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I, Sarvath Ali, hereby submit this original work as part of the requirements for the degree of Master of Public Health in Epidemiology.

It is entitled:

A Retrospective Study to Investigate the Impact of Immigration on Tuberculosis Control Program by DOTS Strategy in Gazan Province, Saudi Arabia

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A Retrospective Study to Investigate the Impact of Immigration on
Tuberculosis Control Program by DOTS Strategy in Gazan province,
Saudi Arabia.

A thesis submitted to the
Graduate School of the University of Cincinnati
in fulfillment of the requirement for the Degree of
Master in Public Health (MPH)

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Abstract

Background: Tuberculosis (TB) is an infectious disease, which is a major global public health concern due to the change in its epidemiological pattern and mode of transmission. Even though tuberculosis is a curable and preventable disease, it is second only to HIV/AIDS as the greatest killer worldwide due to a single infectious agent. Universal migration is one of the risk factors in spreading of the TB infection. Its containment is a challenge for countries of low TB incidence. In low incidence countries, migrants face higher risk of exposure to TB infection due to overcrowded living and working conditions; increased vulnerability to HIV; malnutrition and substance abuse, induced by marginalization and social exclusion. Undocumented migrant patients have difficulty getting healthcare access, have poor health-seeking behavior due to lack of education and health literacy. Stigma and cultural belief are other factors, and they are afraid of getting caught and of deportation. Migrant patients present various challenges in the control of tuberculosis with higher rates of default in treatment which results in drug resistance TB. The aforesaid problems lead to delay in TB diagnosis among migrants and thus leading to spread of disease. Presently, in USA and Western Europe a majority of cases of TB occur in foreign-born individuals, reflecting immigration from countries with high prevalence of TB. To attain effective TB control globally, an understanding of changing epidemiology by public health departments is needed. The use of directly observed therapy of short course (DOTS) is the

strategy recommended by World Health Organization (WHO) which is believed to lead success in reducing TB burden.

Objectives: a) Identify factors influencing the success of DOTS program for the TB treatment in Gazan, Saudi Arabia (SA). b) Assess the success rate of the DOTS program.

Methods: This project is primarily transcribed by a descriptive method. A retrospective review of all the registered cases of tuberculosis in one year 2014 (n=362) enrolled for treatment in the Gazan province is carried out. Logistic regression model is used to identify significant factors of success or non-success of DOTS program.

Results: No predictor is playing a significant role on treatment outcome. The cure rate for study population is 91.7% (after adjusting defaulters and deported patient). Cure rate was calculated based on exclusion of defaulters and deported cases. If we include the 29 defaulters and 68 deported, and assuming that treatment failed for those case, the cure rate would be 67% is far below the WHO goal which is 85%.

Conclusion: Overall success rate of the DOTS program is found to be 67% as per data we have collected for the year 2014. Since the treatment outcome of the defaulters and deported cases is unknown, which has a great impact on DOTS program. We strongly recommend to the Ministry of Health and the Immigration authorities to work together to see that tuberculosis treatment should be completed before deportation of patients who are on treatment under DOTS program.

Keywords: Epidemiology, tuberculosis, immigration, surveillance.

Committee:

Aimin Chen, MD. Ph.D. (Committee Chair)

Marepalli Rao, Ph.D. (Committee Member)

Subjects: Public Health, Epidemiology, Infectious diseases.

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Dedication

I would like to dedicate my work to my parents and to my wife who encouraged me by convincing that a master's degree is achievable.

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Chapter 1

1.1 Background:

Tuberculosis (TB) is an infectious disease and is of an important public health and medical concern. Its epidemiological mode of transmission is also of concern. The bacteria *Mycobacterium tuberculosis* causes tuberculosis that most often affects the lungs but can also affect any organ. Pulmonary TB accounts 70% and extrapulmonary TB 30% of all the cases (Alwani AK, 2015). TB is spread from person to person through air when people with lung TB cough, sneeze, or spit. They propel the TB germs into air. Even though tuberculosis is curable and preventable, it is second only to HIV/AIDs as the greatest killer worldwide due to the single infectious agent (WHO Report 2014). TB is out of control in many parts of the world. The global burden of tuberculosis remains high. Especially so in Southeast Asia, sub-Saharan Africa, and Eastern Europe, because of high rates of *Mycobacterium tuberculosis* and HIV coinfection (Christopher Dye 1999).

In 2013, 9 million people contracted TB and 1.5 million died from the disease around the world, which translates into a global incidence of 128 per 100,000 (WHO 2015). TB occurs in every part of the world and affects all ages. Emergence of multi-drug resistant TB globally is also worrisome; it is estimated about 480,000 people developed multi-drug resistant TB (MDR-TB) in the world in 2013 (WHO 2015). In low-incidence countries, migrants face higher risk of exposure to TB infection due to: overcrowded living and working conditions; increased vulnerability to HIV; and malnutrition and

substance abuse which is induced by marginalization and social exclusion (IOM 2013). Migrants have difficulty in healthcare access and have poor health seeking behavior due to lack of education and health illiteracy, stigma, and cultural belief are other factors. They are afraid of getting caught, losing their jobs, and losing economic sustenance, and finally being deported. All the problems above lead to a delay in a TB diagnosis among migrants and thus spreading the disease among the local population.

TB is a social disease and migration, as a social determinant of health, increases TB-related morbidity and mortality among migrants and surrounding communities (IOM Director General William Lacy Swing, World TB Day 2014).

In 1997, World Health Organization (WHO) had started a new strategy, directly observed treatment short-course (DOTS) to stop spread of TB globally. The goal is to achieve a cure rate of at least 85% by strict implementation of DOTS in all countries' national TB control programs. Strict implementation means a good adherence to the treatment. Currently, more than 200 countries are implementing DOTS in their national TB control program including the USA. The unique features of the program are:

- 1) Permanent reporting system of TB notification to the Ministry of Health (MOH), and thereby to WHO, is mandatory for both physicians and laboratories. This reporting system was enacted when TB came under the direct surveillance of WHO.

2) Contact tracing is conducted through the strict monitoring system and follow-ups are reviewed by case holding until the treatment is complete or TB cured. The MOH policy is to treat all the tuberculosis patients for free. It is mandatory to admit all open cases of TB, i.e., smear positive, and treat patients, its initial intensive phase of first two months or at least patient clings to isolation until sputum conversion from Positive to Negative.

This project investigates the impact of immigration on the TB control program, in the Gazan, Saudi Arabia (SA), which is geographically close to Yemen. Yemen is among the 22 high prevalence TB countries. Many Yemenis enter Saudi Arabia, both legally and illegally, to seek employment and also to seek medical treatment, since primary care is free for all people in Saudi Arabia. However, all the legal immigrants are screened for TB and other infectious diseases at the time of entry, but there is no control over migrants who enter illegally. We need to learn the epidemiology of TB in immigrant population vis-à-vis the citizens.

1.2 Goals:

1. Assess how effective the DOTS program in the Gazan Province using data on Saudi nationals and legal immigrants.
2. Determine factors affecting cure rate using a method based approach.
3. Predict the outcome of the DOTS program for illegal immigrants if they had not been deported.
4. Use the study for policy prescriptions.

