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ABSTRACT

A CROSS-SECTIONAL STUDY TO IDENTIFY FACTORS ASSOCIATED WITH EXTRAPULMONARY TUBERCULOSIS AMONG FOREIGN-BORN IN DEKALB COUNTY GEORGIA DURING 2008-2018

By

Chinedu Francois Egbuonu

12/9/2019

Purpose

Tuberculosis (TB) is a significant health problem in foreign-born and accounted for 57% of all tuberculosis cases in the United States in 2006. Almost 20% of American tuberculosis cases are classified as extrapulmonary tuberculosis (EPTB). Epidemiologic evidence suggests that the prevalence of EPTB in the US is declining at a much slower rate than pulmonary tuberculosis (PTB). This study is designed to examine the factors that are associated with the risk of EPTB in foreign-born residents of DeKalb county.

Methods

In this study, data from the Public Health Information Portal (PHIP), an online system from the Georgia Department of Public Health, was used. A cross-sectional study was conducted on US tuberculosis cases reported in DeKalb county from 2008 to 2018, classified as EPTB and PTB. EPTB encompassed lymphatic, pleural, bone and/or joint, genitourinary, meningeal, peritoneal, and unclassified EPTB cases. The data include demographic information, lifestyle variables, and clinical characteristics of the study subjects. Demographic characteristics and risk factors, including human immunodeficiency virus (HIV) status, were compared across TB status (EPTB vs. PTB).

Results

Foreign-born participants with HIV positive status, homelessness and IV drug users had a much higher chance of developing EPTB.

Conclusion

Awareness of the risk of extrapulmonary tuberculosis may help in developing a prevention strategy among foreign-born.

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TUBERCULOSIS AMONG FOREIGN-BORN IN DEKALB COUNTY GEORGIA DURING 2008-2018

by

Chinedu Francois Egbuonu

M.B.B.S., IGBINEDION UNIVERSITY

A Thesis Submitted to the Graduate Faculty
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of the
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MASTER OF PUBLIC HEALTH

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30303

APPROVAL PAGE

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Author's Statement Page

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_____ Chinedu Francois Egbuonu _____
Signature of Author

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CHAPTER I

Introduction

Tuberculosis (TB) is an airborne disease caused by the bacterium *Mycobacterium tuberculosis*, also called tubercle bacilli (“Trends 2017 | Data & Statistics | TB | CDC,” 2018). The bacteria usually attack the lungs, but TB bacteria can attack any part of the body, such as the kidney, spine, and brain. (“Trends 2017 | Data & Statistics | TB | CDC,” 2018). Extra-pulmonary tuberculosis (EPTB), is when the tuberculous *Mycobacterium* invades areas outside the lungs. Some of the common sites of extra-pulmonary tuberculosis include Lymph node, Pleural, Bone and Joint, Abdominal and Genitourinary, and the Central Nervous System. The clinical findings of extra-pulmonary TB are usually non-specific, develop insidiously, and mimics other noninfectious conditions (Binesh, Zahir, & Bovanlu, 2013).

Tuberculosis remains one of the leading causes of morbidity and the top 10 causes of mortality worldwide, making it an enormous global health problem (World Health Organization, 2012). The World Health Organization estimates that in 2012, there were 8.6 million new cases of TB disease and more than 1.3 million deaths due to TB (WHO | Global tuberculosis report 2018). In the State of Georgia, TB rates are higher than the US average for the last 25 years. In 2013 Georgia had 339 new cases of TB (3.4 per 100,000 population), with half (52%) occurring in the metropolitan Atlanta area (DeKalb, Fulton and East Metro District)(*2015 surveillance report full report*). Extrapulmonary Tuberculosis is a global public health problem due to its broad spectrum of clinical manifestation that remains grossly underreported (Rao et al., 2012).

Most of the resources, diagnosis, and treatment are aimed at pulmonary TB as this form is most common and most important about TB control and public health. However, EPTB in all forms has a significant impact on people suffering from the disease, the families, economy, and health system. This study is aimed at expanding the current knowledge of extrapulmonary tuberculosis to highlight factors contributing to its prevalence in foreign-born at DeKalb County as well as develop a better understanding of preventive measures.

