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Haley E. Kehus Date

Treating Tuberculosis in Haiti's National Prison: A Retrospective Analysis of Who is Less Likely to Complete Treatment in Prison

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Epidemiology

_____

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2015

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Abstract

Treating Tuberculosis in Haiti's National Prison: A Retrospective Analysis of Who is Less Likely to Complete Treatment in Prison
By Haley E. Kehus

Introduction: Tuberculosis remains one of the leading causes of death from an infectious disease worldwide, especially for people who experience incarceration in developing countries. The living conditions in correctional facilities and the overlapping risk factors for tuberculosis and incarceration lead to a concentration of this disease in this setting. Managing tuberculosis within correctional facilities can be difficult due to the resources required compared to what is available, unpredictable lengths of confinement, and largely insufficient tracking systems.
Methods: Data were collected for each tuberculosis patient in Haiti's national prison from January 2016 to December 2018. Each man had been followed from the time of their diagnosis until they completed treatment. Cox regression analysis was conducted to provide insights on who takes longer to complete treatment. Univariate and multivariate logistic regression was conducted to determine factors associated with not completing tuberculosis treatment while in prison.
Results: The overall treatment completion rate was 84.1% for men incarcerated in Haiti's national prison from January 2016 to December 2018. Retreatment cases were significantly likely to take longer to complete treatment than new cases (HR 0.29, 95% CI 0.22-0.36). Extra-pulmonary tuberculosis patients were almost twice as likely to not complete treatment as pulmonary cases (aOR 1.96, 95% CI 1.08-3.52). Patients who were HIV-positive were about three times as likely to not complete treatment as HIV-negative patients (aOR 3.31, 95% CI 1.82-6.02).
Conclusions: Completing treatment for 5 out of 6 patients is an achievement, especially given the setting, and is higher than Haiti's national average of 79%. Nonetheless, this falls short of the World Health Organization's (WHO) TB target of successfully treating 90% of TB cases. Extra-pulmonary and HIV-positive cases are usually the more severe cases that require extra attention, therefore it is foreseeable that these cases are less likely to complete treatment. One limitation of this analysis was the final status of men who were released before completing treatment. Interventions targeting HIV-positive, extra-pulmonary, and/or retreatment cases may improve the prison's TB treatment completion rate and help achieve the WHO's 90% target.

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INTRODUCTION

Tuberculosis (TB) is the leading cause of death from a single infectious disease worldwide. In 2017 alone, there were 1.3 million TB-related deaths[1]. Furthermore, 1.7 billion people, nearly one-fourth of the world's population, is infected with TB.[2, 3] The risk for developing TB is not equally distributed across all demographics, it is a disease of poverty, so there is more disease burden in middle to low income countries, like Haiti, which has the highest TB incidence rate in the Western hemisphere. Haiti's estimated TB incidence was 181/100,000 in 2017[4] and is even greater in Port-au-Prince, the nation's capital and largest city, with an estimated incidence rate of over 1000/100,000.[5] In addition to the high disease burden, the growing epidemic of multiple drug-resistant (MDR) TB is also a great concern. The World Health Organization (WHO) estimates 2.9 percent of new cases and 13 percent of previously treated cases have MDR TB and in 2016, there were 132 new cases of MDR TB in Haiti.[5]

The prevalence of TB is higher within correctional facilities than in the general community[6] and these institutions present numerous complications to managing TB care. Haiti's largest prison is its National Penitentiary, which is located in downtown Port-au-Prince. The conditions within the National Penitentiary and characteristics of the population who are most likely to be incarcerated contribute to the increased concentration of TB in the prison. Completing an entire TB treatment regimen is essential not only for individual's health to improve but also to halt transmission and fight against the rise of MDR TB. The purpose of this evaluation is to determine who is less likely to successfully complete their TB treatment regimen while incarcerated in Haiti's National

Penitentiary, thereby identifying possible points of intervention to improve treatment adherence in this environment.

BACKGROUND

PATHOGENESIS

TB is caused by *Mycobacterium tuberculosis* (Mtb), a bacterium that is transmitted person-to-person via droplet nuclei that are expelled by infectious persons when they cough, sneeze, talk, or sing. The droplet nuclei containing Mtb may stay suspended in the air for long periods of time.[7] When an individual inhales the droplets, Mtb is taken up by the macrophages of the alveolar sacs in the lungs. The bacteria multiply intracellularly and release bacilli, which are ingested by other macrophages. Infected macrophages are then carried to nearby lymph nodes. Bacilli may further disseminate throughout the body, especially if the patient is immunosuppressed.[8] Due to this mechanism of transmission, the lungs are the most common site of TB disease with 80 percent of TB cases characterized as pulmonary TB.[8,9] Other common sites for TB disease include the lymphatic system, pleura, brain and meninges, genitourinary systems, and bones and joints. Miliary TB is characterized by TB disease spread throughout the body. If TB disease spreads beyond the lungs, it is considered extra-pulmonary TB (EPTB). EPTB cases account typically for 20-25 percent of TB cases.[10]

TRANSMISSION

TB infection occurs after a susceptible individual inhales the airborne droplets that contain Mtb. The risk of a successful transmission depends on the duration and the

closeness of the contact with an infectious source, the infectiousness of the source, and the environment in which the contact occurs.[11] Contacts with longer duration and greater closeness are more likely to successfully transmit TB. Additionally, a source case may be more infectious depending on the virulence of the particular strain of bacteria of which they are infected, the frequency of their cough, and the degree of pulmonary cavitation. The infective dose of TB is very low as a single droplet nucleus is sufficient to initiate the development of the primary lesion for TB infection[12] and an infectious TB patient who is not on treatment may release up to 75,000 droplets per day.[7] In addition to proximity to infectious sources, poorly ventilated areas are more likely to transmit TB. Therefore, TB is not only a disease of poverty, but a social disease as well, leading to higher TB rates in overcrowded urban settings. In the urban slums of high burden countries, like many of the neighborhoods in Port-au-Prince, the odds of developing TB are almost five times higher than the national TB incidence rates.[13, 14] Therefore, an overcrowded prison, such as the National Penitentiary, provides the ideal conditions for TB transmission.

The individuals who are most at risk for TB infection and developing active TB disease are the poorest, most vulnerable individuals in the community.[3] There are several risk factors associated with infection as well as several associated with the development of disease as not all of those infected with TB will develop disease. Contact with Mtb may result in active TB disease or latent TB infection (LTBI), where an infected person is showing no symptoms and is usually unaware that they harbor Mtb. About 10 percent of people infected with TB develop active TB disease.[9] The prevalence of infectious TB in the population, population density, and living conditions such as poverty and overcrowding are all associated with infection.[15] Individuals with LTBI or previously

treated active TB disease may develop active disease later in their life, which is commonly referred to as reactivation or recurrence. Failure to adhere to treatment, along with MDR TB and prior TB therapy, is one of the biggest predictors of recurrence of disease.[11] Studies show that some individuals are more at risk for developing active TB disease, especially those who are malnourished or have low body weight, take immunosuppressive drugs, have a history of a prior TB infection, currently smoke, or have a comorbid disease such as HIV/AIDS, diabetes, end stage renal disease, or substance abuse.[9, 14, 16] Symptoms of active pulmonary TB disease may range from mild to severe including cough with or without sputum, fatigue, weight loss, appetite loss, fever, chills, and night sweats.

TESTING AND DIAGNOSIS

A clinician or the patient must suspect TB infection and request an evaluation and diagnostic tests to confirm Mtb is present. If TB is suspected, the patient evaluation involves a detailed medical history including a symptom account and an epidemiologic profile, as well as diagnostic tests to examine the affected site (chest x-ray or CT scan) and to identify the bacteria (microscopy, culture, and molecular assays).[9] Immunologic evidence of TB can be detected using either a tuberculin skin test (TST) or interferon gamma release assays. However, the latter tests do not differentiate between active TB disease and LTBI because they are testing for an immunologic response to Mtb and past infections and LTBI also elicit an immunologic response.[7] Therefore, further clinical tests are needed to distinguish between active TB disease and LTBI.[17] Acid-fast bacilli (AFB) smear and culture are the gold standard test for active TB disease.[18] AFB smear and

cultures require patient specimens, usually a sputum collection. These specimens may or may not be available depending on the main site of infection and the quality of the specimen is a key predictor of the quality of the result. If Mtb is found, then the next step is to conduct drug susceptibility testing to determine if the patient is infected with a TB strain that is susceptible to the first line drugs or if there is any drug resistance. Drug susceptibility testing is typically repeated if patients have a poor response to treatment after three months on the regimen.