1.3 Methods:

Study design:

The data is a retrospective review of all registered cases of tuberculosis in one year (2014) treated in Gazan.

1. We use simple descriptive statistics to assess how effective the DOTS program is using data on Saudi nationals and legal immigrants.
2. We fit a logistic regression model to the data. The response variable is “Outcome” with two levels: Cured and Failure. We assess how good the fit is.
3. We examine the significance of each predictor in the model; we focus especially on “BCG vaccination” and “Diabetes.”
4. We use the fitted logistic regression model for predicting “outcome” of illegal immigrants, who are deported.
5. We assess how effective the DOTS program in the region of study.
6. Multiple imputations: There are 29 defaulters and 68 deported cases, we do not know what will be the out outcome for all these cases. We use a multiple imputation technic to fill in missing values in the outcome variable. We use R package “Mice” to carry out multiple imputations (Van Buuren, S 2000). The acronym MICE stands for multivariate imputation by chained equation. The core idea in the MICE program is, it builds regression model regressing the outcome variable on the rest of variables using all non-missing data. This model is used to fill in the missing values of the outcome variable (Van

Buuren, S 2000). In our analysis we obtain five completed data sets and we analyzed each completed data set.

1.4 Hypothesis:

1. The cure rate of TB in the DOTS program is higher for Saudis than that of legal immigrants.
2. Immigration status (Saudi or non-Saudi) how will it affects implementation of DOTS program.
3. Bacillus Calmette-Guerin (BCG) Vaccination has a significant impact on the success of the DOTS program.
4. Diabetes Mellitus has a significant impact on the success of the DOTS program.

Chapter 2

Gazan-Saudi Arabia profile:

The Kingdom of Saudi Arabia is in the Arab peninsula. It has a total population of 28.7 million, of which 20 million are Saudi nationals and over eight million are foreigners. Saudi Arabia is a rich oil producing country with the world's 25% of oil reserves. The two big cities, Mecca and Medina, which receive approximately four to five million pilgrims year round from all over the world. (The Royal Embassy of Saudi Arabia, Washington, and D.C, USA, 2012). The majority of travelers to Mecca and Medina are adults mostly from high prevalent TB countries having health issues. Due to overcrowding during two seasons, Hajj and Umra, the two religious rituals enhance transmission of

airborne infections including TB (Memish 2003). The most common cause of pneumonia in hospitalized pilgrims during the Hajj is pulmonary TB; one source of TB spreading in the host country is overcrowding (Wilder-Smith, 2005). In the last two decades many developmental activities, like expansion of residential area and mosque, require foreign labor, especially in the construction sector which adds to the problem of TB importation.

Gazan is a southern province in Saudi Arabia. It stretches some 300 km along the southern Red Sea coast, just north of Yemen. The ex-King of Saudi Arabia, Abdallah declared Gazan as an economic city where many developmental projects are slated. It covers an area of 11,671 km² and has a population of 1,365,110 at the 2010 census. Gazan receives more of Yemeni labor force, both legal and illegal.

Saudi Arabia is an active donor and partner of WHO, and is committed to stop TB. Healthcare, primary, secondary and tertiary services are all free of cost to all the Saudi Nationals. But primary care and emergency services are provided free to all Non Saudi, and for the visitors like pilgrims.

Figure 1

Source; "About Saudi Arabia: Facts and figures". The Royal Embassy of Saudi Arabia, Washington, D.C., USA.

Chapter 3

Fig 2. Patient taking daily dose of medications in front of health care worker.

3.1 Definition of DOTS: What is DOTS?

Direct **O**bservation Treatment Short course of tuberculosis.

History and background of Dots;

The major constraint in eradicating TB is due to irregular or insufficient treatment with multiple drug regimens other than standard first line of drugs which are sensitive to TB bacteria. People with tuberculosis require treatment for at least six to eight months with multiple drugs to attain complete cure and to avoid drug resistance. It is difficult with many patients to stick to the treatment to complete their prescribed course of medications. This irregular and non-adherence to treatment results in prolonged infectiousness, relapse of TB, development of drug resistance or even death. When resistance to TB drugs developed it is difficult to treat and it is very expensive with a second

line of drugs. The price may be as high as a thousand times more as the cost of drug sensitive infection (Walsh, 2005). Hence the WHO developed a new strategy DOTS regimen which is patient centered, community based, and cost effective. DOTS is simple to implement, improves patient's compliance, and prevents transmission of the disease and MDR-TB (Jamison, 2006). Prior to implementation of DOTS, cure rate being between 31% and 37%, TB was out of control in many parts of the world, (Alwani AK, 2015). Treatment regimens were not consistent from physician to physician and from center to center (Maher 1997).

A study was done in Ethiopia to assess the knowledge of private practitioners (PPs) with regard to tuberculosis (TB) control and their practice of TB diagnosis, treatment and monitoring. A descriptive survey was conducted among PPs. A total of 120 responded to a self-administered questionnaire. At least two to five TB cases were diagnosed in their clinic per week. The results were, according to 81.5% of the PPs, the correct anti-tuberculosis treatment regimens recommended by the National Tuberculosis Program (NTP) were mentioned by only 9.7% of the doctors, while 63% listed 68 regimens. The majority (41.0%) monitored treatment using chest X-ray (CXR) alone, while 21.0% used CXR in combination with another diagnostic tool. To summarize above study, 80% of the PPs did not keep a TB register, and case holding was non-existent. The conclusion of this study was, PPs in Ethiopia diagnose a high number of TB cases. However, there is a huge lack of information on anti-tuberculosis treatment. This shows the likely irrational

use of the few available anti-tuberculosis drugs, which may lead to the emergence and spread of drug resistance (Sagbakken, 2008). Several other studies show that private providers likely to prescribe antibiotics irrationally, do not monitor the effects of treatment, maintain clinical records, case holding or notify diseases to the public health system, which contribute to a surge in MDR TB (WHO, 2000; Kamath et al., 2001; Mills et al., 2002).

There was no single guideline for using a standard regimen. Usually Patients feel better after three to four weeks of treatment with anti TB drugs, which may make them stop the treatment abruptly. In reality, complete eradication of TB bacteria takes at least six months with multi drug regimen. There were no TB registers and case holding for follow up by the physicians. The chances of registering the same patient at multiple places were happening, when the same patient happened to be seen by another physician or at another treatment center. Duplication of registration misleads the incidence rate and hence increases the prevalence rate.

The DOTS means that a trained health care worker or other designated individual provides the prescribed TB drugs and watches the patient swallow every dose. The DOTS strategy for TB control comprises of five elements: political commitment; diagnosis by direct smear microscopy; a mechanism to secure drug supplies; standardized recording and reporting; and use of standardized short-course chemotherapy with direct observation of treatment. When a TB case is suspected with a patient having cough with fever and malaise for more than three weeks and not responding to antibiotics, it is

mandatory to test smear i.e., sputum for acid fast bacilli (AFB). TB diagnosis is confirmed by smear positive at least two out of three sputum samples. As soon as the case is confirmed registration is done first and foremost, a unique number will be allotted, and TB card is issued for every patient (see figure 3 and 4). Physician-in-charge will decide the category of the disease and the standard first line of 4 drug anti TB regimen HRZE (Isoniazid (H), Rifampicin (R), Pyrazinamide (Z) and Ethambutol (E) or Streptomycin (S)). First two months is followed of treatment includes intensive phase with HRZE and next four months of continuation phase with HR only. For relapse cases Streptomycin is added for re-treatment after testing for sensitivity of drugs. If there is resistance for any two drugs especially of Isoniazid and Rifampicin, then the second line of drugs should be started. Treatment progress is monitored by repeating smear examination every two months to determine whether cured, failure or relapse (Dye, C, 1998).