CHAPTER II

Epidemiology of Tuberculosis

Globally, Tuberculosis (TB) is one of the top ten causes of death. According to the WHO Global Tuberculosis report 2019, an estimated 10.0 million (range, 9.0– 11.1 million) people fell ill with TB in 2018, and the burden of disease varies among countries, from 5 to 500 new cases per 100 000 population per year, with the global average being around 130 (“WHO | Global tuberculosis report 2018,” n.d.) Most TB cases in 2018 were in the WHO regions of South-East Asia (44%), Africa (24%) and the Western Pacific (18%), with smaller percentages in the Eastern Mediterranean (8%), the Americas (3%) and Europe (3%). Eight countries accounted for two-thirds of the global total: India (27%), China (9%), Indonesia (8%), the Philippines (6%), Pakistan (6%), Nigeria (4%), Bangladesh (4%) and South Africa (3%). These and 22 other countries in WHO's list of 30 high TB burden countries accounted for 87% of the world's cases (“WHO | Global tuberculosis report 2019,” n.d.).

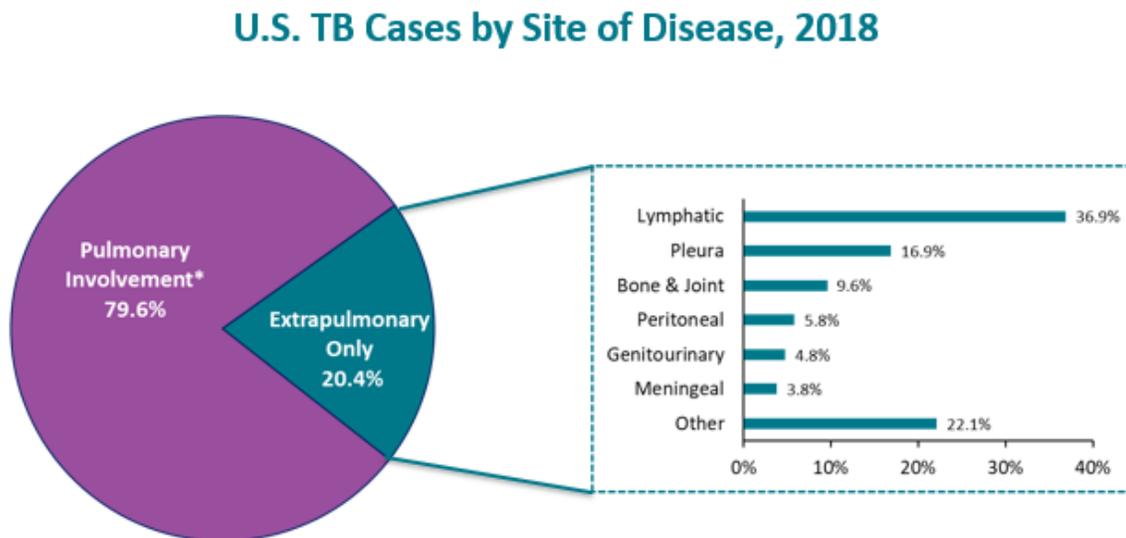
The incidence of Extra-pulmonary TB has increased from overtime from 15.7% of the cases in 1993 to 21.0% in 2006 (Peto, Pratt, Harrington, LoBue, & Armstrong, 2009) (CDC "Trends in Tuberculosis Incidence—the United States, 2006). Of the 7.0 million new and relapse cases notified in 2018, 5.9 million (85%) had pulmonary TB. Extra-pulmonary TB represented 15% of the 7.0 million incident cases that were reported in 2018.

In 2018, the United States had 9,025 (a rate of 2.8 cases per 100,000 persons) reported new cases of TB (Talwar, 2019). Of all the new cases (N=9025) of TB in US 68% (N=6173) were Pulmonary, 20% (N=1828) Extra-pulmonary and 11% (N= 967) both pulmonary and extra-pulmonary TB (Figure 2).

In Georgia, TB rates have been higher than the US average for the last 25 years. (“Trends 2017 | Data & Statistics | TB | CDC,” 2018) In 2017, among the 159 counties in Georgia, four counties in the metropolitan Atlanta area reported the highest number of TB cases: DeKalb (66 cases), Fulton (42), Gwinnett (42), and Cobb (18). These four counties accounted for 57% of all TB cases reported in Georgia in 2017. According to the CDC, in 2018, Georgia ranked fourteenth in the United States for the number of new TB cases. Of the 9,025 reported new TB cases in the US,

272 new TB cases were from Georgia. Seventy-one percent (N=193) of all the new TB cases in Georgia were Pulmonary TB, 20% (N=53) Extra-pulmonary TB and 9% (N= 25) of the new cases had both pulmonary and extra-pulmonary TB (“TB Incidence in the U.S. | Data & Statistics | TB | CDC,” 2018)

Figure 2



*Any pulmonary involvement which includes cases that are pulmonary only and both pulmonary and extrapulmonary. Patients may have more than one disease site but are counted in mutually exclusive categories for surveillance purposes.
 Note: Percentages are rounded.

