 70.2% gave incorrectly responses on TB can be transmitted through smoking while 29.8% had answered correctly.

From the result, 57% correctly answered the question about if a person can get TB through sharing the same dishes while 43% had incorrect response to the question. Also, 47% had correct answers that a person can get TB through eating from the same plate while 53% were incorrect. For the question “Night sweats is one of the signs and symptoms of TB” 74.2%answered correctly while 25.8% were incorrect. There was a high percentage of 92.1% of correct answers that one of the signs and symptoms of TB is coughing up blood than the 7.9% incorrect answers.

Out of the 151 respondents, 77.5% gave incorrect answers that Fever is one of the signs and symptoms of TB while 22.5% gave correct answers. 92.1% have correct

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answers that the loss of appetite is one of the signs and symptoms of TB while7.9% have answered incorrectly. Likewise, 88.7% have answered correctly that one of the signs and symptoms of TB is unintentional weight loss while 11.3%. It also shows that 86.1% of the respondents gave correct answers that TB can be cured through drugs, medicines and pills while there was a 13.9% incorrect answer.

There is a close margin of 51% correct answer on TB can be cured using traditional medicine to a 49% of incorrect answer. Furthermore, 65.6% of the respondents have correct answers that there is no treatment for TB while the incorrect answers were 34.4%. It also shows that 56.3% have correct answers on how long does someone have to take the drugs to cure TB while there was a 43.7% incorrect rate. Lastly, 46.4% of the respondents answered correctly on the question "People with TB are always HIV positive" with a close margin of 53.6% incorrect response. The question "Is it possible to cure TB in people with HIV?" had 82.1% correct answers while it had 17.9% wrong answers.

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Table 4.2: Knowledge of Tuberculosis among Respondents in Ifako-Ijaiye LGA

Variable	Correct	Incorrect
Anybody can get TB	94.0	6.0
People living with HIV are more likely to get TB	87.4	12.6
People that are HIV negative can get TB	87.4	12.6
A person can get TB through handshakes	68.9	31.1
TB is transmitted through the air when a person with TB coughs or sneezes	92.7	7.3
A person can get TB through touching items in public places (doorknobs, handles in transportation, etc)	40.4	49.6
TB can be transmitted through smoking	29.8	70.2
A person can get TB through sharing the same dishes	57.0	43.0
A person can get TB through eating from the same plate	47.0	53.0
Night sweats is one of the signs and symptoms of TB	74.2	25.8
One of the signs and symptoms of TB is coughing up blood	92.1	7.9
Fever is one of the signs and symptoms of TB	82.1	17.9
The loss of appetite is one of the signs and symptoms of TB	77.5	22.5
Cough that lasts longer than two weeks is one of the signs and symptoms of TB	92.1	7.9

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One of the signs and symptoms of TB is unintentional weight loss	88.7	11.3
TB can be cured through drugs, medicines and pills	86.1	13.9
TB can be cured using traditional medicine	51.0	49.0
There is no treatment for TB	65.6	34.4
How long does someone have to take the drugs to cure TB?	56.3	43.7
People with TB are always HIV positive	46.4	53.6
It is possible to cure TB in people with HIV	82.1	17.9

Source: Researcher's Field Survey (2023)

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Table 4.3 shows the knowledge of tuberculosis preventive measures among respondents in Ifako-Ijaiye LGA. TB can be prevented by separating yourself from others and avoiding close contact with anyone was answered correctly at 88.7%. Always covering the mouth and nose with a tissue when coughing and sneezing prevents the spread of TB was answered correctly at 95.4%. A well ventilated room prevents the spread of TB was answered correctly at 94%. Use of medicines regularly according to prescription is one of the TB preventive measures were answered correctly at 90.1%. Early diagnosis and treatment is one of the measures to prevent the spread of TB was answered correctly at 95.4%. Bacille Calmette-Guerin (BCG) vaccination is protective against TB was answered correctly at 90.1%. Opening the room to allow natural light prevents the spread of TB was answered correctly at 84.1%. The use of protective masks prevent the spread of TB was answered correctly at 92.7%. People with TB become non-infectious soon after initiating appropriate treatment was answered correctly at 8.6%, Only patients with active TB can spread the disease was answered correctly at 86.1%. With the exception of the 9th question, this table shows good knowledge of TB preventive measures among the respondents, with them having between the rate of 84-95% of correctly answered questions.

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Table 4.3 Knowledge of Tuberculosis Preventive Measures among Respondents in Ifako-Ijaiye LGA

Variable	Correct	Incorrect
TB can be prevented by separating yourself from others and avoiding close contact with anyone	88.7	11.3
Always covering the mouth and nose with a tissue when coughing and sneezing prevents the spread of TB	95.4	4.60
A well ventilated room prevents the spread of TB	94.0	6.0
Use of medicines regularly according to prescription is one of the TB preventive measures	90.1	9.9
Early diagnosis and treatment is one of the measures to prevent the spread of TB	95.4	4.6
Bacille Calmette-Guerin (BCG) vaccination is protective against TB	90.1	9.9
Opening the room to allow natural light prevents the spread of TB	84.1	15.9
The use of protective masks prevent the spread of TB	92.7	7.3
People with TB become non-infectious soon after initiating appropriate treatment	8.6	91.4
Only patients with active TB can spread the disease	86.1	13.9

Source: Researcher's Field Survey (2022)

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Figure 4.4 shows the percentage of respondents on their knowledge about tuberculosis through the use of a pie chart indicating how there is 93.4% knowledge about tuberculosis among the respondents higher than others. In other words, there is a 93.4% good knowledge and a 6.6% poor knowledge among the youths and adolescents in Ifako-Ijaiye LGA