TREATMENT

The goals of TB treatment are to halt transmission by rendering the patient non-infectious as soon as possible, to cure the patient to prevent mortality and limit morbidity, and to prevent the emergence of drug resistance.[19] Getting an infectious patient on treatment is time-sensitive because prompt treatment reduces the spread and impact of TB as a person infected with TB becomes significantly less infectious after the first two weeks of treatment.[7,20] Haiti's National TB Control Program, the Programme National de Lutte contre la Tuberculose (PNLT), recommends a six-month treatment regimen of isoniazid, rifampin, pyrazinamide, and ethambutol for drug-susceptible TB disease in accordance with the 2010 WHO TB Treatment Guidelines.[10, 20] The WHO recommends the same treatment regimen for EPTB cases; however, testing for HIV is especially important for these cases because EPTB is more likely to occur in patients with immunosuppression.[10] The first phase of treatment is more intensive and consists of 60 doses (one dose per day) of all four drugs. The second phase of treatment is the maintenance phase and involves 120 doses (one dose per day) of just isoniazid and

rifampin. This regimen aims to rapidly destroy bacilli and treatment success is defined by the disappearance of infectiousness, culture negative sputum at two months, alleviation of the patient's symptoms, and improvement of their overall health. TB treatment is usually well tolerated with cure rates around 95 percent.[9] However, treatment may take longer than the prescribed six months depending on drug resistance, disease severity, the patient's health, and treatment adherence. Drug susceptibility testing helps clinicians determine to which drugs a particular patient's TB is susceptible. Clinicians may use second line drugs if the strain is resistant to first line drugs (isoniazid, rifampin, pyrazinamide, and ethambutol). It is imperative that at least two and never a single drug are added to an already failing regimen as adding one drug at a time provides opportunity for drug resistance to emerge. Ensuring treatment adherence is also vital in mitigating the risk of developing drug resistance.

DIRECTLY OBSERVED TREATMENT, SHORT COURSE

Directly Observed Treatment, Short course (DOTS) is the recommended strategy for TB control and elimination. DOTS, endorsed by the WHO, is an efficient and cost-effective strategy. There are five components to DOTS including: "sustained political and financial commitment, diagnosis by quality ensured sputum-smear microscopy, standardized short-course anti-TB treatment given under direct and supportive observation (DOT), a regular and uninterrupted supply of high-quality anti-TB drugs, and standardized recording and reporting."[21] Directly observed therapy, or DOT, involves a health care worker or trained community member supervising a TB patient swallowing each dose of their medication.[21] This requires the observer to be accessible to the patient

every day, for at least six months, to complete the regimen. DOT is designed to improve treatment adherence but is very costly in terms of time and resources. This strategy also allows for the potential for intensified stigma associated with TB and impedes on a patient's privacy because their TB status is more likely to be disclosed or suspected.[22] Furthermore, there are many environments in which DOT is not feasible given the limited resources available for hiring health care workers and traveling to patients to supervise them take their medication.

VIDEO DIRECTLY OBSERVED THERAPY

Given the many difficulties and high cost associated with DOT, video directly observed therapy (VDOT) may be a cost-effective alternative. VDOT is similar to DOT in that a TB patient is observed taking their medication every day of their prescribed regimen; however, VDOT utilizes a smart phone or tablet instead of an in-person health care worker. The patient uses a smart phone or tablet to record a short video of them taking their medication and sends the video to a health care worker so they may document that the medication was taken. There are several smart phone applications specifically designed for VDOT that automatically encrypt the video and sends it only to a secure database, thereby protecting patient confidentiality. Several studies have shown that not only is VDOT feasible in low-resource settings, but it has also resulted in high levels of treatment adherence.[23-26] VDOT may be especially helpful in areas that are more difficult to reach and have unpredictable or intermittent access. In settings with unstable political climates, there may be ongoing protests and demonstrations or violence that prevent health care workers from traveling to prisons to supervise DOT. When such

violence occurs, such as the civil unrest seen in Haiti in 2018 and early 2019, streets may be shut down or prisons may not allow visitors for safety and security purposes. Therefore, VDOT may be the best strategy to use in low-resource prisons like the prisons in Haiti.

TREATMENT ADHERENCE

The factors associated with poor treatment adherence differ based on the population and it is important to understand these influencing factors in order to properly control TB in that given population.[27] Several factors including HIV co-infection, smoking, alcoholism, low income, and lack of family support may affect TB treatment completion in prisons.[28, 29] One study conducted in Nigeria found that "unfriendly attitudes of health care workers" was a major barrier to treatment adherence as well as the patient's knowledge of the treatment duration and distance from the health worker.[29] Other studies have found that social risk factors, such as social deprivation and mental health concerns, may also contribute to poor treatment adherence.[30-35] Mental health concerns, particularly depression and psychological distress, negatively impact health behaviors like medication adherence. When clinical depression and TB disease occur simultaneously, there is increased morbidity, mortality, TB transmission, and MDR TB.[33] The relationship between depression and TB is somewhat bidirectional, meaning depression may increase the risk of TB recurrence and contribute to TB disease progression and depression may be triggered by TB-related stigma. Clinical depression that is comorbid with TB disease is exacerbated by any social vulnerabilities.[34]

Unfortunately said social vulnerabilities are quite common in the incarcerated populations so comorbid depression may be equally as common.

Ensuring that TB patients adhere to their treatment regimen is particularly difficult within correctional facilities due to the short duration of stay in some facilities, inadequate tracking of individuals who are transferred to other facilities, and lack of resources at the facility. Overcrowding and lack of healthcare staff also negatively impact an institution's ability to properly manage TB care as there are usually not enough staff available given the number of patients. Tracking systems are largely insufficient in Haitian prisons so patients may be easily lost to follow-up if transferred to another facility, making continuity of care very difficult. If individuals are transferred or released before completing their TB treatment, the status of their treatment may be incomplete or unknown, which may contribute to the development of drug-resistant tuberculosis strains if they remain untreated.[27] One study in Ethiopia found that some prisons reported 24 percent of their known TB cases to be harboring MDR TB from 2011 to 2015.[28] Another study demonstrated that TB treatment was successful if completed while in prison, 94 percent completed treatment, but if incarcerated persons were transferred or released during their treatment then they were lost to follow-up and the outcome of their treatment was unknown. Furthermore, the majority of incarcerated persons and prison staff (64 percent) were unaware that interrupting TB treatment may lead to MDR TB.[28, 35]

MULTI-DRUG-RESISTANT TUBERCULOSIS

MDR TB is TB that is resistant to at least two of the first line drugs (isoniazid or rifampin). Extensively-resistant TB (XDR TB) is TB that is MDR and is also resistant to

fluoroquinolone as well as a second-line injectable drug such as amikacin, kanamycin, or capreomycin.[36] There are several risk factors associated with primary drug resistance including contact with a case with known drug-resistant TB, infection in areas with high rates of drug resistance, history of prior treatment with TB drugs, poor TB treatment compliance, previous hospitalizations, history of incarceration, and positive cultures even after three months of treatment.[9, 36] MDR and XDR TB are significantly more difficult to treat as there is no standard proven regimen and the drugs are less effective, more toxic, and more expensive. The average direct treatment cost for drug-susceptible TB in the United States is $19,000 per case.[37] This cost jumps to $164,000 for MDR TB, a 763 percent increase, and jumps even more to $526,000 for XDR TB, a staggering 2,668 percent increase. Furthermore, 73 percent of persons with drug-resistant TB require hospitalization and 9 percent die during treatment. Other side effects from the more severe treatment include depression and psychosis, hearing impairment, hepatitis, and kidney impairment.[38] Drug resistance is particularly concerning in prisons like the National Penitentiary due to the close quarters and poor living conditions. Overcrowding further complicates treating MDR TB as there are very few places where an MDR TB patient could be isolated to prevent further transmission. Additionally, if drug resistance is not promptly identified, then these cases do not receive proper treatment and remain infectious, potentially spreading drug-resistant TB to those around them.[38, 39]