Diagram sourced from the CDC Tuberculosis Report 2019

Foreign-Born and TB Transmission

Human migration has had a significant effect on the spread of tuberculosis throughout human history, and it is no different today (Blumberg, Migliori, Ponomarenko, & Heldal, 2010). In modern times, geographic barriers have been easily overcome, and mass migration reached unprecedented levels in recent times with nearly 1 billion—or one of seven—people being migrants (UNDP, 2009). An estimated 740 million are internal migrants, and 200 million are international migrants, with most (130 million) moving from one developing country to another and 70 million moving from a developing to a developed country (UNDP, 2009). With the steady increase in migration, it is estimated that the prevalence of extrapulmonary tuberculosis (EPTB) could increase as well, posing a significant public health issue (Rieder, 2016).

Among the 9,029 TB cases reported in the United States in 2018, approximately two thirds (6,276 [69.5%]) occurred in foreign-born persons, whereas 2,662 (29.5%) occurred in U.S.-born persons; 91 (1.0%) cases occurred in persons for whom no national origin was documented. This distribution is like that in 2017 when 6,392 (70.3%) incidents occurred in foreign-born persons, 2,693 (29.6%) occurred in U.S.-born persons, and 9 (0.1%) occurred in persons for whom no national origin was documented (“WHO | Global tuberculosis report 2018,” n.d.).

Among foreign-born persons with TB, the incidence in 2018 (seen in figure 1) was highest among Asians, followed by Native Hawaiians/Pacific Islanders, non-Hispanic blacks (blacks), Hispanics, and American Indian/Alaska Natives, and was lowest among non-Hispanic whites (whites). The top five countries of birth of non-U.S.-born persons with TB were Mexico (1,195 cases; 19.0% of all non-U.S.-born cases), Philippines (781; 12.4%), India (616; 9.8%), Vietnam (503; 8.0%), and China (374; 6.0%). Among TB cases in non-U.S.-born persons, 2,905 (46.3%) were diagnosed ≥ 10 years after the patient first arrived in the United States (“WHO | Global tuberculosis report 2018,” n.d.).