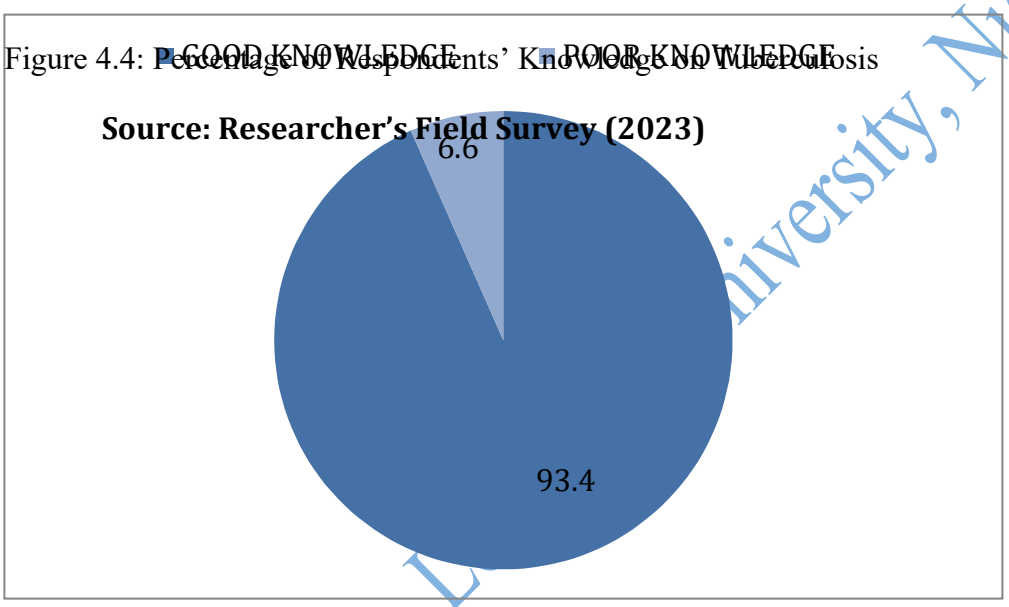

Figure 4.4: Percentage of Respondents' Knowledge on Tuberculosis

Source: Researcher's Field Survey (2023)

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Figure 4.5 illustrates the percentage of respondents' knowledge about tuberculosis Preventive measures through a representation with a pie chart showing a high percentage (97%) of knowledge about tuberculosis preventive measures among respondents. Thus, there is a 97% good knowledge and a 3% poor knowledge among the youths and adolescents in Ifako Ijaiye LGA.

Figure 4.5: Chart Illustrating the Percentage of Respondents' Knowledge about Tuberculosis Preventive Measures

Source: Researcher's Field Survey (2023)

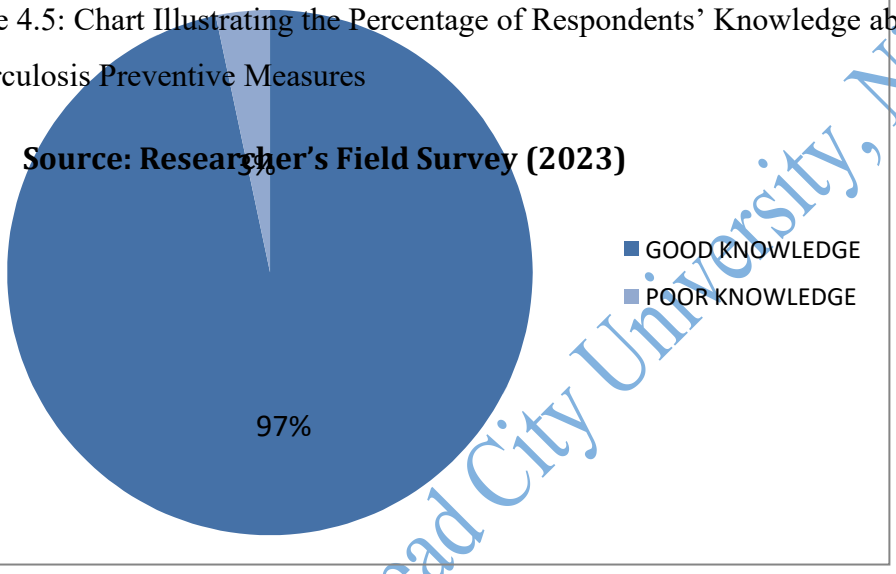

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Table 4.4 shows the association between selected socio-demographic characteristics and the knowledge on tuberculosis among adolescents and youth in Ifako-Ijaiye LGA. It is observed from the result of the analysis that there is no significant association between the religion and the knowledge on tuberculosis among the respondents at a P-value of 0.366. The result shows that there is no association between age and the knowledge of tuberculosis at a P-value of 0.302. However, there is a significant relationship between the education level and the knowledge of tuberculosis among the respondents at P-value of 0.008. The study presents that there is no association between marital status and the knowledge of tuberculosis at a P-value of 0.676. Also there is no association between type of relationship and the knowledge of tuberculosis at a P-value of 0.590. It is seen to however have a significant relationship between the occupation and the knowledge of tuberculosis among the respondents at P-value of 0.010.