In the DOTS program, the WHO recommends smear microscopy as the most rapid and inexpensive method for the diagnosis of TB and for the detection of AFB. In Saudi Arabia, all the primary care health care centers are equipped with microscopes and trained technicians. However, difficult cases and undiagnosed cases are referred to higher treatment centers where all modern lab facilities are available to assist diagnosis of TB. As soon as a TB case is confirmed it is registered and notification process starts. There are 12 forms to be filled out and sent to the district headquarters and from there to the National TB Program control center (NTP). NTP will then send

quarterly reports to the WHO. At the same time the patient, his or her family members and other close contacts receive health education. Contact tracing is very important. Immediate contacts are those who live in the same household, classroom or working place. If a contact is found to have symptoms of TB, their sputum should be tested for AFB. If it is positive, treatment should be started immediately. If smear is negative, do sputum culture and chest X-ray. If still negative follow up them periodically. If symptoms appear any time later, ask them to see a doctor immediately. One of the important tasks of the DOTS team workers is to find the defaulters and put them back on treatment (see figure 2) (Sia, I. G., & Wieland, M. L. 2011, April).

Figure2:

The objectives of this program are; a) achieve universal access to high-quality care for all people with TB; b) address the most vulnerable and hard-to-reach groups; c) reduce the human suffering and socioeconomic burden associated with TB; d) address special needs of migrants and cross-border issues; e) undertake screening for active TB and latent TB infection (LTBI) in TB contacts and selected high-risk groups, and provide appropriate treatment; f) optimize the prevention and take care of drug-resistant TB; g) ensure continued surveillance, program monitoring and evaluation and case-based data management; h) invest in research and new tools; i) support global TB prevention, care and control; and j) protect and promote human rights in TB prevention, care and control. The overall approach needs to be multi sectoral, focusing on equitable access to high-quality diagnosis and care, and on addressing the social determinants of TB. Since the globalization and mobilization of population have been increasing, the response needs to have both national and global dimensions (Maher, D., 1997).

The WHO in the year 1997 has set the following target; 1) to reach a cure rate of 85% by the year 2015, and to halt and begin to reduce the incidence of TB by 2015; 2) to reduce the prevalence and deaths due to TB by 50% by 2015 compared with a baseline of 1990; 3) to eliminate TB as a public health problem by 2050. The eventual goal of DOTS is treatment completion of tuberculosis patients, and in order to achieve that goal, a

partnership among clinical, public health, and social services is crucial (WHO 2009).

3.2 Summary of why use DOTS:

- We cannot predict who will and will not take medications as directed. People from all social classes, educational background, ages, genders, and ethnicities can have problems taking the medications correctly as prescribed by the doctors.
- Studies show that 86-90% of patients receiving DOTS, complete therapy, compared to 61% for those on self-administered therapy.
- DOTS helps patients finish TB therapy as quickly as possible, without unnecessary gaps.
- DOTS helps prevent TB from spreading to others.
- DOTS decreases the risk of drug-resistance resulting from erratic or incomplete treatment.
- DOTS decreases the chances of treatment failure and relapse (WHO 2009).

3.3 Disease classification and definitions for terms used in the DOTS:

Latent Tuberculosis infection (LTBI);

A person has tuberculosis infection without any signs and symptoms of disease. TB bacteria remains in the body as dormant inactive state without expressing tuberculosis disease.

Smear Positive patient; a patient with at least 2 sputum specimens positive for AFB by microscopy or a patient with one sputum specimen positive for

AFB and radiographic abnormalities determined by a medical officer to be consistent with active pulmonary TB.

Smear Negative patient; a patient with radiographic abnormalities determined by a medical officer to be consistent with active pulmonary TB, sputum exam was negative at least 3 times, and the physician decides to treat with anti TB drugs.

Pulmonary TB; a patient with at least 2 sputum specimens positive for AFB by microscopy or a patient with one sputum specimen positive for AFB and radiographic abnormalities determined by a medical officer to be consistent with active pulmonary TB.

Extra pulmonary TB; a patient with one mycobacterial culture positive specimen from an extra pulmonary site. OR a patient with histological or clinical evidence consistent with active tuberculosis.

New Case; a patient who has been diagnosed with TB for the first time in his life, by history he was never considered having active TB in the past.

Cured; a patient received full course of anti TB drugs and his smear becomes negative after two months of the initial phase and remains negative at the 4th month and 6th month intervals, considered as cured.

Failure; a patient received the full course of anti TB drugs and his smear remains positive after two months of initial phase and remains positive at the end of the 4th month and 6th month is then considered as Failure.

Relapse; a patient who had been diagnosed and received complete course of treatment and has been considered cured from TB, but now is smear positive.

Defaulter; a patient on treatment who did not show up for more than three days.

Multiple drug resistance TB (MDR-TB); a patient is resistant to first line of drugs at least to two drugs Rifampicin and Isoniazid.

Extensive drug resistance TB (XDR-TB); extensively drug-resistant TB is a rare type of **MDR-TB**, that is resistant to isoniazid and rifampin, plus any fluoroquinolone and at least one of three injectable second-line drugs (i.e., amikacin, kanamycin, or capreomycin) (Francis J. 2003).

Category I:

Initial Intensive Phase 2 months with HRZE(S) and Continuation Phase 4 Months HR

1. Pulmonary TB whose Sputum is positive
2. Seriously ill patients with severe forms of smear negative PTB with extensive parenchymal involvement or

Extra Pulmonary TB like meningitis, TB pericarditis, peritonitis, spinal disease with neurological complications, intestinal TB and genito-urinary TB.

Category II:

Initial Intensive Phase 3 months with HRZE+ Continuation Phase 4 Months HR

Supplemented by streptomycin for the first 2 months and continuation phase of 5 months HR.

This regimen is to be prescribed to previously treated patients who are:
Relapse or Failure.

Category III:

This regimen is to be prescribed to;

1. PTB patients whose smear negative for three times, and
2. Extra Pulmonary TB patients
3. Initial Intensive Phase 2 months with HRZ
4. Continuation Phase 4 Months HR.