Figure 3

Percentage of extrapulmonary cases among new and relapse TB cases, 2018

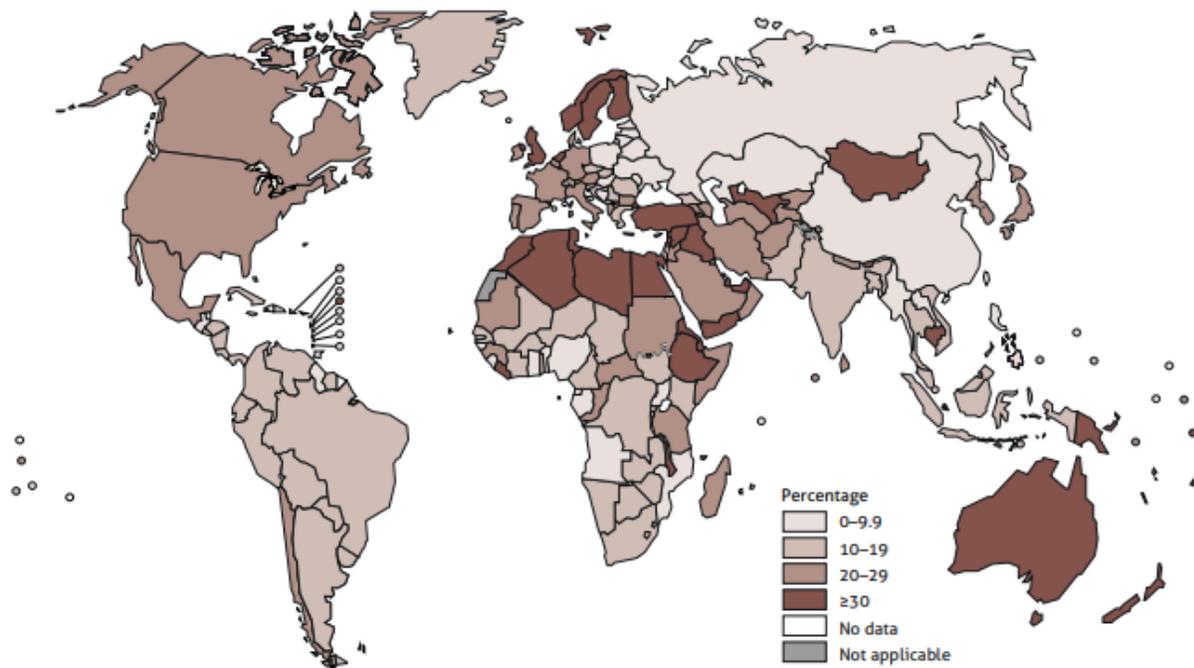


Diagram sourced from CDC Tuberculosis Report 2019

Chapter III- Literature Review

Brief Pathogenesis on TB

Infection occurs when a person inhales droplet nucleus containing tubercle bacilli that reach the alveoli of the lungs. These tubercle bacilli are ingested by alveolar macrophages; most of these bacilli are destroyed or inhibited. A small number may multiply intracellularly and are released when the macrophages die. If alive, these bacilli may spread by way of lymphatic channels or through the bloodstream to more distant tissues and organs (including areas of the body in which TB disease is most likely to develop: regional lymph nodes, the apex of the lung, kidneys, brain, and bone).

Figure 2. Pathogenesis of TB

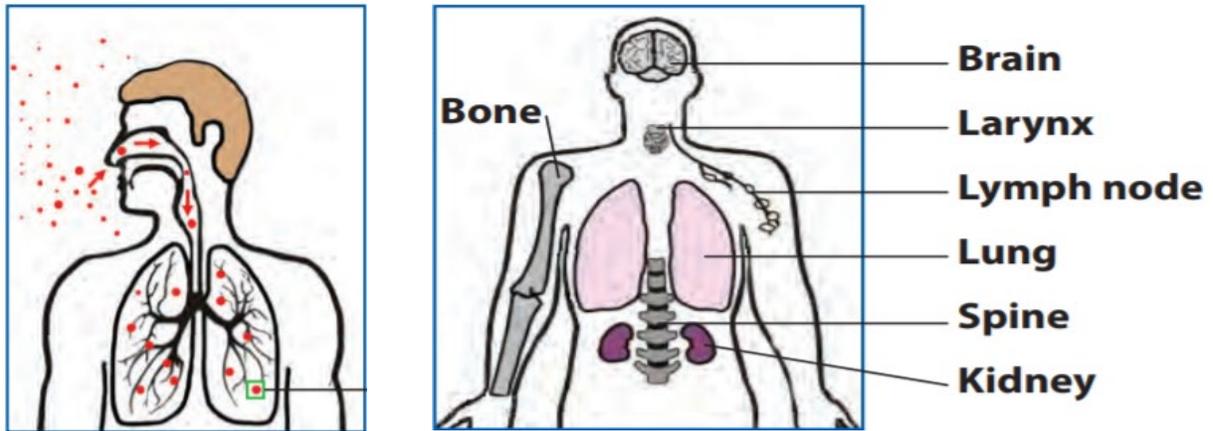


Diagram sourced from <https://www.cdc.gov/tb/webcourses/tb101/page1699.html>

In the United States, EPTB is not evenly distributed among the US population. Foreign-born are disproportionately affected by tuberculosis, usually a reflection of the high rate of disease in their country of origin due to poverty and, or by limited healthcare and public health infrastructure (Hargreaves et al., 2014). Migration has tremendously affected the epidemiology of tuberculosis here in the USA, which has a low incidence of tuberculosis but with most cases now occurring in foreign-born individuals

Most of the resources, diagnosis, and treatment are aimed at pulmonary TB as this form is most common and most important about TB control and public health. However, EPTB in all types has a significant impact on people suffering from the disease, the families, economy, and health system.

This study is aimed at expanding the current knowledge of extrapulmonary tuberculosis to highlight factors contributing to its prevalence in foreign-born at DeKalb County as well as develop a better understanding of preventive measures.