TUBERCULOSIS-RELATED STIGMA

TB has been a leading cause of death for centuries, particularly in developing countries like Haiti. As long as it has been around, TB has been stigmatized due to its

association with poverty, misery, and infectiousness.[40-42] The emergence of the HIV/AIDS epidemic added to stigmatization of those with TB due to the co-infectivity of the illnesses. Furthermore, "exaggerated notions of transmissibility" has led to societal attitudes towards TB to be "infused with shame, rejection, discrimination, and neglect."[40] Persons living with TB report experiences of shame and social isolation associated with their diagnosis. In Haiti specifically, TB-related stigma was related mostly to economic issues such as poverty and malnutrition. The perceived inability to take care of a loved one is a source of great shame in the Haitian context.[40] Disease-related stigma contributes to depression in patients, which, as stated before, has important implications for health outcomes and treatment adherence.[41, 42]

TUBERCULOSIS IN HAITI

As previously mentioned, Haiti has the highest TB incidence rate in the Western hemisphere.[4] From 2005 to 2010, the PNLT reported approximately 14,000 cases each year.[43] In 2010, the earthquake in Port-au-Prince killed over 200,000 people and destroyed most of the city, displacing nearly 1.5 million individuals. Most of these individuals were settled into shelters and camps that quickly became overcrowded and the poorer living conditions increased disease transmission. Following the earthquake, the PNLT focused their efforts on the settlements and worked to improve case detection and diagnosis techniques. PNLT surveillance found that from 2010 to 2015, TB incidence increased by 20 percent. During this time period, 52.2 percent of TB cases were male, 94.9 percent were new cases, 19 percent were HIV positive, the majority of cases were 15-24 years old (24.6 percent) or 25-34 years old (28.2 percent), and most were from the

western region of Haiti (43. 4 percent),[43] which includes Port-au-Prince (Figure 1). It is likely that the increased surveillance efforts and improved diagnostics contributed to the higher reported prevalence, however, the public health consequences of the earthquake likely made the larger impact. A systematic review of crisis-affected populations found an increased burden of TB disease and a pattern of excess risk following crises like the 2010 earthquake.[44] The displacement of 1.5 million people led to many of them being without their medications and many more of them living in overcrowded tent cities. Since the earthquake, the PNLT and non-governmental organizations have been working to improve case detection and treatment completion. In 2018, Haiti's national TB budget was $11 million, of which $1.2 million was from domestic sources, 7.4 million from international sources, and the remaining 2.4 million was "unfunded" meaning the budget was ultimately limited to the funded $8.6 million.[45] Non-governmental organizations like Health through Walls (HtW), the Stop TB Partnership, and the Endtb Partnership work in Haiti with the common goal of ending the TB epidemic.

TUBERCULOSIS IN CORRECTIONAL FACILITIES

Incarceration is associated with increased risk of TB disease.[46-50] As previously mentioned, the increased risk is due to the conditions of correctional facilities as well as the overlapping of risk factors for developing TB and experiencing incarceration. TB is more easily spread within correctional facilities, especially in low-resource settings, due to the higher prevalence of HIV infection, overcrowding, insufficient ventilation, poor hygiene, inadequate nutrition, and the worse overall health of incarcerated persons.[46-50] Poor nutrition is linked to a greater risk of developing disease from TB infection and low

body weight has been found to be a significant predictor of death among TB patients.[28] More specifically, patients who were underweight at the beginning of their TB treatment are at greater risk of death than patients at normal weight or above. This relationship between nutrition/body weight and TB is bidirectional, meaning TB contributes to patients being malnourished and malnourished patients are more likely to develop severe TB disease and face more unfavorable outcomes. A further complication to TB management in corrections is the nature of prison releases and transfers that may interrupt treatment. The length of stay in correctional facilities may be somewhat unpredictable, which makes it difficult to plan for a person's health care and treatment. Therefore, correctional facilities are an important- and largely overlooked- reservoir for drug susceptible and resistant TB that poses a substantial risk to the community at large.

INFECTION CONTROL IN CORRECTIONAL FACILITIES

The Centers for Disease Control (CDC) recommends several measures for effective TB control in correctional facilities including: routine screenings to identify all those with TB with a focus on early detection, successful treatment of active TB disease and LTBI, airborne precautions, comprehensive discharge planning, and thorough contact investigation for each case identified.[6] These measures are more difficult to achieve in low-resource settings, especially in overcrowded prisons where there are many competing priorities such as safety and security. Many prisons in these settings lack the funds and staff to effectively accomplish the preventative measures recommended by the CDC. Even with the assistance of non-governmental organizations, the National Penitentiary is overwhelmed with illness, malnutrition, and overcrowding. A modeling

study investigating the dynamics of TB epidemics found that case detection and effective treatment alone were insufficient in mitigating epidemics involving institutional amplifiers, like prisons.[51] However, Basu et al found that reducing the total population size entering institutional amplifiers significantly reduced TB incidence. Therefore, interventions for low-resource prison settings must be practical and work in conjunction with advocating policy changes that systemically reduce prison population sizes. Correctional staff are much more likely to accept, and perhaps even assist with, interventions if they are perceived to be achievable in scope and do not disrupt the safety or security of the prison.

THE NATIONAL PENITENITARY

The National Penitentiary in downtown Port-au-Prince is comprised of several buildings and cell blocks (Figure 2). The prison buildings sustained a great deal of damage during the 2010 earthquake when the entire roof caved in and several administrative buildings collapsed. This prison is for men only and is consistently overcrowded, housing over 4,000 men on average when it was built to house only 800.[47] Cells designed for only 20 men are forced to accommodate between 80 and 100 at a time and these individuals are typically locked up 22 hours a day.[52] With such extreme overcrowding, there are not enough beds or space for beds for everyone inside the facility. Individuals must create makeshift hammocks using linens and other found materials. Overcrowding is exacerbated by the clogged judicial system. About 90 percent of the individuals within the National Penitentiary have yet to be convicted of a crime and are still awaiting trial.[47] Nutrition provided to incarcerated men is inadequate as it is

limited to two meals a day with the meals consisting mostly of cornmeal and vegetables. Protein, such as chicken or fish, is sometimes available but only in small quantities and rarely reaches the entire prison population. Several cases of beriberi, a thiamine deficiency disorder, have occurred in the prison due to the inadequate nutrition. The symptoms of beriberi include constipation, fatigue, memory loss, peripheral neuropathy, muscle weakness and pain, foot drop, and heart failure.[53] Many of the incarcerated men rely on their family or friends to supplement their prison meals by bringing food when they visit; however, not everyone is afforded this opportunity. Additionally, hygiene is an issue within the facility for the individual as well as the facility overall. The facility uses three water pumps to provide water and currently only one of the three pumps works properly. There are no latrines inside the cells, so the only options are to defecate on the ground or in plastic bags. Moreover, access to soap is severely limited and can be quite costly for the individual, making bathing a luxury.

The National Penitentiary has a separate holding cell for individuals experiencing extreme malnutrition. This cell is much larger than the other holding cells, is separated from the others, and provides much better ventilation with windows on all four walls. Persons housed in this cell are still somewhat cramped but have significantly much more room than the other housing cells. This cell would be a better environment to house TB patients in the prison given the ventilation that would deter transmission.

STOP TB PARTNERSHIP

Founded in 2001, the Stop TB Partnership is an international organization that aims to reach people vulnerable to TB and improve the quality of TB diagnosis,

treatment, and care.[55] The Global Plan to End TB is a series of five-year investment plans by the Stop TB Partnership that lay out specific benchmarks and targets to achieve as part of the WHO End TB Strategy. The people-centered global targets of the 90(90)90 WHO End TB Strategy are to 1) reach at least 90 percent of all people with TB; 2) reach at least (90) percent of key populations with TB meaning the most vulnerable; and 3) achieve at least 90 percent treatment success.[55] The WHO's definition of the most vulnerable to target includes incarcerated individuals due to their increased risk of TB. In order to end TB, a 10 percent reduction in TB cases per 100,000 per year must be achieved; however, the current global trend is only a 1.5 percent reduction TB cases per 100,000 per year.[38] Therefore, to close this gap and end TB, more radical and innovative measures must be taken.