The Following is the TB Card assigned to patients:

Figure 3

Kingdome of Saudi Arabia
Ministry of Health
National program for tuberculosis control
Form No: 3

Tuberculosis treatment card

Directorate of health affairs in: Name of the treating health unit: T.B registration No:

Patient's full name : Tel:

Address (in full): Tel:

Name and address of contact person: Tel:

Sex: Male ☐ Female ☐ Age: Nationality:

Disease classification

Pulmonary ☐ extra pulmonary ☐

Site:

Type of patient

New ☐ Relapse ☐

Transfer in ☐ Failure ☐

Treatment after default ☐ Other (specify) ☐

1-INITIAL INTENSIVE PHASE – Prescribed regimen and dosage :
Tick appropriate regimen box, and indicate daily dosage:

CAT-1 ☐ ☐ ☐ ☐ ☐ H R Z S (E)

CAT-2 ☐ ☐ ☐ ☐ ☐ H R Z E S

CAT-3 ☐ ☐ ☐ ☐ H R Z

H: Iso niazed
R: Rifampicin
Z: Pyrazinamide
E: Ethambutol
S: Streptomycin

Month	Result of sputum examination						Weight (Kg)
	Local lab			Reference lab			
	Date	Smear	Lab No	Smear	Cult.	Sensitivity Sens. Res.	
0							
2							
4							
6							

Tick appropriate box after the drugs have been administered:

Month	Day																																
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	3	

Please turn over for continuation phase

Table 1. The six components of the Stop TB Strategy (WHO 2007).

	<ol style="list-style-type: none"> 1. Pursuing high-quality DOTS expansion and enhancement. Making high-quality services widely available and accessible to all those who need them, including the poorest and most vulnerable, requires DOTS expansion to even the remotest areas. In 2004, 183 countries (including all 22 of the high-burden countries which account for 80% of the world's TB cases) were implementing DOTS in at least part of the country. 2. Addressing TB/HIV, MDR-TB and other challenges. Addressing TB/HIV, MDR-TB and other challenges requires much greater action and input than DOTS implementation and is essential to achieving the targets set for 2015, including the United Nations Millennium Development Goal relating to TB (Goal 6; Target 8). 3. Contributing to health system strengthening. National TB control programs must contribute to overall strategies to advance financing, planning, management, information and supply systems and innovative service delivery scale-up. 4. Engaging all care providers. TB patients seek care from a wide array of public, private, corporate and voluntary health-care providers. To be able to reach all patients and ensure that they receive high-quality care, all types of health-care providers are to be engaged. 5. Empowering people with TB, and communities. Community TB care projects have shown how people and communities can undertake some essential TB control tasks. These networks can mobilize civil societies and also ensure political support and long-term sustainability for TB control programs. 6. Enabling and promoting research. While current tools can control TB, improved practices and elimination will depend on new diagnostics, drugs and vaccines.
--	--

Source; WHO 2007

3.4 Natural History of Tuberculosis and Diagnosis:

Time line:

1865: Understanding of the pathogenesis of tuberculosis began with the work of Théophile Laennec.

1865: The demonstration of the transmissibility of *Mycobacterium tuberculosis* infection by Jean-Antoine Villemin.

1882: the identification of the tubercle bacillus as the etiologic agent by Robert Koch

1891: Tuberculosis Koch's tests Fail. Robert Koch

1904: Attenuation of Bacterium by Albert Calmette and Jean Marie Camille Guerin (Attenuation definition is to weaken the bacteria)

1907: Clemens von Pirquet developed the tuberculin skin test

1910: Clemens von Pirquet demonstrate latent tuberculous infection in asymptomatic children.

1921: Albert Calmette and Camille Guerin began their first test of their attenuated tuberculosis bacilli BCG (Bacillus Calmette-Guerin) in human.

1945: Streptomycin was discovered, which marked a big step forward in the treatment of tuberculosis.

1952: Isoniazid (INH) was invented.

1970: Rifampicin was invented, which began the era of short course therapy. The duration of treatment for tuberculosis could be shortened from more than two years to a period of six months.

Many studies have been recognized that clinical disease may follow soon after initial infection with Mycobacterium TB known as primary disease or many years thereafter known as post-primary disease, may be either through endogenous reactivation or after exogenous reinfection, but often it is disputed (Vynnycky, E. 1997).

It is not necessary that everyone infected with TB bacteria becomes sick. TB-related two conditions exist: latent TB infection and TB disease. In LTBI results are positive on either a tuberculin skin test or an interferon- γ release assay, where tuberculosis bacteria stays in a dormant condition, that is bacteria are alive but not active.

Clinical manifestations may vary accordingly, signs and symptoms of active TB include: (CDC 2000)

- Coughing that lasts three or more weeks.
- Coughing up blood
- Chest pain, or pain with breathing or coughing.
- Unintentional weight loss.
- Fatigue.
- Fever.
- Night sweats.
- Chills.
- Loss of appetite.

3.5 The risk factors for developing tuberculosis: (CDC 2002).

Number of factors are known to increase the risk of developing TB.

1. Immune system dysfunction;

Diseases and medications that disrupt the immune system include HIV/AIDS, diabetes, certain cancers, end-stage renal disease, cancer drugs and medications that prevent transplant rejection.

2. Travel to endemic areas.

There are 22 countries are declared high prevalence TB by WHO.

3. Poverty, Low socio-economic communities.
4. substance abuse and work location
5. Alcohol and tobacco smoking
6. Healthcare workers have regular contact with people who are sick and, therefore, have a higher risk for contracting tuberculosis.
7. Nursing Homes & Old age residential health facilities.
8. Refugee Camps.
9. Prisons and detention centers.
10. Crowded Housing.

Elizabeth. L., et al., in their study after extensively reviewing data which were gathered from notifications of TB cases, cohort treatment outcomes, surveys of *Mycobacterium tuberculosis* infection, and HIV prevalence in patients with TB and other subgroups, from relevant sources like WHO, the Joint United Nations Program on HIV/Acquired Immunodeficiency Syndrome (UNAIDS), the US Census Bureau, and the US Centers for Disease Control and Prevention, revealed HIV infection is a potent risk factor for TB and also increases the risk of reactivating latent *Mycobacterium tuberculosis* (MTB) infection. Further they conclude that Tuberculosis is one of the most common causes of morbidity and the most common cause of death in HIV-positive adults living in less-developed countries (Elizabeth 2003).

The risk of active tuberculosis is substantially elevated in people who drink more than 40 g alcohol per day, and/or have an alcohol use disorder. This

may be due to both increased risk of infection related to specific social mixing patterns associated with alcohol use, as well as influence of alcohol on the immune system itself and of alcohol related conditions (Lönnroth, K., 2008).

Lin H-H, et al., in their paper revealed there is consistent evidence that tobacco smoking is associated with an increased risk of TB (Lin H-H, 2007). Several studies have suggested that diabetes mellitus increases the risk of active tuberculosis. The mounting prevalence of DM in TB-endemic areas may critically affect TB control. According to Jeon 2008, DM was associated with an increased risk of TB regardless of study design and population. People with DM may be important targets for interventions such as active case finding and treatment of latent TB and efforts to diagnose, detect, and treat DM may have a beneficial impact on TB control (Jeon CY, 2008)

3.6 Conceptual and theoretical framework:

Universally, immigrants such as migrant workers are an accelerating population of mounting social, demographic, and political concern. Specifically these demographic shifts may lead to worst consequences affecting health. In relation to health determinants, disparities often exist between a migrant population's place of origin and its destination. Globally the epidemiology of certain infectious and non-infectious diseases has an impact on the disparities related to migration. The increasing number of diverse group of migrants is bridging existing and developing gaps in health outcome indicators. If global health disparities and prevalence differentials continue to exist, national health programs and policies in migrant receiving nations will continue to be

challenged by illness and disease rising beyond their control. The health challenges related to migration may be more effectively addressed through cooperative global activities (Diderichsen, F. 2001).