Factors attributing to EPTB

Despite extensive research, screening, education, and continuous efforts to try to eradicate and control the infection, tuberculosis is still one of the most prevalent infections throughout the world. Even the cases of extrapulmonary dissemination are seen to have increased. Part of the challenges faced with extrapulmonary tuberculous dissemination is the varying presentation that depends on the organ involved (García-Rodríguez et al., 2011)

In numerous studies, risk factors identified for extra-pulmonary dissemination include cirrhosis, malignancy, immunosuppressive drug use, alcoholism, HIV infection, chronic obstructive pulmonary disease (COPD), congestive heart failure, intravenous drug use, previous history of pulmonary tuberculosis, and history of cerebrovascular accident. Still, there is no statistical analysis that linked these causes as a direct risk factor for disseminated infection (Rock, Olin, Baker, Molitor, & Peterson, 2008).

A study by Donald et al. found that the incidence of extrapulmonary tuberculosis is higher in populations with reduced immune function especially in very young children with the immature immune system and in older people in whom the worse function of the immune system in advanced age is observed (Donald, Marais, & Barry, 2010). Also, any disease impairing the immune function, in particular, HIV infection (Harris, Li, Hanna, & Munsiff, 2010), as well as kidney failure, favor the development of extrapulmonary tuberculosis (Lin et al., 2009).

Genetic factors may also influence the incidence of extrapulmonary tuberculosis (Rowińska-Zakrzewska, 2011). Most studies found that extrapulmonary tuberculosis is significantly more common in females (Lin et al., 2009). This applies to all types of the disease except for pleural tuberculosis, which occurs more often in males. Extrapulmonary tuberculosis occurs very rarely in Caucasians (Mohammed, Al-Rubeai, Yaseen, Ghazi, & Khaz'al, 2015).

Zhang et al. found that in their study that in the United States, extrapulmonary tuberculosis was particularly common in people originating from South Asia in the absence of HIV infection or other immunosuppressive factors (Zhang et al., 2011). Studies have found that among persons with tuberculosis, blacks and women have a higher proportion of extrapulmonary disease compared with non-blacks and men, respectively (Forssbohm, Zwahlen, Loddenkemper, & Rieder, 2008).

In a retrospective study conducted by Lin and colleagues, patients with EPTB and PTB were compared in Southern Taiwan. They found using multivariate logistic regression that being female, non-diabetic, end-stage renal disease, and nonsmoking were independent risk factors to EPTB development.

Chapter IV

Methodology

A retrospective cross-sectional study was conducted using secondary data from the Public Health Information Portal (PHIP), an online system from the Georgia Department of Public Health, which was collected. Data included demographic information, lifestyle variables, and clinical characteristics of the reported TB case in DeKalb county from 2008 to 2018.

Inclusion criteria were all persons with a verified case of incident TB disease reported to the Georgia Department of Health from January 1, 2008, through December 31, 2018, examining TB case frequency by US Census Bureau categorization of US- or foreign-born origin (an individual is classified as a US-born person if he or she was born in the United States or associated jurisdictions or was born in a foreign country, but at least one parent was a US citizen.¹³ All other individuals are classified as foreign-born, according to patient age, gender, race, and ethnicity per self-report or parental report (Hispanic, or non-Hispanic white, black, Asian/Pacific Islander, American Indian/Native Alaskan), disease site (pulmonary, extrapulmonary, or both), hierarchical TB verification criteria (i.e., [1] positive culture or [2] nucleic acid amplification test for Mycobacterium tuberculosis, [3] positive smear or examination for acid-fast bacilli, [4] clinical confirmation by tuberculin skin test or interferon γ release assay results and chest radiograph or scan, or [5] provider diagnosis in the absence of clinical results), HIV infection status (positive, negative, or not reported to TB surveillance).

Result

A total of 771 reported culture-proven tuberculosis cases were diagnosed in DeKalb County from 4 January 2008 through 31 December 2018. Two hundred three were EPTB, and 566 were PTB. Most of the patients were male, accounting for 62.0% of the study population, female making up 37.9%. There were 28 non-Hispanic whites (3.6% of subjects), 407 non-Hispanic blacks (52.8%), 220 Asians/Pacific Islanders (28.5%), 107 Hispanics (13.9%), 5 Multiracial Non-Hispanic (0.6%) 1 American Indians (0.1%) and 2 Unknown (0.3%). The majority (648 [92%]) of the study, patients were not born in the United States. The 771 included patients who came