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Table 4.4 Association between the Selected Socio-demographic Characteristics and Knowledge on Tuberculosis Prevention among Adolescents and Young Adults in Ifako-Ijaiye LGA

Variable	Good Knowledge	Poor Knowledge	Chi square	P-value
Age			1.063	0.302
Less than 20	95.7%	4.3%		
20 and above	91.5%	8.5%		
Level of education			9.785	0.008
Primary	76.5%	23.5%		
Secondary	93.2%	6.8%		
Tertiary	97.3%	2.7%		
Religion			0.818	0.366
Christianity	91.8%	8.2%		
Islam	95.5%	4.5%		
Marital Status			0.175	0.676
Single	93.9%	6.1%		
Not single	91.9%	8.1%		
Type of partner			0.278	0.590
Steady	91.8%	8.2%		
Casual	94.1%	5.9%		
Occupation			6.710	0.010
Student	97.8%	2.2%		
Non student	87.1%	12.9%		

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The overall table (table 4.5) shows the association between the knowledge of tuberculosis preventive measures among the selected socio-demographic characteristics among youths and adolescents in Ifako-Ijaiye LGA.

It is observed that respondents that are less than 20 have 97.1% of good knowledge and 2.9% have poor knowledge on TB, while respondents that are 20 and above have 96.3% knowledge on TB and 3.7% have poor knowledge. Also, tertiary level educated respondents have the highest percentage of good knowledge on TB while primary level educated respondents have 76.5% good knowledge level. Respondents practicing Christianity had 91.8% good TB knowledge while respondents practicing islam had 95.5% good knowledge on TB. 96.5% of respondents who are single have good knowledge on TB while 97.3% of respondents who are not single have good knowledge on TB. Respondents who have steady partners have 95.9% good knowledge on TB while respondents that have casual partners have 97.1% good knowledge. Respondents that are students have 98.9% good knowledge while those that are non-students have 93.5% good knowledge.

From that, it is observed from the result of this study that there is no significant association between religion and the knowledge of tuberculosis Preventive measures at 0.818 p-values. At p-value of 0.068, there are no significant associations between the age and the knowledge of tuberculosis Preventive measures among respondents. However, there is a significant association between the level of education and the knowledge of tuberculosis Preventive measures with a p-value of 0.008.

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Table 4.5: Association between the selected socio-demographic characteristics and knowledge on tuberculosis preventive measures among adolescents and young adults in Ifako-Ijaiye LGA

Variable	Good Knowledge	Poor Knowledge	Chi square	P-value
Age			0.795	0.068
Less than 20	97.1%	2.9%		
20 and above	96.3%	3.7%		
Level of education			9.758	0.008
Primary	76.5%	23.5%		
Secondary	93.8%	6.2%		
Tertiary	97.3%	2.7%		
Religion			0.366	0.818
Christianity	91.8%	8.2%		
Islam	95.5%	4.5%		
Marital Status			0.057	0.812
Single	96.5%	3.5%		
Not single	97.3%	2.7%		
Type of partner			0.134	0.714
Steady	95.9%	4.1%		
Casual	97.1%	2.7%		
Occupation			3.240	0.072
Student	98.9%	11.1%		
Non student	93.5%	6.5%		

Source: Researcher's Field Survey (2023)

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4.2.2 Practice of Tuberculosis Preventive Measures

Table 4.6 shows the respondents' practice of tuberculosis Preventive measures and the result from the study shows that out of 151 respondents, there is a high percentage of 94.7 that opened window regularly. It also shows that 64.8% have frequent TB test while 35.8% do not. Likewise, it was seen to have 73.5% have people smoking around them while 26.5% do not have. Furthermore, it is shown that 82.1% of the respondents have received health education while 17.9% have not received.

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Table 4.6: Respondents' Practice of Tuberculosis Preventive Measures

Variable	yes	No
Opened window regularly	(143)94.7%	(8)5.3%
Frequent TB test	(97)64.2%	(54)35.8%
People smoking around you	(111)73. 5%	(40)26.5%
Ever received health education	(124)82.1%	(27)17.9%

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Figure 4.6 illustrates the practice of preventive tuberculosis measures among the youths and adolescents in Ifako Ijaiye LGA and these shows a average of 67.5% respondents have good practices on tuberculosis preventive measures higher than the 32.5% of poor practice.

Figure 4.6 Practices Tuberculosis Preventive Measures among the Respondents

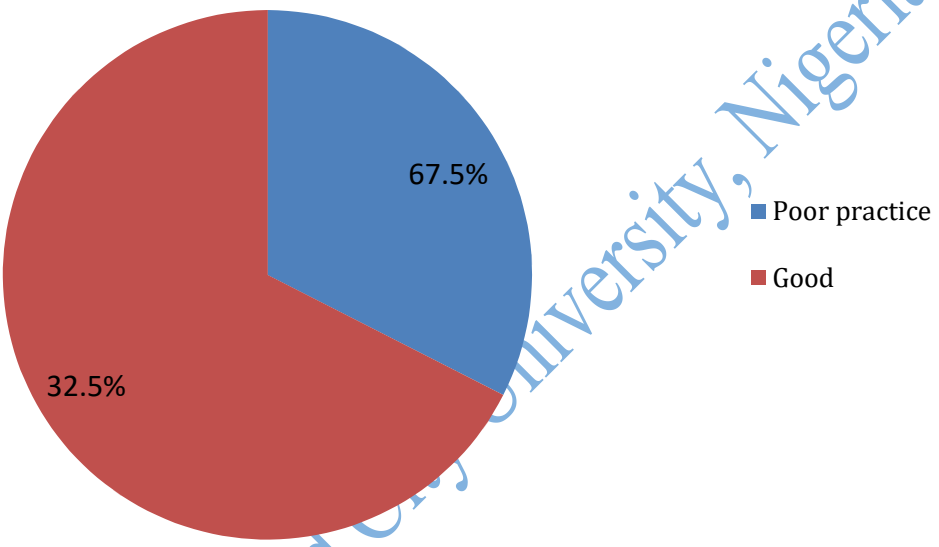

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Table 4.7 highlights the association between selected socio-demographic characteristics and practices of tuberculosis preventive measure among respondents in Ifako-Ijaiye LGA. This result shows that there is no significant association between the practices on tuberculosis preventive measures and religion, (0.618 p-value). Furthermore, there is no significant association between the practices on tuberculosis preventive measures and educational level. Also, there is no significant association between the practices on tuberculosis preventive measures and marital status at 0.998 p-value. There is no significant association between the practices on tuberculosis preventive measures and type of partner and occupation with P-values of 0.436.