We can apply theories of international migration and correlate the nature of problems discussed in this thesis. Saudi Arabia is a developing country which is economically rich and has a low incidence of TB like many other western European countries. There is always a demand for laborers and skilled workers. Because of the wage differences people will migrate to a rich country in search of jobs which pays more wages than the country of origin. The Neoclassical economic theory of international migration theories, helps explains this occurrence of differences in wages between poor countries and rich developing countries (MacPherson, D. W., 2006).

The social cognitive theory, a model described by Bandura (1997), examines numerous factors in the unorganized and unsecured life style of immigrant workers. Immigrants do not perceive the risk of becoming sick, hence the negative impact of the disease was not a factor for motivation to seek medical advice or adherence to treatment. The principal strength of the social cognitive theory have been postulated, that human thoughts and feelings developed in reaction to environmental factors, however at the same time influenced the environment (Bandura 1997).

The Health Belief Model (HBM) by Hoch Baum, Rosen Stock and Kegels can be applied to a broad range of health behaviors and subject populations. HBM encompasses five theories representing the perceived threat

and net benefits: perceived susceptibility, perceived severity, perceived benefits, perceived barriers and self-efficacy. HBM is a psychological model that tries to explain and predict health behaviors. For example sick role behaviors, which reference to compliance with recommended medical regimens, usually following professional diagnosis of illness; as well as the use of Health care services, which includes doctor visits for a variety of reasons (Becker, M. H 1988).

Chapter 4

4.1 Statistical Analysis:

Data source: Directorate of Health Services. Gazan, Saudi Arabia.

4.2 Data summary:

Study sample size; n=362

Nationality	Male	Female	total
Saudi	(104) 61%	(65) 39%	169
Non Saudi (immigrants)	(162) 84%	(31) 16%	193
Total	(266) 73%	(96) 27%	362

Immigrants	Male	Female	total
Legal immigrants (residence permit)	(27) 57%	(20) 43%	47
Non legal immigrants (no residence permit)	(135)92.2%	(11).8%	146
Total	162	31	193

Outcome	Cured	Failure	Deported	Defaulters	Total
	(243)67%	(22)6%	68	29	362

Smear	Positive	Negative	NA
	(176)49%	(185)51%	1

BCG	Received	Not Received
	(172)48%	(190)52%

Diabetes	Yes	No
	(48)13%	(314)87%

Figure: 4

Figure: 5

Figure: 6

Figure; 7

4.3 Results: Summary;

Age	Nationality	BCG	Symptoms
Min. : 0.17	NS: 193	Min. : 0.0000	Min. : 2.00 1st Qu.:23.00
1st Qu.:1.000	S: 169	1st Qu.: 0.0000	1st Qu.: 6.00
Median: 28.00		Median: 0.0000	Median: 8.00
Mean : 32.13		Mean : 0.4751	Mean: 11.43
3rd Qu.:37.00		3rd Qu.:1.0000	3rd Qu.: 12.00
Max. : 86.00		Max. : 1.0000	Max. : 104.00
Smear	Diabetes	HIV	Outcome
Neg: 185	Min. : 0.0000	Neg: 362	Cured: 243
POS: 176	1st Qu.:0.0000		Failure: 22
NA's: 1	Median: 0.0000		NA's : 97
	Mean :0.1326		
	3rd Qu.:0.0000		
	Max. :1.0000		

Nationality	Male	Female	total
Saudi	(104) 61%	(65) 39%	169
Non Saudi (immigrants)	(162) 84%	(31) 16%	193
Total	(266) 73%	(96) 27%	362

1. Response Variable is outcome.
2. There are many predictors.
3. Association between the response variable and each predictor is examined.
4. No predictor is significant.

Tables;

a. Symptoms vs outcome

	Disease	Non disease	Total
Exposed	17	4	21
Non exposed	226	18	244
Total	243	22	265
OR =0.34, 95% CI (0.1- 1.11), p =0.34 RR = 0.87			

b. Sex vs outcome

	Disease	Non disease	Total
Exposed	166	18	184
Non exposed	77	4	81
Total	243	22	265
OR =0.48, 95% CI (0.16- 1.46), p =0.19 RR= 0.94			

c. Nationality vs outcome

	Disease	Non disease	Total
Exposed	104	6	110
Non exposed	139	16	155
Total	243	22	265

OR =2.0, 95% CI (0.75- 5.27), p =0.16 RR =1.05

d. BCG vs outcome

	Disease	Non disease	Total
Exposed	117	11	128
Non exposed	126	11	137
Total	243	22	265

OR =0.93, 95% CI (0.39-2.22), p =0.87 RR = 0.99

e. Smear vs outcome

	Disease	Non disease	Total
Exposed	121	11	132
Non exposed	122	11	133
Total	243	22	265

OR =0.99, 95% CI (0.41-2.37), p =0.99 RR = 0.99

f. Diabetes vs outcome

	Disease	Non disease	Total
Exposed	201	21	222
Non exposed	42	1	43
Total	243	22	265

OR =0.23, 95% CI (0.03-1.74), p =0.12 RR = 0.88

Fisher exact test OR =0.23, 95% CI (0.01-1.5), p =0.22

g. Logistic regression

Coefficients:

	Estimate	Std. Error	z value	Pr (> z)
(Intercept)	-2.55549	1.00404	-2.545	0.0109 *
Age	0.01859	0.01518	1.225	0.2207
Sex	-0.90952	0.59406	-1.531	0.1258
Nationality	0.90615	0.53777	1.685	0.0920
BCG	0.13162	0.54081	0.243	0.8077
Symptoms	0.01797	0.01598	1.125	0.2606
Smear POS	-0.13980	0.47073	-0.297	0.7665
Diabetes	-1.72518	1.05133	-1.641	0.1008

5. A logistic Regression Model is fitted. No predictor is significant.
6. Model selection procedure is implemented, 3 predictors are chosen, but none is significant.
7. Conclusion: No predictor is playing a significant role on outcome.

The cure rate for study population is 67% (n=362). However, the cure rate was calculated based on the total number of cases including the 68 deported cases who didn't complete the required treatment regimen for the whole 6 months period, and 29 cases lost to follow up (defaulters). The cure rate without the deported cases would be 86%, and the cure rate without deported cases and defaulters is as high as 91.7%, that would have met the WHO goals (see multiple imputation analysis below).