HEALTH THROUGH WALLS

HtW is a non-profit volunteer organization that works in the prisons of developing countries. Founded in 2001, HtW assists with the implementation of sustainable improvements in prison health care. In the National Penitentiary specifically, HtW creates and maintains medical records for each incarcerated individual, supports staff training, and provides medical supplies.[56] One of their main initiatives in the National Penitentiary is to identify and treat infectious diseases such as TB, HIV, syphilis, and cholera. Since 2013, HtW has had trained medical staff working full-time in the prison alongside prison authority medical staff to help manage prison health care. HtW conducts routine TB screenings using a portable digital x-ray machine for chest x-rays. Additionally, with the cooperation of the PNLT, they use a GeneXpert machine for

laboratory confirmation of TB diagnoses and to identify drug susceptibility and resistance.

In 2018, the Stop TB Partnership awarded a grant to HtW to perform a non-inferiority study of VDOT in Haitian prisons. The purpose of the project is to demonstrate that VDOT can achieve the same levels of treatment compliance as DOT in low-resource prison settings. Many prisons in Haiti do not have the resources required for implementing DOT, which is why VDOT may be a cost-effective alternative for managing TB care in these settings. HtW subcontracted Emory researchers to evaluate the project and to determine the acceptability attitudes towards VDOT among incarcerated individuals with TB as well as the correctional officers working in the prisons. The evaluation will include comparisons of treatment adherence and acceptability attitudes of VDOT prisons to DOT prisons. The project will take place in prisons in Port-au-Prince, Carrefour, Petit Goave, Gonaives, Mirebalais, Jacmel, Saint-Marc, Croix-des-Bouquets, and Les Cayes (Figure 1). As part of this evaluation, baseline data were collected of TB-infected individuals who were incarcerated at the National Penitentiary and underwent treatment for TB. This analysis aims to identify predictive factors of who will not complete TB treatment in prison thereby providing valuable insight for the next phases of the demonstration project and improving TB treatment in low-resource prisons.

METHODS

DATA SOURCE

In 2018, HtW recruited Emory researchers to conduct an epidemiologic evaluation of their TB Reach project funded by the StopTB Partnership. The data for this analysis were provided by HtW as a part of the larger evaluation ongoing in Haitian prisons with the intention that this analysis may inform next phases of the project as it may provide insight into who is less likely to successfully complete treatment in prison. The investigators traveled to Port-au-Prince in December 2018 and January 2019 to visit the National Penitentiary, meet with HtW staff to discuss the evaluation, and collect data for this analysis. HtW staff working in the prison maintain a hand-written registry of all TB patients in the prison. Cases are found with routine screening conducted by HtW staff. The registry follows each suspected and confirmed TB case in the prison until they complete their treatment (successfully or unsuccessfully), are released or transferred from the National Penitentiary, die, or are lost to follow-up. HtW staff scanned the registry pages from January 2016 to December 2018 and sent them to Emory.

DATA SECURITY

The investigators undertook several measures to secure data and protect patient confidentiality. A separate Emory staff member redacted all identifiable information from the registry pages, including the patient's full name and previous address, and then sent the de-identified data to the investigator for analysis. Registry data with identifiable information was kept in a locked cabinet in a secure office on Emory's campus. The investigator assigned a study identification number to each subject and entered all the de-

identified into a secure Excel database. All data were kept on password-protected computers.

DATA CLEANING AND ANALYSIS

The registry pages from January 2016 to December 2018 included data on 661 patients on treatment for suspected or laboratory-confirmed TB in the National Penitentiary. The outcome of interest for this analysis is completing or failing to complete TB treatment while in the prison. Completing treatment includes patients classified as "treated" and "treatment terminated." Patients are classified as "treated" if they show a positive smear result prior to starting treatment and test negative after treatment. In accordance with the WHO guidelines, patients who do not have smear-positive bacilli prior to starting to treatment are considered suspected TB cases. Since these patients cannot show a change in smear post-treatment- as they were negative at the beginning of treatment- their treatment outcome is classified as "treatment terminated" instead of "treated." For the purposes of this analysis, these patients were considered successfully treated. Patients who failed to complete treatment included treatment failures, deaths, prison release and transfers, and unknown outcomes. If a patient is transferred to another correctional facility or released prior to completing their six-month regimen, their treatment outcome is unknown and these patients are typically lost to follow-up as there is no mechanism to link patients and ensure continuity of care. Additionally, the medications in the prison are provided by HtW so treatment is more difficult to obtain once released. These patients were classified as failing to complete treatment based on the recommendation by the HtW physicians and staff in the National Penitentiary.

Since the registry was hand-written, there were some fields that were left blank or were unreadable. These variables were counted as missing for the purpose of this analysis. Possible covariates and confounders were identified based on a review of the literature concerning TB treatment adherence and TB treatment in correctional settings, however, variable specification was limited to the covariates available on the hand-written registry. For each patient, the registry included the following variables:

Variables Recorded for Each Tuberculosis Patient at the National Penitentiary

Age	Smear at 2 months
Housing location	Weight at 2 months
Treatment start date	Smear post-treatment
TB case category	Weight post-treatment
TB type	HIV status
Pre-treatment GXP	Date of HIV test
Pre-treatment weight	Treatment outcome

Housing cell number was considered to be not identifiable information because as many as 100 individuals may be in a cell at one time. Furthermore, housing cell assignments are not permanent so it would not be feasible to identify a patient based on a housing cell number from previous months or years. Patients were categorized as new TB cases if they had no history of prior TB diagnosis or as retreatment cases if they did have a history of prior TB diagnosis. TB types included pulmonary (laboratory-confirmed and non-laboratory confirmed) and EPTB cases. Weight measurements were recorded in pounds or kilograms on the registry. When entering these measurements into the Excel database, any weight measurement recorded in pounds was converted to kilograms for measurement consistency. Dates included in the registry were written in the French date format (DD/MM/YYYY). These were converted to the American date format

(MM/DD/YYYY) when entered into the Excel database for convenience of analysis. All data entered into the excel database were reviewed for errors and inconsistencies.

Data were transferred from Excel to SAS version 9.4 for further data cleaning and analysis. Change in weight was found using the end of treatment weight and the pre-treatment weight. Age, pre-treatment weight, and change in weight were categorized into quartiles based on their relative distribution. Housing cells were grouped based on housing location, meaning all cells in Titanic were grouped together. Change in weight was initially considered for analysis to determine if there was a significant association with treatment outcome, however, any result would be biased as the patient would be required to reach the sixth month of treatment to be measured for end of treatment weight.

Time-to-event analysis was used to determine predictors of who may take longer to complete their treatment in prison. The event in this analysis is completing the TB regimen. Patients who did not complete treatment were censored at the time of their treatment outcome whether that was death, prison release or transfers, treatment failures, or loss to follow-up (unknown treatment outcome). Kaplan-Meier curves were generated for each variable (age groups, TB case category, TB type, HIV status, housing location, and pre-treatment weight groups). The log-rank test was used to determine whether survival curves were significantly different from each exposure classification for every variable. The proportional hazards assumption was assessed for each variable considered for the Cox regression analysis using the graphical method, goodness of fit testing, and time-dependent variables. Then Cox regression analysis was used to determine covariates that significantly affected the time to complete treatment in prison.