At a p-value of 0.966, there is no significant association between the practices on tuberculosis preventive measures and occupation. However, there is a significant association between practices on tuberculosis preventive measures and age at p-value of 0.060. There is also a significant association between practices on tuberculosis preventive measures and anyone in household ever had at 0.04 p-value.

At a p-value of 0.000, there is a significant association between practices on tuberculosis preventive measures and ever had TB.

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Table 4.7: Association between the Selected Socio-demographic Characteristics and the Practice of Tuberculosis Preventive Measures

Variable	Poor practice	Good practice	Chi square	P-value
Age			3.538[a]	0.060
Less than 20	24.6%	75.4%		
20 and above	39.0%	61.0%		
Religion			0.247	0.618
Christianity	34.1%	65.9%		
Islam	30.3%	69.7%		
Level of education			3.142	0.207
Primary	47.1%	52.9%		
Secondary	25.4%	74.6%		
Tertiary	34.7%	65.3%		
Marital Status			0.000	0.998
Single	32.5%	67.5%		
Not single	32.4%	67.6%		
Type of partner			0.607	0.436
Steady	36.7%	63.3%		
Casual	30.4%	69.6%		
Occupation			0.002	0.966
Student	32.6%	67.4%		
Non student	32.3%	67.7%		
Anyone in household ever had TB			4.213	0.040
No	38.9%	61.1%		
Yes	23.0%	77.0%		

Source: Researcher's Field Survey (2023)

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4.2.3 Factors Associated with the Practice of Tuberculosis among the Respondents in Ifako-Ijaiye LGA

Table 4.8 illustrates the logistic regression coefficient of selected socio-demographic characteristics showing the factors associated with the practice of tuberculosis among adolescents and young adults in Ifako-Ijaiye LGA, Lagos. This shows that there is no significant association between practices on tuberculosis preventive measures and religion (0.421, 1.675%), educational level of the respondent at primary level (0.206, 1.731%) and secondary level (0.732, 3.311), marital status (0.452, 2.206%), type of partner (0.367, 1.542%), occupation (0.493,1.97%) and anyone in the household ever had TB (0.134, 0.567%)

At UOR, there is significant association between age and practices of tuberculosis preventive measures. This result shows from the table that the respondents less than 20 years are two times more likely to not practice tuberculosis preventive measure at (0.97,3.96%) Confidence interval compared to their counterpart who are 20 year and above. The result shows that the respondent who practice Christianity are 1 time less likely to not practice tuberculosis preventive measures at (0.421,1.675%) confidence interval compared to their counterparts who are practicing Islam. It is seen that the educational level of the respondent at primary level are 2 times less likely to not practice tuberculosis preventive measures at (0.206, 1.731%) confidence interval compared to their counterparts at tertiary level and the educational level of the respondent at secondary level are 2 times more likely to not practice tuberculosis preventive measures at (0.732, 3.311%) confidence interval compared to their counterparts at tertiary level.

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The result shows that the respondent that are single are 1 times less likely to not practice tuberculosis preventive measures at (0.452,2.206%) confidence interval compared to their counterparts who are married. Respondents who have steady partners are 1 times less likely to not practice tuberculosis preventive measures at (0.367, 1.542%) confidence interval compared to their counterparts who are casual partners. Also, students are 1 times less likely to not practice tuberculosis preventive measures at (0.493, 1.97%) confidence interval compared to their counterparts who are non-students. The result shows that respondents who have no one in their household to have TB are 2 times less likely to not practice tuberculosis preventive measures at (0.225, 0.973%) confidence interval compared to their counterparts who have anyone in their household to have TB. The result shows that respondents who have never had TB are 4 times less likely to not practice tuberculosis preventive measures at (0.134,0.567%) confidence interval compared to their counterparts who have had TB. The result shows that respondents who have good knowledge on tuberculosis are 9 times more likely to practice tuberculosis preventive measures at (1.968. 47.916%) confidence interval compared to their counterparts who have bad knowledge on tuberculosis.

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Table 4.8: Logistics Regression Coefficient of selected Socio-demographic Characteristics showing the Factors Associated with the Practice of Tuberculosis among Adolescents and Young Adults in Ifako-Ijaiye LGA, Lagos

Variable	Practice of TB preventive Measure					
	UOR	95%CI	P-Value	AOR	95% CI	P value
Age						
Less than 20	1.96	0.97,3.96	0.062	2.207	1.02, 4.747	0.043
20 and above						
Religion						
Christianity	0.84	0.421,1.675	0.620			
Islam						
Level of Education						
Primary	0.597	0.206,1.731	0.342			
Secondary	1.556	0.732,3.311	0.251			
Tertiary						
Marital Status						
Single	0.999	0.452,2.206	0.998			
Not Single						
Type of Partner						
Steady	0.752	0.367,1.542	0.436			
Casual						
Occupation						
Student	0.985	0.493,1.97	0.966			
Non Student						
Anyone in Household Ever had TB						
No	0.468	0.225,0.973	0.436			
Yes						
Knowledge						
Good Knowledge	9.758	1.98, 47.91	0.005	4.904	0.93, 25.67	0.0060
Poor Knowledge						