8. Multiple imputation results:

Imputation # 1:

```
> summary (Imp1)
```

Age	Sex	Nationality	BCG	Symptoms
Min. : 0.17	Min. :1.000	NS:193	Min. :0.0000	Min. : 2.00
1st Qu.:23.00	1st Qu.:1.000	S :169	1st Qu.:0.0000	1st Qu.: 6.00
Median :28.00	Median :1.000		Median :0.0000	Median : 8.00
Mean :32.13	Mean :1.265		Mean :0.4751	Mean :11.43
3rd Qu.:37.00	3rd Qu.:2.000		3rd Qu.:1.0000	3rd Qu.:12.00
Max. :86.00	Max. :2.000		Max. :1.0000	Max. :104.00

Smear	Diabetes	Outcome
Neg:186	Min. :0.0000	Cured :329
POS:176	1st Qu.:0.0000	Failure: 33
	Median :0.0000	
	Mean :0.1326	
	3rd Qu.:0.0000	
	Max. :1.0000	

```
> CureRate <- (329/362)*100
```

```
> CureRate
```

```
[1] 90.88398
```

```
> Imp1Reg <- glm (Outcome ~, family = binomial, data = Imp1)
```

```
> summary (Imp1Reg)
```

Call:

```
glm (formula = Outcome ~ ., family = binomial, data = Impl)
```

Deviance Residuals:

Min	1Q	Median	3Q	Max
-0.8316	-0.4953	-0.3960	-0.3042	2.6489

Coefficients:

	Estimate	Std. Error	z value	Pr(> z)
(Intercept)	-2.93556	0.81700	-3.593	0.000327 ***
Age	0.01921	0.01332	1.442	0.149204
Sex	-0.45832	0.46869	-0.978	0.328143
Nationality2	0.34070	0.40386	0.844	0.398883
BCG	0.69288	0.43681	1.586	0.112690
Symptoms	0.01282	0.01609	0.797	0.425380
Smear2	0.04545	0.37951	0.120	0.904678
Diabetes	-1.83264	1.03786	-1.766	0.077432

Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

(Dispersion parameter for binomial family taken to be 1)

Null deviance: 220.97 on 361 degrees of freedom

Residual deviance: 210.48 on 354 degrees of freedom

AIC: 226.48

Number of Fisher Scoring iterations: 6

Imputation # 2:

```
> summary (Imp2)
```

Age	Sex	Nationality	BCG	Symptoms
Min. : 0.17	Min. : 1.000	NS:193	Min. : 0.0000	Min. : 2.00
1st Qu.: 23.00	1st Qu.: 1.000	S :169	1st Qu.: 0.0000	1st Qu.: 6.00
Median : 28.00	Median : 1.000		Median : 0.0000	Median : 8.00
Mean : 32.13	Mean : 1.265		Mean : 0.4751	Mean : 11.43
3rd Qu.: 37.00	3rd Qu.: 2.000		3rd Qu.: 1.0000	3rd Qu.: 12.00
Max. : 86.00	Max. : 2.000		Max. : 1.0000	Max. : 104.00

Smear	Diabetes	Outcome
Neg:186	Min. : 0.0000	Cured :329
POS:176	1st Qu.: 0.0000	Failure: 33
	Median : 0.0000	
	Mean : 0.1326	
	3rd Qu.: 0.0000	
	Max. : 1.0000	

```
> CureRate <- (329/362)*100
```

```
> CureRate
```

```
[1] 90.88398
```

```
> Imp2Reg <- glm(Outcome ~ ., family = binomial, data = Imp2)
```

```
> summary (Imp2Reg)
```

```
Call:
```

```
Glm (formula = Outcome ~ ., family = binomial, data = Imp2)
```

Deviance Residuals:

Min	1Q	Median	3Q	Max
-0.8562	-0.4625	-0.4039	-0.3222	2.8075

Coefficients:

	Estimate	Std. Error	z value	Pr(> z)
(Intercept)	-2.64572	0.78432	-3.373	0.000743 ***
Age	0.01905	0.01300	1.465	0.142858
Sex	-0.38180	0.46911	-0.814	0.415709
Nationality2	0.49314	0.41792	1.180	0.237997
BCG	-0.18411	0.44327	-0.415	0.677893
Symptoms	0.01076	0.01541	0.698	0.485022
Smear2	0.03468	0.38070	0.091	0.927422
Diabetes	-1.88425	1.04133	-1.809	0.070378 .

Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

(Dispersion parameter for binomial family taken to be 1)

Null deviance: 220.97 on 361 degrees of freedom

Residual deviance: 209.77 on 354 degrees of freedom

AIC: 225.77

Number of Fisher Scoring iterations: 6

Imputation # 3:

> summary (Imp3)

Age	Sex	Nationality	BCG	Symptoms
Min. : 0.17	Min. : 1.000	NS:193	Min. : 0.0000	Min. : 2.00

```

1st Qu.:23.00 1st Qu.:1.000 S :169 1st Qu.:0.0000 1st Qu.: 6.00
Median :28.00 Median :1.000 Median :0.0000 Median : 8.00
Mean :32.13 Mean :1.265 Mean :0.4751 Mean :11.43
3rd Qu.:37.00 3rd Qu.:2.000 3rd Qu.:1.0000 3rd Qu.:12.00
Max. :86.00 Max. :2.000 Max. :1.0000 Max. :104.00

```

```

Smear      Diabetes      Outcome
Neg:185 Min. :0.0000 Cured :334
POS:177 1st Qu.:0.0000 Failure:28

```

```
Median :0.0000
```

```
Mean :0.1326
```

```
3rd Qu.:0.0000
```

```
Max. :1.0000
```

```
> CureRate <- (334/362)*100
```

```
> CureRate
```

```
[1] 92.26519
```

Imputation # 4:

```
> summary(Imp4)
```

```

Age      Sex      Nationality  BCG      Symptoms
Min. : 0.17 Min. :1.000 NS:193  Min. :0.0000 Min. : 2.00
1st Qu.:23.00 1st Qu.:1.000 S :169  1st Qu.:0.0000 1st Qu.: 6.00
Median :28.00 Median :1.000 Median :0.0000 Median : 8.00
Mean :32.13 Mean :1.265 Mean :0.4751 Mean :11.43
3rd Qu.:37.00 3rd Qu.:2.000 3rd Qu.:1.0000 3rd Qu.:12.00

```

Max. :86.00 Max. :2.000 Max. :1.0000 Max. :104.00

Smear Diabetes Outcome

Neg:185 Min. :0.0000 Cured :333

POS:177 1st Qu.:0.0000 Failure: 29

Median :0.0000

Mean :0.1326

3rd Qu.:0.0000

Max. :1.0000

```
> CureRate <- (333/362)*100
```

```
> CureRate
```

```
[1] 91.98895
```

```
> Imp4Reg <- glm(Outcome ~ ., family = binomial, data = Imp4)
```

```
> summary(Imp4Reg)
```

Call:

```
glm (formula = Outcome ~ ., family = binomial, data = Imp4)
```

Deviance Residuals:

Min	1Q	Median	3Q	Max
-0.9671	-0.4356	-0.3676	-0.2752	2.7518

Coefficients:

	Estimate	Std. Error	z value	Pr(> z)
(Intercept)	-2.51392	0.86199	-2.916	0.00354 **
Age	0.01582	0.01410	1.122	0.26184
Sex	-0.73108	0.53025	-1.379	0.16798

Nationality2 0.71346 0.43782 1.630 0.10320

BCG 0.15672 0.46883 0.334 0.73817

Symptoms 0.01888 0.01493 1.265 0.20587

Smear2 -0.22043 0.40623 -0.543 0.58739

Diabetes -1.74854 1.04297 -1.677 0.09364.

Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

(Dispersion parameter for binomial family taken to be 1)

Null deviance: 202.02 on 361 degrees of freedom

Residual deviance: 190.77 on 354 degrees of freedom

AIC: 206.77

Number of Fisher Scoring iterations: 6

Imputation # 5:

> summary(Imp5)

Age	Sex	Nationality	BCG	Symptoms
Min. : 0.17	Min. : 1.000	NS:193	Min. : 0.0000	Min. : 2.00
1st Qu.: 23.00	1st Qu.: 1.000	S :169	1st Qu.: 0.0000	1st Qu.: 6.00
Median : 28.00	Median : 1.000		Median : 0.0000	Median : 8.00
Mean : 32.13	Mean : 1.265		Mean : 0.4751	Mean : 11.43
3rd Qu.: 37.00	3rd Qu.: 2.000		3rd Qu.: 1.0000	3rd Qu.: 12.00
Max. : 86.00	Max. : 2.000		Max. : 1.0000	Max. : 104.00

Smear	Diabetes	Outcome
Neg:185	Min. : 0.0000	Cured :327
POS:177	1st Qu.: 0.0000	Failure: 35

Median :0.0000

Mean :0.1326

3rd Qu.:0.0000

Max. :1.0000

```
> CureRate <- (327/362)*100
```

```
> CureRate
```

```
[1] 90.33149
```

Imputation 5:

```
> Imp5Reg <- glm(Outcome ~ ., family = binomial, data = Imp5)
```

```
> summary (Imp5Reg)
```

Call:

```
glm(formula = Outcome ~ ., family = binomial, data = Imp5)
```

Deviance Residuals:

Min	1Q	Median	3Q	Max
-0.9203	-0.4782	-0.4275	-0.3853	2.3651

Coefficients:

	Estimate	Std. Error	z value	Pr(> z)
(Intercept)	-2.66826	0.77435	-3.446	0.000569 ***
Age	0.01075	0.01330	0.809	0.418681
Sex	-0.27963	0.43994	-0.636	0.525037
Nationality2	0.22622	0.39797	0.568	0.569735
BCG	0.32874	0.41900	0.785	0.432700
Symptoms	0.01978	0.01368	1.446	0.148220

Smear2 -0.02116 0.36716 -0.058 0.954033

Diabetes -0.66294 0.64003 -1.036 0.300299

Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

(Dispersion parameter for binomial family taken to be 1)

Null deviance: 230.04 on 361 degrees of freedom

Residual deviance: 225.76 on 354 degrees of freedom

AIC: 241.76

Number of Fisher Scoring iterations: 5

For each imputed data set we calculated the cure rate as (# of cured/# total)*100. The cure rates are 1=90.88%, 2= 90.88%, 3=92.26%, 4=91.99, and 5=90.33.

We conducted logistic regression on each of completed data set, none of the prediction is significant in every one of the completed data set.

Our conclusions;

- 1) Demographically age sex and nationality did not play any significant role.
- 2) BCG vaccination did not have any impact on the treatment outcome.

The disease outcome in BCG vaccinated and non-vaccinated groups was 91.96%, 89.19 respectively. A chi square test was performed to examine the relationship between BCG vaccination and disease outcome. There was no significant relationship between these variables. X^2 (1, N=362) 0.41, $p=0.52$. 1= Degree of freedom, N= Sample size, 0.41 chi square value. P value = 0.52.

- 3) In our study population Diabetes mellitus did not have any significant impact on treatment outcome. We assume by using DOTS regime while patients on directly

observed for a period until the completion of TB treatment also facilitated the diabetics to keep their DM under control (this is one of our observations).

4) There was no significant impact on the outcome regardless of their duration of symptoms at the time of diagnosis of TB.

5) The box plot below outlines the age distribution of patients in our study. 75% of patients are in the age range of 22 to 38 years. There is one infant (see figure 8).

Figure: 8

6) Kernel density curves of age given below indicate that the age distributions are similar among cured and non-cured patients.

Figure:9

4.4 Trend Analysis;

Figure: 10

In the year 2014 the Incidence Rate of TB was 27.84/100,000. (Population of Jazan 1.3 Million).

Mortality Rate was 1.7/100,100.

In general population incidence rate has been increasing over a span of 8 years culminating in 2014. In the year 2014, the number of cases in Non Saudi's especially undocumented immigrants is higher than Saudi's.

There is no change in the incident cases of TB among the documented Non Saudi immigrants (see graphs below).

Trend from 2006 to 2014.

The total number of cases are increasing in the general population; this increase is due to an increase of the number of un-documented immigrants. There is no change in incidents of TB among documented immigrants. In the year 2014, the number of cases

in Non-Saudis, especially undocumented immigrants, was higher than the Saudi nationals.

Chapter 5

5.1 Discussion:

1. We want the authorities in the Ministry of Health and the teams of DOTS in the regional sectors to understand the barriers to access health care by immigrants; the risk of deportation of active cases; and the risk to the general local population. One active case can give a TB infection to at least 10 people (CDC website). We emphasize prioritizing screening for the vulnerable population.
2. The efficacy of BCG Vaccine can be determined from this study. As part of the policy of the MOH, it is mandatory to give BCG to all the newborns in SA. We study its impact on the DOTS program. In the literature, BCG efficacy is known to be from 0 to 70 % (Ponnighaus, J. M 1992). In this study, we discovered no difference in the outcome between the BCG vaccinated group and the unvaccinated group.
3. Multiple studies of tuberculosis treatment have indicated that patients with diabetes mellitus may experience poor outcomes (Baker, M. A., 2011). We want to explore the impact of diabetics associated with TB infection on the overall outcome of the DOTS program. In this study, we discovered no significant difference in the treatment outcomes between TB patients with or without DM.

Further research is warranted in the aforementioned subject more efficiently study the implementation of the DOTS to understand TB well to prevent and stop this disease.

5.2 Significance/Relevance to Public Health:

Since TB is a curable and preventable disease, if risk factors are identified properly and dealt with appropriately, the spread of tuberculosis can be stopped or at least good control can be achieved. The message for the public health workers is to optimize the DOTS program implementation and to reach out to the underprivileged population who are always at risk. Even though the USA has an effective control strategy of tuberculosis by implementing DOTS, still faces immigration as one of the challenges that need to be identified to achieve effective results. Immigrants reported high levels of stress due to fear of deportation, which affected the access to health care service; thereby, this affects their emotional well-being, which is a public health concern. (Esposito, F.2015). Removing the barriers to health care access and educating them about their rights, is the top priority for the vulnerable populations anywhere in the globe for their social and emotional well-being.

5.3 Limitations:

Our study sample is a convenient sample, since the majority of the patients are self-reported to the health care facilities. Patients visited by themselves or were brought by their family members or the patients' employers, to seek medical advice, except for a few cases of contact who were traced by DOTS health workers. This study is limited, because of the likelihood that many TB patients go unreported due to fear of deportation, stigma and other factors.

5.4 Conclusions:

The importation of tuberculosis as a result of immigration from high-incidence countries had a slight influence on the transmission of this pathogens in SA, the receiving low-incidence country. To prevent future increases of TB transmission in the receiving low-incidence countries, we recommend public health authorities and immigration authorities to work together in implementing the DOTS strategy, and not to discontinue the required treatment to the targeted population. Also, targeted patients' education is needed to address noncompliance in TB treatments and to help ensure adherence to the prescribed treatment regimen by the DOTS program. We assume there are more unreported cases, who might have been avoiding seeking medical advice; these patients must be traced by passive case finding to treat them successfully to help stop TB. We emphasize intensive screening to identify latent TB infection among immigrants, as well as the local population. Further research should be directed towards identifying the pathogen strains circulating in the local and migrant populations, in order to understand whether the strain is the same or different, before we blame migrants as the culprits in spreading TB.