Univariate logistic regression procedures were used to determine which, if any, covariates were significantly associated with not completing treatment in prison. Odds ratios were considered significant if the corresponding p-value was less than alpha level 0.05. Then a final model was compiled using multivariate logistic regression and backwards elimination to determine risk factors for not completing treatment in the prison. Based on the results of the univariate logistic regression results and the literature review, the following covariates were considered for the full model: age, TB case category, TB type, and HIV status (Figure 3). These covariates were first assessed for collinearity. Then, a chunk test of likelihood ratios was used to evaluate whether there was any evidence of effect modification. The chunk test involved a full model with interaction terms for each combination of the covariates in the model and a reduced model with no interaction terms. No evidence of statistically significant interaction was found so the model was then assessed for confounding by comparing different combinations of the covariates against the fully parameterized model to determine if the models differed meaningfully. If the odds ratio varied more than 10 percent from the fully parameterized then it was determined this was evidence of confounding by the dropped variable. Adjusted and unadjusted estimates were found using the final multivariate logistic regression model.

INSTITUTIONAL REVIEW BOARD

The Emory Institutional Review Board reviewed and approved the broader evaluation of the project in Haiti and this additional analysis.

RESULTS

Out of the 661 patients, 556 (84.1 percent) completed treatment while in prison and 105 (15.9 percent) did not complete treatment while in prison. Ages ranged from 18 to 71 years old at the start of treatment. The average age at the start of treatment was 31 years old with a standard deviation of 8.00. Out of the 661 patients, 536 (81.2 percent) were new TB cases and 124 (18.8 percent) were retreatment TB cases (Table 1). The majority of cases were characterized as pulmonary TB (85.9 percent) and only 88 cases were characterized as EPTB (14.1 percent). Additionally, 554 patients (89.1 percent) were identified as HIV-negative and 68 (10.9 percent) were HIV-positive. The average pre-treatment weight was 54.27 kilograms (119.65 pounds) with a standard deviation of 7.46. The average change in weight during treatment was a gain of 1.99 kilograms (4.39 pounds). Most patients with a known housing location were housed in Titanic (32.2 percent), Dispensair (29.8 percent), or Brick (20.1 percent). Figure 2 provides a snapshot of the distribution incarcerated men in the different housing location on a single day (January 16, 2019). The majority of individuals on that day were housed in Titanic (37.2 percent). Out of the 105 patients who did not complete treatment in prison, 52 (49.5 percent) were released, 32 (30.5 percent) died, 2 (1.9 percent) were transferred, 3 (2.9 percent) had treatment failures, and 16 (15.2 percent) were lost to follow-up (Table 2). During the January 2016 to December 2018 time frame, only one patient was determined to have MDR TB (0.15 percent).

COX REGRESSION ANALYSIS

Time-to-event analysis was conducted to determine predictors of who may take longer to complete treatment in prison. The Kaplan Meier curves and corresponding log-rank tests found only TB case category (new versus retreatment cases) to be significantly associated with time to completing treatment (Table 3). Age, TB type, HIV status, housing location, and pre-treatment weight were not significantly associated with time to complete treatment in prison. The crude Kaplan-Meier curve demonstrates the shorter time-to-complete treatment for new cases compared to retreatment cases (Figure 4). Using Cox regression analysis, it was found that retreatment cases (those with a history of TB diagnosis) were significantly likely to take longer to complete the TB treatment regimen (hazard ratio 0.29, 95% CI 0.22-0.36) than new cases (no history of prior TB diagnosis). New TB cases had a shorter average time to complete treatment than retreatment cases with a mean [standard deviation] of 193.85 [±15.57] days to complete treatment for new cases compared to 227.68 [±29.89] days to complete for retreatment cases (Figure 5).

UNIVARIATE LOGISTIC REGRESSION

To investigate which covariates were significantly associated with not completing treatment while in prison, univariate logistic regression was conducted (Table 4). The odds of failing to complete treatment increased with increased age at start of treatment, however, this association was not significant at alpha level 0.05. Retreatment cases were slightly more likely to complete treatment than new cases, but this association was also not significant. The association between TB type and failing to complete treatment was

significant. EPTB cases were 1.76 times less likely to complete treatment than pulmonary TB cases (p-value 0.0424). The association of HIV status and failure to complete treatment was also significant. HIV-positive individuals were 3.19 times less likely to complete treatment than those who are HIV-negative (p-value <0.0001). Cell block and pre-treatment weight were not significantly associated with failure to complete treatment. However, individuals living in the "Dispensair" cell block were much less likely to complete treatment than any other cell block (OR 4.91 compared to 1.56, 1.17, 3.11, 2.00, and 0.90. This could be because the individuals housed in "Dispensair" are kept in the clinic due to comorbid conditions. It should be noted that while these results were not significant and a large majority of patients (n=403) were missing cell block location.

MULITVARIATE LOGISTIC REGRESSION

To further investigate the relationship between the given covariates and not completing treatment while in prison, multivariate logistic regression was conducted, and a final model was created (Table 5). Based on the results of the univariate logistic regression and the aforementioned literature review, age, TB case category, TB type, and HIV status were considered for the full model. A chunk test demonstrated there was no statistically significant evidence of interaction among any of the selected covariates. TB case category and age were not significantly associated with the outcome and were dropped from the model. The confounding assessment showed evidence that age may be a confounder of the relationship between TB type, HIV status, and not completing treatment in prison. Estimates were adjusted for patient's age at the start of treatment. The adjusted estimates provide more precise measures (narrower confidence intervals) of

the association between TB type, HIV status, and not completing treatment in prison. Multivariate logistic regression indicated that EPTB patients were almost twice as likely to not complete treatment as pulmonary cases (aOR 1.96, 95% CI 1.08-3.52). Additionally, patients who were HIV-positive were about three times as likely to not complete treatment as HIV-negative patients (aOR 3.31, 95% CI 1.82-6.02).

DISCUSSION

During the January 2016 to December 2018 timeframe, the National Penitentiary achieved 84.1 percent treatment completion with the assistance of HtW. This level of treatment completion is commendable, especially given the setting, and is higher than Haiti's national average of 79 percent.[4] However impressive, there is still room for improvement to reach the WHO's end TB target of successfully treating 90 percent of people with TB. The results of the multivariate logistic regression analysis indicate that the individuals who are least likely to complete treatment prison are EPTB cases and HIV-positive individuals. These cases are usually more severe and require extra attention. Thus it is not surprising that they are less likely to complete treatment. It is likely that these individuals were more at risk of death due to the advanced disease and that lead to failing to complete treatment. Furthermore, Cox regression analysis demonstrated that retreatment cases were significantly likely to take longer to complete treatment than new cases. Interventions targeting these types of cases (HIV-positive, EPTB, and/or retreatment) may improve the prison's TB treatment completion rate and help achieve the WHO's 90 percent target. Possible interventions could involve discussions with these

particular patients about the importance of treatment adherence in their circumstances and VDOT to ease treatment monitoring.

LIMITATIONS

There are several limitations to this analysis and its findings. Firstly, the data were collected from the National Penitentiary where prison health care is supported by HtW staff. HtW regularly screens and oversees TB treatment so the results of this analysis may not be as generalizable to other prisons throughout Haiti, especially in rural locations with fewer resources. Additionally, there is the possibility that patient outcomes were misclassified as the data were extracted from a hand-written registry that is susceptible to human error. It is also conceivable that patients who were released or loss to follow-up did complete their TB treatment. Due to the manner of record keeping, the year of entry for the patients was unknown and therefore unavailable for analysis. It is hypothesized that time spent in the prison (calculated from year of entry) may have an effect on treatment completion, but these data were unfortunately not available for this analysis. Without the date of prison entry, it is not possible to determine if TB cases were diagnosed during entry or at some other time during their confinement. Most screening occurs during entry procedures so individuals with LTBI or treated TB may pass through intake screening but later develop active TB disease due to malnutrition and the conditions inside the prison, especially if HIV-positive. A delay in diagnosis could explain why HIV-positive individuals were less likely to complete treatment in prison. Furthermore, adherence data was not available for this analysis; though adherence is expected to be high given the assistance from HtW. And finally, there is also the

possibility for selection bias if TB screening efforts in the prison were not comprehensive enough and some TB patients were missed.

RECOMMENDATIONS

Based on the findings of this analysis, it is recommended patients with more advanced disease, such as EPTB cases and those who are HIV-positive, are prioritized when monitoring treatment adherence and treatment outcomes. These patients are less likely to successfully complete treatment while in prison and should therefore be more closely managed. It should be noted that treatment completion levels in the National Penitentiary are impressive, especially considering the setting; however, there is room for improvement and these data provide possible patients to target for intervention.