Source: Researcher's Field Survey (2023)

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4.3 Discussion of Findings

4.3.1 Socio-demographic Information

This study aimed to assess the knowledge and practice of TB preventive measures among adolescents and young adults in Ifako-Ijaiye Local Government. Nearly 15 million active TB cases are reported each year, with India, Indonesia, South Africa, Nigeria, the Philippines, Pakistan, Bangladesh, and China bearing the heaviest burden. In Nigeria, the prevalence of tuberculosis in adults aged 15 and older was predicted to be 318 per 100,000 population for smear-positive cases and 524 for bacteriological confirmed cases[1]. Findings show that many of the respondents are Christians, taking up 85 (56.3%) of the respondents. However, only almost half of the respondents are tertiary educated. It also has the highest percentage of 49.7% while primary level has a percentage of 11.3 and secondary level is 39.1%. Likewise, 75.5% of the respondents are single. Similarly, Kalu employed the use of simple and systematic random sampling techniques in the selection of schools and students who consented to participate in the study[2]. The result of this study showed that, respondents were predominantly within the age bracket of 15-19 years 224 (61.0%), Christians 382 (95.5%), males 227 (56.7%) and reside with both parents 139 (34.8%). The study presents that 32.5% of respondents have steady partners while 62.5% have casual partners.58.9% of the respondents in this study are student while 41.1% are shown to be non students. Idris conducted a dissimilar study among solely secondary school students where socio-demographic groups were used as necessary tools for KAP scores in areas of gender, ethnicity and smoking status for post-TB educational programme[3].

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Furthermore, out of 151 respondents, 40.4% has someone in their household with TB, leaving 59.6% of the respondents without. Tuberculosis patients are frequently drawn from the most vulnerable groups in society. Those living in poverty, in prisons, and in poor working circumstances are among them. Stress reduction, exposure to pollutants, overpopulation, poverty reduction, improved nutrition, and engagement with health care providers all lessen the risk of infection and illness development[4].

4.3.2 Knowledge of Tuberculosis and its Preventive Methods

Tuberculosis is still the most common cause of mortality worldwide, with the majority of new cases occurring in low- and middle-income nations. Despite achievements, the WHO Global Tuberculosis Report 2019 emphasizes major and persistent gaps in detection and treatment, including human rights and gender hurdles[5]. The age at the time of infection, as well as the presence of any other medical condition linked to TB progression, define a human's long-term likelihood of reactivation TB from latent TB infection (LTBI). Smear-positive, pulmonary TB is a continuous infection that kills 70% of people within 10 years if left untreated[6].

From this result, the overall knowledge of tuberculosis preventive measures among adolescents and young adults in Ifako-Ijaiye LGA was 97% with (95% CI 1.968. 47.916%). However, the result is higher than a study finding in the Philippines which had a percentage of 65.22[6]. This could have been caused by respective socio demographic characteristics like age, level of education, religion, culture etc that differs in each country.

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Shamu, 2019 also found some of the factors that are associated with TB knowledge are female, younger, a student etc, which is similar to our findings on good knowledge in socio demographic characteristics like religion, age and education level at 91.8%, 97.1% and 76.5% respectively [AOR = 2.207, 95% CI at 1.026, 4.747%][7]. This finding was also similar in a study conducted by Kalu 2015 that showed a 6.9% lack of knowledge of tuberculosis which is closer to the 6.6% poor knowledge findings[2]. The similarity could be due to both the research being done primarily in Nigeria. Also, the present findings revealed that the respondents reported that loss of appetite 77.5%, anybody can get TB 94% and weight loss 88.7% were related signs of tuberculosis. This, however, is not in agreement with the study conducted by Kalu 2015 which had its findings at 8.2%, 16.5% and 11.9% respectively. However, there was a close range in the question "smoking can cause TB" where our findings was at 29.8% which is almost similar to Kalu, 2015 at around 30%[2].

Shamu, 2019 showed an average knowledge result by the respondent which contradicts the high level [97%] of knowledge on tuberculosis preventive measures[7]. Differences in country, age range, level of education and social norms could play huge factors on the overall knowledge of tuberculosis. Sellah 2018 deduced that culture can also affect behaviors like good attitudes and practices in relations to health and disease preventive measures[8]. With the studies being done in Malaysia, it opens up the disparity cultural and social backgrounds.

4.3.3 Practices of Tuberculosis Preventive Measures

The findings are higher than a study conducted in Iraq which had unfavorable attitudes and practices towards tuberculosis[9]. Unlike our result which had a 65% positive

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response from the acquired data. Similarly like in Iraq, Saudi Arabia had negative attitude towards TB and not enough knowledge or practice that does not tally with our findings of 65% practice of tuberculosis preventive measures from the respondents[10].

The present findings revealed that there is significant association between age and practices of tuberculosis preventive measures from the respondents less than 20 years, who are two times more likely to not practice tuberculosis preventive measure at (0.97,3.96%) Confidence interval compared to their other counterpart. This shows that the older a person gets, the more a person gets and understands all information regarding tuberculosis and the preventive measures. A lower age would equal to a lower level of knowledge from the respondents.

In this study, it is revealed that those who have no one in their household are 2 times less likely to not practice tuberculosis preventive measures at (0.225, 0.973%) confidence interval compared to their counterparts who have anyone in their household. This illustrates how the study shows the presence of having people around as a more possible chance to adhering to tuberculosis preventive measures. This could be due to a number of factors like sex, which could greatly affect it.

A small sample size was used to conduct this research and however might not represent the whole country. A local government in Lagos state is the study location which is used to target a particular population of adolescents and young adults within the state.