from came from 55 countries. About 23.7% were from Africa, 28.8% from Asia and 47.5% from the Americas; the most common countries of origin were Ethiopia (19.4%), Burma (11.1%), Mexico (10.5%), Bhutan (7.7%), and India (7.1%). A portion of the study patients was ≥ 65 years old (88 patients; 11%). The disease site constituting the largest proportion of EPTB cases was lymphatic tuberculosis. (Figure1). The mean age of patients with EPTB was 44 years (Table 1). The total of patients with bone and/or joint tuberculosis was 18 (11.9%), meningeal tuberculosis 20(13.2%), genitourinary 8 (5.2%), and 'others' 21 (13.9%). About 60% of the EPTB patients were male (Table1). Most EPTB cases (82%) occurred in nonwhite racial and/or ethnic groups (Table 1), with blacks constituting the largest racial and/or ethnic group (55.6%), followed by Asians. Among EPTB cases, proportions of foreign-born and US-born patients were different, with Foreign-born making up 23.4% of cases compared to 16.0% in the US-born (Table 1).

Among EPTB patients reported, 39.3% were HIV-infected (Table 1).

Table 1. Characteristics of Patients with Extrapulmonary Tuberculosis (EPTB), Compared with Patients with Pulmonary Tuberculosis (PTB) in DeKalb County, Atlanta. 2008-2018

variable	PTB N(%)	EPTB N(%)
Age, years		
Median (IQR)	37(25-54)	35(26-49)
Mean	39	38
Gender		
Female	219(75.5)	71(24.5)
Male	346(72.4)	132(27.6)
Country of birth		
US	206(76.9)	62(23.1)
Foreign	360(71.9)	141(28.1)
Race		
Non-Hispanic Black	296(73.1)	109(26.9)
Non-Hispanic White	19(67.9)	9(32.1)
Non-Hispanic Asian	168(76.9)	52(23.6)
Other Hispanics	78(72.9)	29(27.1)
American	1(100)	0(0.0)
Indian/Alaska Native		
2 or more races	3(60.0)	2(40.0)
Regions		
Africa	124(67.8)	59(32.2)
Asia	166(74.8)	56(25.2)
Americas	276(75.8)	88(24.2)
HIV status		
Negative	479(75.2)	158(24.8)
Positive	51(60.7)	33(39.3)
Homelessness		
No	517(72.4)	197(27.6)
Yes	49(90.7)	5(9.3)
Injection drug use		
No	541(73.9)	191(26.1)
Yes	12(66.7)	6(33.3)
Drug use		
No	523(73.2)	191(26.8)
Yes	30(83.3)	6(16.7)
Alcohol abuse		
No	493(72.7)	185(27.3)
Yes	58(84.1)	11(15.9)

% = row percentage

Chapter V

Recommendation

Healthy People 2010 objectives emphasize improving health by modifying the individual, social, and environmental determinants of health. Actions and policy initiatives that can be undertaken to ameliorate extrapulmonary tuberculosis in foreign-born in DeKalb county will include;

- Collaboration with international and national agencies and organizations as well as state and local health departments to develop profiles of immigration trends and patterns at the global, federal, state, and local levels
- Early recognition of the disease process and prompt treatment would be of help to prevent the debilitating complications of the disease. The focus on TB has been almost exclusively as pulmonary disease, causing fever, cough, and hemoptysis in national awareness campaigns. This might lead to delayed seeking of medical care in cases with atypical presentations of pulmonary disease and extrapulmonary involvement
- Though the government provides sputum tests and first-line antitubercular treatment free of cost to all patients, other diagnostic tests for extrapulmonary TB require a patient to pay by themselves, which is an economic burden to them and may lead to compromised treatment. More must be done with regards to access to a diagnostic test that is critical to care for EPTB patients
- A new vision of health and migration is necessary if we want to go beyond what (little) is done today. Each country should first ensure that, everywhere, all patients with tuberculosis have easy access to diagnosis and treatment free of charge
- The clear focus on the health needs of foreign-born populations is needed to prevent inequalities in health outcomes for extrapulmonary tuberculosis due to limited access to health care, which prevents migrant communities from accessing information that would enable them to avoid tuberculosis or to obtain early diagnosis and treatment.

- Another strategy is to invest in global tuberculosis control, strengthening national tuberculosis programs, in line with the Global Plan to Stop TB. Additionally, we must invest in the development of better tools (new drugs, diagnostics, and a vaccine) to enhance tuberculosis control.
- State and local health departments should develop area-specific, cost-effective strategies for TB screening targeted to foreign-born populations at high risk and ensure that resources are targeted to areas of greatest need.

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