More broadly, improving linkage systems and continuity of care is highly recommended. Such a linkage system would ideally identify incarcerated persons living with a disease, such as TB, when they are being transferred and would notify the correctional facility to which they are being transferred. And wherever possible, the health care staff at the correctional facility would be notified of any known cases that arrive at their facility. This would allow for the continuity of care for patients and would alleviate disruptions in TB treatment and other treatment regimens. Another important facet of continuity of care is linking incarcerated persons living with TB disease to health care once they are released from prison into the community. This includes assisting incarcerated persons with identifying where they may access care and what care they will need once released. Accessing care can be an obstacle for many previously incarcerated persons given the cost and resources needed. HtW has established a community clinic in

downtown Port-au-Prince with the mission of improving continuity of care for previously incarcerated individuals. Additionally, one aspect of the TB Reach project funded by the StopTB Partnership is exploring VDOT for individuals incarcerated in the National Penitentiary who have TB and are about to be released into the community. HtW staff believe VDOT may be part of the solution for continuity of care for this population as it will help establish patient autonomy and responsibility with taking their medications. VDOT will also allow health care staff to continue monitoring treatment adherence if patients are released prior to completing their regimen. Patients participating in the project will receive a smartphone equipped with VDOT software upon their release from prison and will then use the smartphone to record taking their daily TB medications so that HtW staff may monitor their treatment adherence. Based on the findings of this analysis, it is recommended that patients with EPTB and/or patients who are HIV-positive should be targeted for participation in the VDOT project and given assistance with discharge planning.

PUBLIC HEALTH IMPACT

This analysis demonstrates the impact of non-governmental organizations like HtW that work in prisons and assist with prison health care and possible points for intervention to achieve the WHO's end TB targets. Without the routine screening conducted by HtW, case detection would be substantially lower. Furthermore, it is reasonable to assume that the same completion rates would not have been achieved without their assistance. Since this analysis found that HIV-positive individuals were less likely to complete treatment in prison, these results also emphasize the importance of

HIV testing in prisons like the National Penitentiary and the need for the continued support of organizations like HtW that make widespread testing possible. The analysis conducted indicates patients who should be more closely monitored during treatment as they are less likely to complete treatment in prison. Targeting patients with EPTB and/or are HIV-positive will likely improve the treatment completion rate. And with a higher treatment completion rate, the risk of TB transmission is lowered and the potential for MDR TB is lessened, thereby improving the safety for all incarcerated individuals at this facility and for the communities to which they are released.

Table 1. Characteristics of Men Incarcerated in Haiti's National Penitentiary and Diagnosed with Tuberculosis from January 2016 to December 2018

Variable		No.	%
Age (years)			
	Missing	18	
	15-25	173	26.9
	26-29	163	25.4
	30-34	151	23.5
	35+	156	24.3
TB Case Category			
	Missing	1	
	New Case	536	81.2
	Retreatment Case	124	18.8
TB Type			
	Missing	38	
	Pulmonary	535	85.9
	Extra-Pulmonary	88	14.1
HIV Status			
	Missing	39	
	Negative	554	89.1
	Positive	68	10.9
	HIV-Positive & Pulmonary	*51*	
	HIV-Positive & Extra-Pulmonary	*12*	
	HIV-Positive & New Case	*53*	
	HIV-Positive & Retreatment Case	*15*	
Cell Block			
	Missing	403	
	Admission	15	5.8
	Bois Vena	10	3.9
	Brick	52	20.1
	Dispensair	77	29.8
	Greffe	2	0.8
	Hall	11	4.3
	Klinik	8	3.1
	Titanic	83	32.2
Pre-treatment weight (kg)			
	Missing	163	
	38-49	130	26.1
	50-54	137	27.5
	55-60	115	23.1
	60-83	116	23.3

Table 2. Tuberculosis Treatment Outcomes of Men Incarcerated in Haiti's National Penitentiary from January 2016 to December 2018

Treatment Outcome	No.	%
Completed Treatment	556	84.1
Treated	405	61.3
Treatment Terminated*	151	22.8
Did Not Complete Treatment	105	15.9
Released	52	7.9
Died	32	4.8
Transferred	2	0.3
Treatment Failure	3	0.5
Unknown	16	2.4

**In accordance with WHO guidelines, suspected TB cases without a positive smear prior to starting treatment are classified as treatment terminated after 6 months of treatment*

Table 3. Cox Regression Analysis of Time-to-Complete Tuberculosis Treatment and TB Case Category among Men Incarcerated in Haiti's National Penitentiary and Diagnosed with Tuberculosis from January 2016 to December 2018

	Log-Rank Test		
Variable	**Chi-Square**	**DF**	**P-value**
Age	1.95	3	0.5826
TB Case Category	114.93	1	<0.0001*
TB Type	2.16	1	0.1414
HIV	2.77	1	0.0960
Housing Location	5.96	7	0.5450
Pre-treatment weight	2.10	3	0.5526

	Cox Proportional Hazard Model			
	Estimate	**P-value**	**HR**	**(95% CI)**
TB Case Category				
Retreatment vs. New Case	-1.25	<0.0001*	0.29	(0.22, 0.36)

**Significant at alpha level 0.05*

Table 4. Univariate Regression Analysis of Not Completing Tuberculosis Treatment and Covariates among Men Incarcerated in Haiti's National Penitentiary and Diagnosed with Tuberculosis from January 2016 to December 2018

	Completed Treatment		Did Not Complete Treatment			
Variable	**No.**	**%**	**No.**	**%**	**OR (95% CI)**	**P-value**
Age (years)						
15-25**	148	27.2	25	25.3	1	
26-29	140	25.7	23	23.2	1.11 (0.92, 1.35)	0.2719
30-34	130	23.9	21	21.2	1.24 (0.85, 1.81)	0.2719
35+	126	23.2	30	30.3	1.38 (0.78, 2.43)	0.2719
TB Case Category						
New Case**	450	80.9	86	82.7	1	
Retreatment Case	106	19.1	18	17.3	0.89 (0.51, 1.54)	0.6739
TB Type						
Pulmonary**	454	87.1	81	79.4	1	
Extra-Pulmonary	67	12.9	21	20.6	1.76 (1.02, 3.02)	0.0424*
HIV Status						
Negative**	490	91.1	64	76.2	1	
Positive	48	8.9	20	23.8	3.19 (1.78, 5.71)	<0.0001*
Cell Block						
Admission**	14	6.2	1	3.0	1	
Bois Vena	9	4.0	1	3.0	1.56 (0.08, 28.15)	0.7649
Brick	48	21.3	4	12.1	1.17 (0.12, 11.30)	0.8942
Dispensair	57	25.3	20	60.6	4.91 (0.61, 39.78)	0.1348
Greffe	2	0.9	0	0.0	0	0.9888
Hall	9	4.0	2	6.1	3.11 (0.24, 39.54)	0.3816
Klinik	7	3.1	1	3.0	2.00 (0.12, 36.95)	0.6414
Titanic	79	35.1	4	12.1	0.71 (0.07, 6.82)	0.7658
Pre-treatment weight, kg						
60-83**	104	24.1	12	18.2	1	
38-49	110	25.5	20	30.3	1.01 (0.80, 1.28)	0.9287
50-54	115	26.6	22	33.3	1.02 (0.63, 1.64)	0.9287
55-60	103	23.8	12	18.2	1.03 (0.50, 2.11)	0.9287