5.5 References

- Alwani A. K, Abdelsadek H Al-Aarag, Magdy M Omar, Nabil A Abdelghaffar Hibah. Incidence of tuberculosis before and after DOTS implementation in El-Behira Governate, Egypt. *J Bronchol* 2015-9:101-8
- About Saudi Arabia: "Facts and figures". The royal embassy of Saudi Arabia, Washington, D.C., USA.
- Bandura, A. (1998). Health promotion from the perspective of social cognitive theory. *Psychology and Health*. 13, 623-649.
- Baker, M. A., Harries, A. D., Jeon, C. Y., Hart, J. E., Kapur, A., Lönnroth, K., ... Murray, M. B. (2011). The impact of diabetes on tuberculosis treatment outcomes: A systematic review. *BMC Medicine*, 9, 81. <http://doi.org/10.1186/1741-7015-9-81>
- Campbell, Jonathon R., Thenuga Sasitharan, and Fawziah Marra. "A Systematic Review of Studies Evaluating the Cost Utility of Screening High-Risk Populations for Latent Tuberculosis Infection." *Applied health economics and health policy* 13, no. 4 (2015): 325-340.
- Center for disease control. <http://www.cdc.gov/tb/topic/basics/>
- Christopher Dye, DPhil; Suzanne Scheele, MS; Paul Dolin, DPhil; Vikram Pathania, MBA; Mario C. Raviglione, MD; for the WHO Global Surveillance and Monitoring Project *JAMA*. 1999; 282(7):677-686. doi:10.1001/jama.282.7.677.
- Corbett, E. L., Watt, C. J., Walker, N., Maher, D., Williams, B. G., Raviglione, M. C., & Dye, C. (2003). The growing burden of tuberculosis: global trends

- and interactions with the HIV epidemic. *Archives of internal medicine*, 163(9), 1009-1021.
- Dye, C., Garnett, G. P., Sleiman, K., & Williams, B. G. (1998). Prospects for worldwide tuberculosis control under the WHO DOTS strategy. *The Lancet*, 352 (9144), 1886-1891.
- “DOT Essentials: A Training Curriculum for TB Control Programs”, Francis J. Curry National Tuberculosis Center, 2003
- Esposito, F., Ornelas, J., & Arcidiacono, C. (2015). Migration-related detention centers: the challenges of an ecological perspective with a focus on justice. *BMC International Health and Human Rights*, 15, 13. <http://doi.org/10.1186/s12914-015-0052-0>
- Gushulak, B. D., & MacPherson, D. W. (2006). The basic principles of migration health: population mobility and gaps in disease prevalence. *Emerg Themes Epidemiology*, 3(3), 1742.
- International Organization for Migration (IOM) 2014 Migration and Tuberculosis: A Pressing Issue. IOM, Geneva. Available from: www.iom.int/files/live/sites/iom/files/WhatWe-Do/docs/Migration-Tuberculosis-APressing-Issue.pdf.
- Jamison, D. T., Breman, J. G., Measham, A. R., Alleyne, G., Claeson, M., Evans, D. B., & Klugman, K. P. (2006). Drug Resistance.
- Jeon CY, Murray MB (2008) Diabetes Mellitus Increases the Risk of Active Tuberculosis: A Systematic Review of 13 Observational Studies. *PLoS Med* 5(7): e152. doi:10.1371/journal.pmed.0050152

- Lin H-H, Ezzati M, Murray M (2007) Tobacco Smoke, Indoor Air Pollution and Tuberculosis: A Systematic Review and Meta-Analysis. *PLoS Med* 4(1): e20. doi:10.1371/journal.pmed.0040020
- Lönnroth, K., Williams, B. G., Stadlin, S., Jaramillo, E., & Dye, C. (2008). Alcohol use as a risk factor for tuberculosis—a systematic review. *BMC public health*, 8(1), 289.
- MacPherson, D. W., & Gushulak, B. D. (2006). Balancing prevention and screening among international migrants with tuberculosis: population mobility as the major epidemiological influence in low-incidence nations. *Public health*, 120(8), 712-723.
- Maher, D., Chaulet, P., Spinaci, S., & Harries, A. (1997). Treatment of tuberculosis: guidelines for national programmes. *Treatment of tuberculosis: guidelines for national programmes. Second edition.* (Ed. 2), 1-77 Diagnosis and management of tuberculosis by private practitioners in Manila, Philippines. Auer C, Lagahid JY, Tanner M, Weiss MG.
- Memish, Z. A., Zumla, A., Alhakeem, R. F., Assiri, A., Turkestani, A., Al Harby, K. D., & Al-Tawfiq, J. A. (2014). Hajj: infectious disease surveillance and control. *The Lancet*, 383(9934), 2073-2082.
- Ponnighaus, J. M., Msosa, E., Gruer, P. J. K., Liomba, N. G., Fine, P. E. M., Sterne, J. A. C., ... & Lucas, S. B. (1992). Efficacy of BCG vaccine against leprosy and tuberculosis in northern Malawi. *The Lancet*, 339(8794), 636-639.

- Rosen Stock, I. M., Strecher, V. J., & Becker, M. H. (1988). Social learning theory and the health belief model. *Health Education & Behavior*, 15(2), 175-183.
- Sagbakken, M., Frich, J. C., & Bjune, G. A. (2008). Perception and management of tuberculosis symptoms in Addis Ababa, Ethiopia. *Qualitative health research*.
- Sia, I. G., & Wieland, M. L. (2011, April). Current concepts in the management of tuberculosis. In *Mayo Clinic Proceedings* (Vol. 86, No. 4, pp. 348-361). Elsevier.
- Sudre, P., ten Dam, G., & Kochi, A. (1992). Tuberculosis: a global overview of the situation today. *Bulletin of the World Health Organization*, 70(2), 149–159.
- Van Buuren, and Groothuis-Oudshoorn, C. G. M (2000). Flexible multivariate imputation by chained equation: MICE V1.0 user's manual. Technical Report PG/VGZ/00.038, TNO Prevention and Health Leiden.
- Vynnycky, E., & Fine, P. E. M. (1997). The natural history of tuberculosis: the implications of age-dependent risks of disease and the role of reinfection. *Epidemiology and infection*, 119(02), 183-201.
- Wilder-Smith, Annelies, Foo, Winnie, Earnest, Arul and Paton, Nicholas I. High risk of *Mycobacterium tuberculosis* infection during the Hajj pilgrimage 2005
- World Health Organization. (2009). WHO policy on TB infection control in health-care facilities, congregate settings and households.

- World Health Organization. (2014a). Global tuberculosis report executive summary. http://www.who.int/tb/publications/global_report/gtbr14_executive_summary.pdf?ua=1. World Health Organization. (2014b) the stop TB strategy.
- World Health Organization: Global Tuberculosis Control 2009, Epidemiology, Strategy, Financing. <http://www.who.int/mediacentre/factsheets/fs104/en/>
- Wyss, L. L., & Alderman, M. K. (2006). Using theory to interpret beliefs in migrants diagnosed with latent TB. *Online J Issues Nurs*, 12(7).