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Chapter Five

Conclusion

5.1 Summary of Findings

The study examined the socio-demographic, knowledge and practices of TB preventive measures among adolescents and young adults in Ifako-Ijaiye LG. The targeted population for the study was 151 AYAs receiving treatment in selected facilities in Ifako-Ijaiye LG and the community. A sample size of 151 respondents was recruited. Cluster sampling technique was used to select the participants for the study. The recruitment was done on their general/DOTS clinic days. Due to the sample size, the recruitment was done for 5 general/DOTS clinic days in selected private and public facilities and it was done such that no individual was recruited more than once. For each day, 25 or more AYAs were recruited.

In the study, we found the Respondent ages with majority 20-24, 82(54.3%), with the least being less than 20, 69(45.7%). It was shown that 85 (56.3%) were Christians while 66(43.7%) were Muslims, 114(75.5%) reported to be single while 37(24.5%) said they are not single, majority of the AYAs with 75(49.7%) reported to have tertiary level of education 59(39.1%) have secondary level with the least 11.3(17%) having primary level of education. 102(67.5%) majority reported to have casual partners and 49(32.5%) had steady partners. Furthermore, it was revealed that 89(58.9%) of the respondents are student while 62(41.1%) are shown to be non-students. Out of 151 respondents, 61(40.4%) has someone in their household with TB, leaving 90(59.6%) without anyone in their household with TB. Likewise, it was

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reported that 70(46.4%) have never had a TB test while 81(53.6%) have been screened for TB.

According to this study, the findings depicted that 93.4% of AYAs had good knowledge about tuberculosis and 6.6% had poor knowledge. However, 97% had good knowledge about tuberculosis preventive measures and 3% had poor knowledge. Furthermore, there is a significant relationship between the education level and the knowledge of tuberculosis and preventive measures among the respondents at P-value of 0.008. 67.5% of AYAs in Ifako-Ijaiye LGA have good practices on tuberculosis preventive measures and 32.5% have poor practices. There is a significant association between practices on tuberculosis preventive measures and age at 0.060 of P-value. Also, there is a significant association between practices on tuberculosis preventive measures and anyone in household ever had TB and ever had TB at P-value of 0.040 and 0.000 respectively.

In addition, the findings of this study shows that individual who have good knowledge about tuberculosis are 9 times more likely to practice tuberculosis preventive measures at (1.968.47.916%) CI compared to their counterparts who have bad knowledge on tuberculosis.

5.2 Conclusion

The study assesses the socio-demographic, knowledge and practices of TB preventive measures among AYAs attending general/DOT clinic in Ifako-Ijaiye LGA. It was evident that the participants have knowledge of TB, preventive measures and

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practices; although the respondents are less than 20 according to the findings of the study.

These finding is in similitude with the findings of Shamu, which indicated a significant association on good knowledge in socio demographic attributes like religion, age and educational level. The knowledge and practice of TB preventive measures contributes to the alleviation of the spread of TB.

5.3 Recommendations

The result of this study suggests that;

1. The management of Ifako-Ijaiye PHC department should review the adequacy of communication at their disposal and dissemination which will enable individuals and communities to be more autonomous when making informed choices regarding tuberculosis preventive measures and practices.
2. The risk of tuberculosis (TB) infection progressing to TB disease is much higher for groups, such as PLWHIV, adolescents as well as young adults. Treatment always carries some risk of adverse drug reactions, so being informed and understanding the practices of TB preventive treatment/measures helps to make well-informed decision. Consequently, it is important to sensitize AYAs infected with the TB and their families on TB, preventive measures and its practices.
3. The findings of the study showed that the respondents have excellent knowledge on TB practices and preventive measures but few have never screened for TB, therefore it is imperative to screen them regularly. This can

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be achieved by training HWs often on recent knowledge and practices of TB preventive measures. Resources for screening AYAs should be made readily available by the government for TB test.

The role of health education and community engagement should not be undermined in ascertaining that individuals and communities make informed decisions regarding the prevention of TB infection/disease, its treatment and practices; therefore, the following should be carried out by health workers:

- Frequent health talks on TB, preventive measures and practices.
- Explanation on the cause of the disease and how it is transmitted should be explicit
- The result of the sputum test and the type of disease diagnosed should be made known to the patient once confirmed
- The disease is curable provided the correct drugs and dosages are taken for stipulated 8months without a break
- Explain the types of the drugs and the number of times they ought to be taken
- There is the need to bring symptomatic contacts for screening
- The patient's family members should know the signs and symptoms of TB and should be willing to bring any suspect to the health care service providers
- The family should also be ready to support the patients in order to be regular on the treatment
- It should be stressed that the patient is no longer infectious as long as he/she complies with the treatment regularly

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- Explanation on the duration and the nature of the treatment in the hospital and at home should be explicit
- Educate the patient on the side effects of drugs which may include: skin rash, joint pains, yellow colouration of the conjuctiva, poor vision, imbalance, and red colouration of urine. Instruct patient to report any of these signs promptly.
- Sputum examination should be repeated at the end of 2nd, 5th and 7th month to determine the effectiveness of the drugs taken. It should however be noted that, if the results still identify the TB organism, the treatment may change.
- The health workers should obtain feedback by allowing patients to recall facts, identify possible problems and deal with the decisively at the end of each health talk session.

5.4 Contribution to Knowledge

Although many researchers have been working on TB, its preventive measures, treatment and practices, not many studies have been carried out on adolescents and young adults especially in Nigeria; this study was able to add data on knowledge and practices of TB preventive measures among AYAs.