**Significant at alpha level 0.05*

***Reference group*

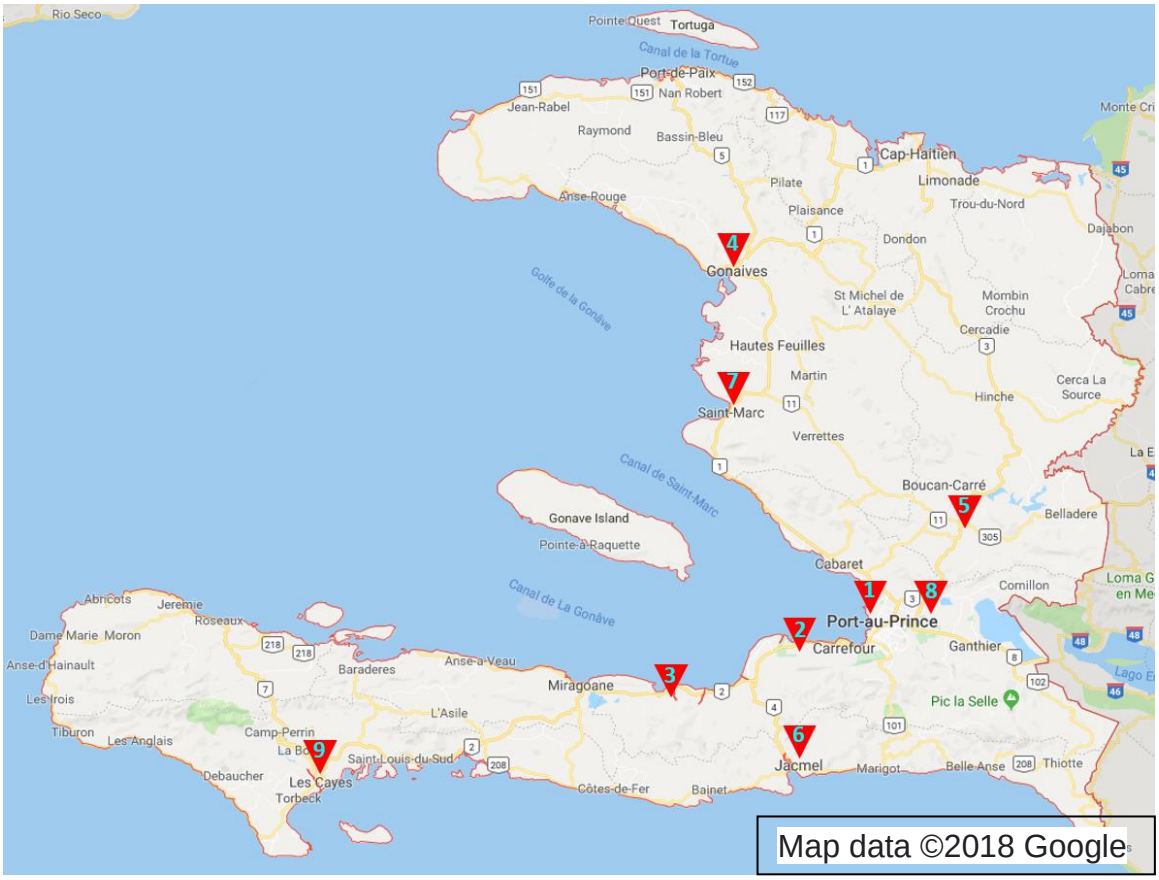
Table 5. Adjusted and Unadjusted Multivariate Models for Failing to Complete TB Treatment and Covariates among Men Incarcerated in Haiti's National Penitentiary and diagnosed with Tuberculosis from January 2016 to December 2018

Exposure Classification	Estimate	P-value	OR	(95% CI)
TB Type				
Adjusted**				
EPTB v. Pulmonary TB	0.72	0.0179*	2.05	(1.13, 3.72)
Unadjusted				
EPTB v. Pulmonary TB	0.67	0.0250*	1.96	(1.08, 3.52)
HIV Status				
Adjusted**				
Positive v. Negative	1.09	0.0006*	2.98	(1.60, 5.54)
Unadjusted				
Positive v. Negative	1.20	<0.0001*	3.31	(1.82, 6.02)

**Significant at alpha level 0.05*

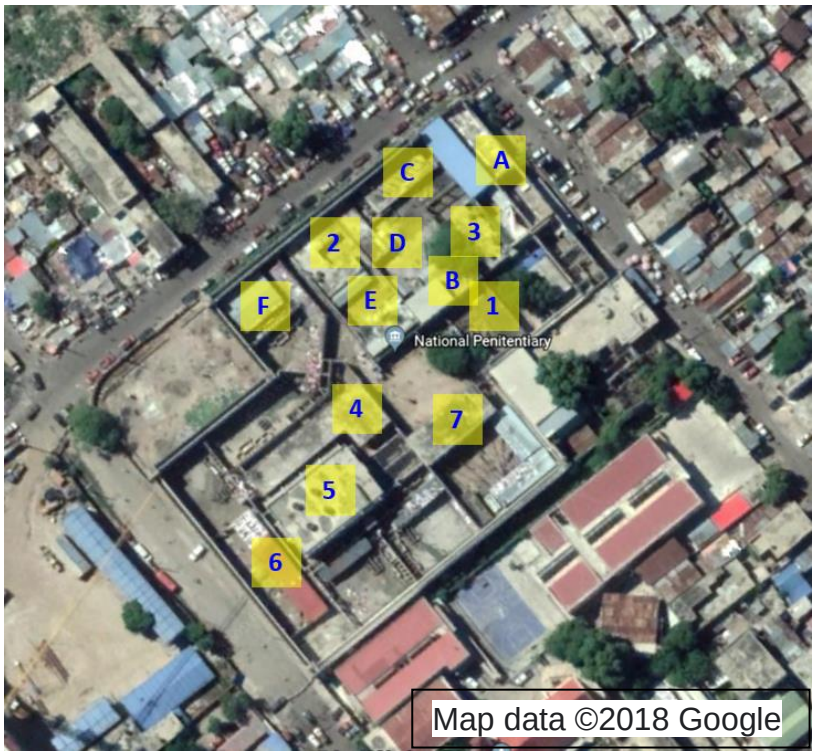
***Adjusted for patient's age at start of treatment*

Figure 1. Map of Haiti and locations of prisons (Google Maps 2019)



1. Port-au-Prince
2. Carrefour
3. Petit Goave
4. Gonaives
5. Mirebalais
6. Jacmel
7. Saint-Marc
8. Croix-des-Bouquets
9. Les Cayes

Figure 2. Aerial View of the National Penitentiary and locations of prison buildings (Google Earth 2019)



Housing buildings

1. Admission
2. Dispensair/Klinik
3. Greffe
4. Brick
5. Titanic
6. Bois Vena
7. Hall

Other buildings

A. Entrance
B. Administration
C. Kitchen
D. Medical buildings
E. TB treatment ward
F. Malnutrition ward

Housing Distribution of Men Incarcerated in Haiti's National Penitentiary on January 16, 2019

Housing Location	No.	%
Admission	973	24.0
Bois Vena	338	8.3
Brick	386	9.5
Dispensair	215	5.3
Greffe	131	3.2
Hall	451	11.1
Klinik	2	0.0
Titanic	1506	37.2
Isolation	51	1.3

Figure 3. Directed Acyclic Graph of Factors Affecting Treatment Completion among Men Incarcerated in Haiti's National Penitentiary and Diagnosed with Tuberculosis from January 2016 to December 2018