5.5 Suggested Areas for Further Research

1. Focused research in endemic areas on knowledge and practices of TB preventive measures among AYAs globally.
2. Data on AYAs TB in endemic areas.

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Appendix I

Informed

Consent

Title of Study

Knowledge and Practice of Tuberculosis Preventive Measures among Adolescents and Young Adults in Ifako-Ijaiye Local Government, Lagos State, Nigeria.

Principal Investigator

Christianah Temilola **OLAWOYIN**

Public Health Department, Lead City University

Lead City University, Toll Gate, Ibadan,

+2348137978418

Purpose of Study

My name is Olawoyin Christianah Temilola, a master of public health student at the Faculty of public health, Lead City University, Ibadan. I am conducting a study on diet knowledge and practice of tuberculosis preventive measures among adolescents and young adults in Ifako-Ijaiye local government, Lagos State, Nigeria. I hereby solicit your support in completing this questionnaire.

Research Procedure

If you agree to be in this study, you will be asked to answer questions about yourself pertaining to the purpose of this study described above. These questions will be asked

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using a structured questionnaire. The questionnaire will take about 5 to 10 minutes of your time to complete.

Risks and Benefits

There are no known risks if you take part in this study. There are also no incentives but the information you provide would hopefully serve as an important input to intervene in programs that aim at improving children health.

Compensation

Participant will not be compensated for participation in this study. Participation is voluntary.

Confidentiality

All information you provide will be confidential and used for research purpose only. Your name will not be required and will never be used in connection with any information you give. Your response is completely anonymous. No personal identifying information will be collected. Every effort will be made by the researcher to preserve your confidentiality. Only the research team will have access to the answered questionnaires. Confidentiality and privacy will be maintained.

Contact Information

If you have questions at any time about this study, or you experience adverse effects as the result of participating in this study, you may contact the researcher whose contact information is provided on the first page. If you have questions regarding your rights as a research participant, or if problems arise which you do not feel you

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can

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discuss with the Primary Investigator, please contact the Supervisor at olowolafe.tubosun@lcu.edu.ng

Voluntary Participation

Your decision to participate in this study is completely voluntary. It is up to you to decide whether or not to take part in this study. If you decide to take part in this study, you will be asked to sign a consent form. After you sign the consent form, you are still free to withdraw at any time and without giving a reason.

Withdrawal from the Study/Withdrawal of Authorization

If you decide to participate in this study, you may withdraw from your participation at any point without penalty. Withdrawing from this study will not affect the relationship you have, if any, with the researcher. If you withdraw from the study before data collection is completed, your data will be returned to you or destroyed.

Consent

I have read and I understand the provided information and have had the opportunity to ask questions. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving a reason and without cost. I understand that I will be given a copy of this consent form. I voluntarily agree to take part in this study.

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Appendix II

Questionnair

e

Section 1: Socio – Demographic Characteristics.

Kindly tick (√) or fill in the space provided in the statements below;

1. Age: _____
2. Religion: Christianity ( ) Islam ( ) Others (Please specify)_____
3. Educational level: None ( )Primary level ( ) Secondary level ( ) Tertiary level ( )
4. Marital status: Single ( )Married ( ) Divorce ( ) Widowed ( ) Separated ( )
5. Type of partner: Spouse ( ) Steady ( ) Causal ( ) None ( )
6. How will you describe your Occupation:
   i. Professional / Technical/ Managerial ( )
   ii. Clerical Job ( )
   iii. Sales and Services ( )
   iv. Skills Manual Job ( )
   v. Unskilled Manual Job ( )
   vi. Agricultural ( )
   vii. Housewife ( )
   viii. Student( )
   ix. Others, Pls. specify _____
7. Has anyone in your household ever had TB? Yes ( ) No ( ) Don't know ( )
8. Have you ever had a TB test? Yes ( ) No ( ) Don't know ( )
9. If your answer to Question 8 is **YES**, where did you get your TB test done? Pharmacy( )Primary HealthCare Center ( ) At a clinic/hospital ( )

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Traditional Healer ( ) Community Outreach ( )

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10. What specimen did they collect to test for TB? Blood( )Sputum ( ) Others (Please specify)_____

11. How long ago did you have a TB test? 0 to 2 months ( ) 4 to 6 months ( ) 7 to 11 months ( ) More than a year ago ( )

Section 2: Knowledge of Tuberculosis (Tb)

Kindly tick (√) or fill in the space provided in the statements below;

1. Anybody can get TB: Yes ( ) No ( ) Don't know ( )
2. People living with HIV are more likely to get TB: Yes ( ) No ( ) Don't know ( )
3. People that are HIV negative can get TB: Yes ( ) No ( ) Don't know ( )
4. A person can get TB through handshakes: Yes ( ) No ( ) Don't know ( )
5. TB is transmitted through the air when a person with TB coughs or sneezes: Yes ( ) No ( ) Don't know ( )
6. A person can get TB through touching items in public places (doorknobs, handles in transportation, etc.): Yes ( ) No ( ) Don't know ( )
7. TBcan be transmitted through smoking: Yes ( ) No ( ) Don't know ( )
8. A person can get TB through sharing the same dishes: Yes ( ) No ( ) Don't know ( )
9. A person can get TB through eating from the same plate: Yes ( ) No ( ) Don't know ( )
10. Night sweats is one of the signs and symptoms of TB: Yes ( ) No ( ) Don't know ( )

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11. One of the signs and symptoms of TB is coughing up blood: Yes ( ) No ( ) Don't know ( )
12. Fever is one of the signs and symptoms of TB: Yes ( ) No ( ) Don't know)
13. The loss of appetite is one of the signs and symptoms of TB: Yes ( ) No ( ) Don't know ( )
14. Cough that lasts longer than two weeks is one of the signs and symptoms of TB: Yes ( ) No ( ) Don't know ( )
15. One of the signs and symptoms of TB is unintentional weight loss: Yes ( ) No ( ) Don't know ( )
16. TB can be cured through drugs, medicine and pills: Yes ( ) No ( ) Don't know ( )
17. TB can be cured using traditional medicine: Yes ( ) No ( ) Don't know ( )
18. There is no treatment for TB: Yes ( ) No ( ) Don't know ( )
19. How long does someone have to take the drugs to cure TB? One month or less ( ) Two to five months ( ) Six months or longer ( ) Others (Please specify) _____
20. People with TB are always with HIV positive: Yes ( ) No ( ) Don't know ()
21. It is possible to cure TB in people with HIV: Yes ( ) No ( ) Don't know ( )

Section 3: Knowledge of Tuberculosis (Tb) Preventive Measures

Kindly tick (√) or fill in the space provided in the statements below;

1. TB can be prevented by separating yourself from others and avoiding close contact with anyone: Yes ( ) No ( ) Don't know ( )

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2. Always covering the mouth and nose with a tissue when coughing and sneezing prevents the spread of TB: Yes ( ) No ( ) Don't know ( )
3. A well-ventilated room prevents the spread of TB: Yes ( ) No ( ) Don't know ( )
4. Use of medicines regularly according to prescription is one of the TB preventive measures: Yes ( ) No ( ) Don't know ( )
5. Early diagnosis and treatment is one of the measures to prevent the spread of TB: Yes ( ) No ( ) Don't know ( )
6. BacilleCalmette-Guérin (BCG) vaccination is protective against TB: Yes ( ) No ( ) Don't know ( )
7. Opening the room to allow natural light prevents the spread of TB: Yes ( ) No ( ) Don't know ( )
8. The use of protective masks prevent the spread of TB: Yes ( ) No ( ) Don't know ( )
9. People with TB become non-infectious soon after initiating appropriate treatment: Yes ( ) No ( ) Don't know ( )
10. Only patients with active TB can spread the disease: Yes ( ) No ( ) Don't know ( )

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Section 4: Practice of Tuberculosis (Tb) Preventive Measures

Kindly tick ( ) or fill in the space provided in the statements below;

1. Have you ever received health educationabout TB: Yes ( ) No ( ) Don't know ( )

√

2. Which of the following best describes your house: Bungalow ( ) Flat ( ) Duplex ( ) Storey building ( )Boysquarter ( )
3. How many people are living in your room?_____
4. Do you have window in your house?Yes ( ) No ( )
5. Do you open your home window regularly? Yes ( ) No ( )
6. Do you frequently test for TB: Yes ( ) No ( ) Don't know ( )
7. After coughing for more than two weeks, it is important to see a doctor or a community health provider: Yes ( ) No ( ) Don't know ( )
8. Smoking is very harmful: Yes ( ) No ( ) Don't know ( )
9. Smokers and those who take alcohol are at risk of contracting TB: Yes ( ) No ( ) Don't know ( )
10. Do you have people smoking around you: Yes ( ) No ( ) Don't know ( )
11. Do you know smoking around others put them at a risk of contracting TB: Yes ( ) No ( ) Don't know ( )
12. People living with HIV are more vulnerable to contracting HIV: Yes ( ) No ( ) Don't know ( )

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Bio-data

Olawoyin Christianah Temilola
1, Sunday Olawoyin Close, Baale Akinosi Ajuwon,Ogun State.
Tel: +2348137978418, +2348058555276
E-mail: temilolaolawoyin@gmail.com

Career Objective

To make contributions to the success and growth of an organization whose mission is centered on providing adequate health care services, serving the community and providing a platform for mentorship. To strive for excellence in all position while adding value.

Bio Data:

Date of Birth: 7th may, 1977

Marital Status: Single

Sex: Female

State: Lagos

Local Government: Agege

Religion: Christianity

Nationality: Nigerian

Key Skills and Expertise

- Strong interpersonal, leadership and management skills complemented with sound oral, written communication skills.
- Counseling and advising patients on health related conditions and need for compliance to medications
- Ability to work under pressure and with minimal supervision.
- Excellent attention to details
- Interpretation of prescriptions
- Clerkship of patients/clients
- Methodical and logical approach, ability to plan work and meet deadlines

Education

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- *B.Sc Community Health* 2020

Lead City University, Ibadan, Oyo State

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vi. *HND Community Health* 2016
Lagos State University Teaching Hospital, Lagos State

- *ND Community Health ExtensionWorker* 2001

College HealthTechnology, Ijebu-Ode, Ogun State

- *WAEC* 1995

State High School, Oyewole, Mulero Agege, Lagos State

- *FLSC* 1989

Ibukun Only Primary School, Agege, Lagos State

Experience:

- **Lagos State Primary Health Care Board, Yaba, Lagos** 2016 till date
  Post: Community Health Officer
- **Lagos State Primary Health Care Board, Yaba, Lagos** 2007-2016
  Post: Community Health Extension Worker
- **Balda Hospital & Maternity Home.** 1995-1998

Referees:

Mrs. Olaonipekun Nosimot
Ifako-Ijaiye PHC

Dr. Sanni F.O
Ifako-Ijaiye PHC

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The University Compliance Certification

This is to certify that this thesis by Christianah Temilola OLAWOYIN with Matric No. LCU/PG/002176 in the Department of Public Health, Faculty of Basic Medical and Applied Sciences, Lead City University, Ibadan is in full compliance with the approved university format.

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Signature	**Date**