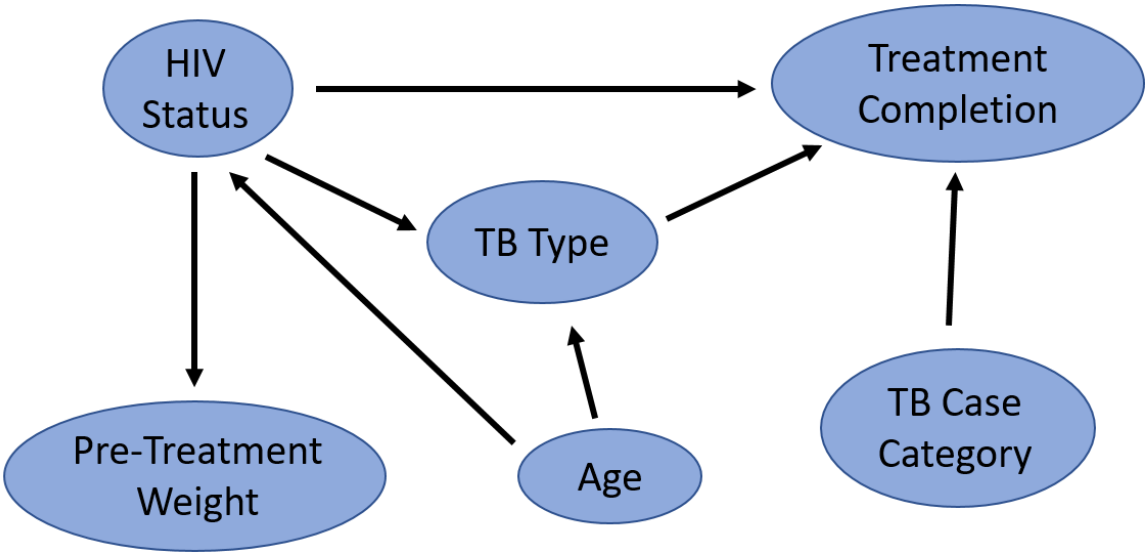


Figure 4. Kaplan Meier Curve: Time-to-Complete Treatment of New TB Cases compared to Retreatment TB Cases among Men Incarcerated in Haiti's National Penitentiary and Diagnosed with Tuberculosis from January 2016 to December 2018

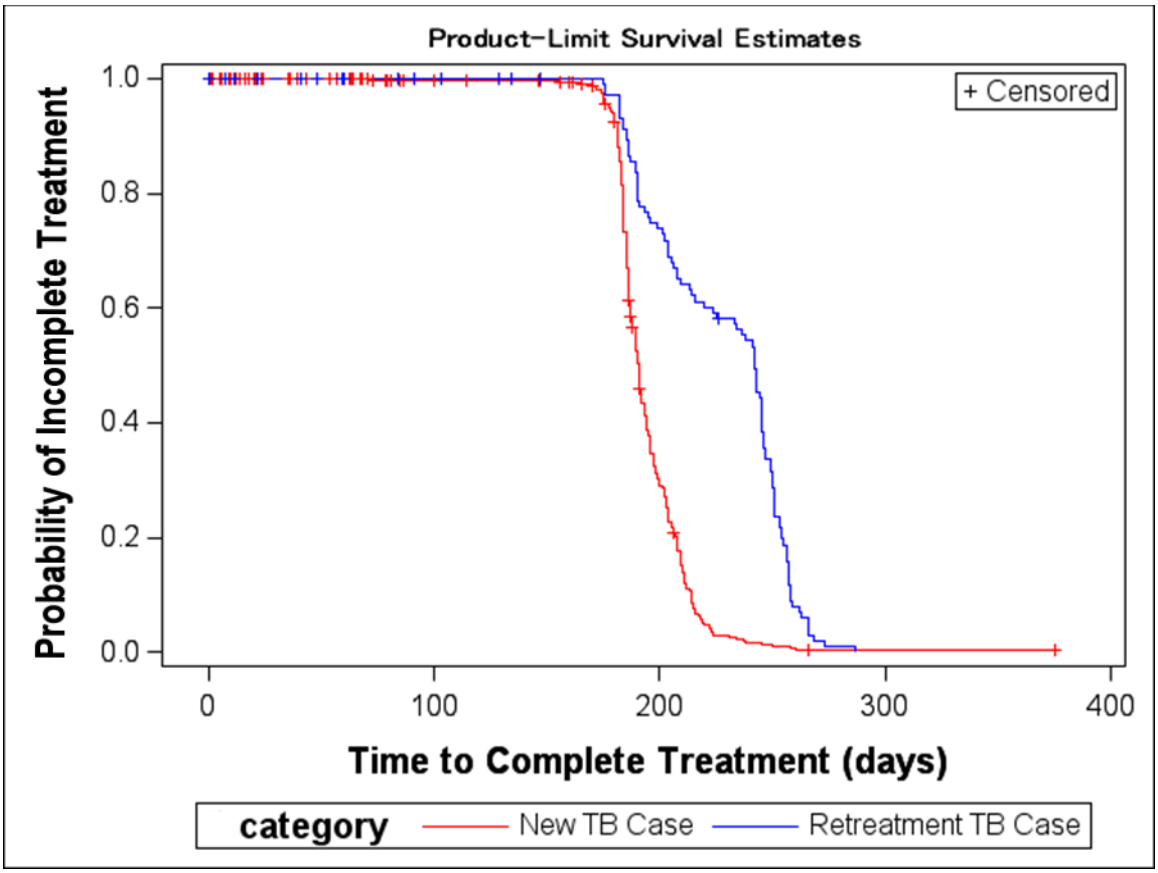
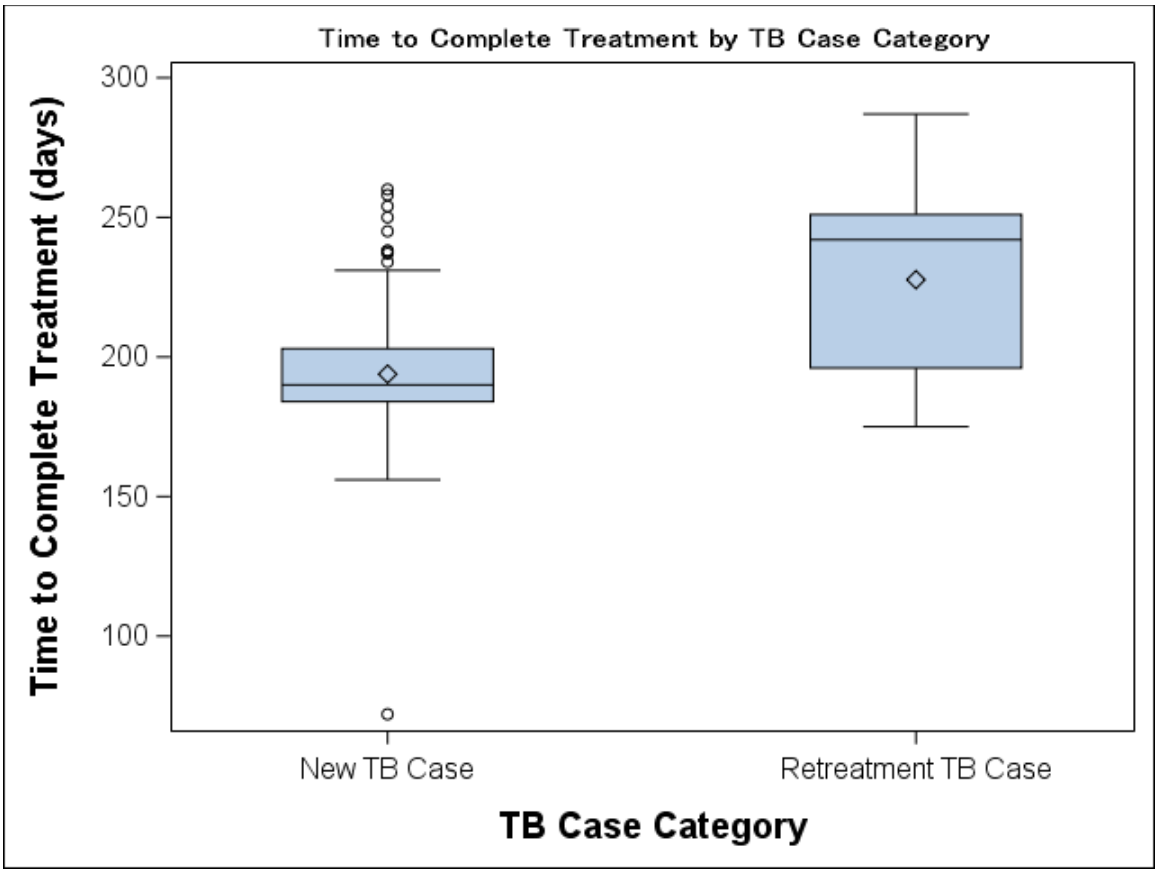


Figure 5. Boxplots of Time to Complete Treatment of New Cases compared to Retreatment Cases among Men Incarcerated in Haiti's National Penitentiary and Diagnosed with Tuberculosis from January 2016 to December 2018



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