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Tuberculosis (TB) Trends Among Refugee, Other Foreign-Born, and US-Born Cases in DeKalb County During 2004-2015

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ABSTRACT

TUBERCULOSIS (TB) TRENDS AMONG REFUGEE, OTHER FOREIGN-BORN, AND US-BORN CASES IN DEKALB COUNTY DURING 2004-2015

By

MARYAM AHMAD

May 4, 2016

BACKGROUND: On World TB Day 2016, CDC reported an increase in number of US tuberculosis (TB) cases in 2015, the first time in 23 years. TB is the largest cause of mortality from any bacterial disease worldwide, with 95% of cases and deaths in low and middle-income countries, where it remains endemic. The recent increase in US TB cases highlights the fact that TB is a global issue, thus requiring a global effort to achieve elimination, with particular focus on active TB and Latent TB Infection (LTBI) identification and treatment among populations at high risk. The refugee population requires particular attention, considering TB disproportionately afflicts refugees and there are more refugees worldwide today than in the past 20 years. Georgia is among the top 10 US states for refugee arrivals, with majority resettling in DeKalb County, approximately 90% in 2010. There is a lack of data on TB rates among these populations and effects of implementation of the 2007 expanded CDC Technical Instructions on imported TB and LTBI reactivation.

OBJECTIVES: (1) Estimate and compare TB disease incidence rates among refugee, other foreign-born, and US-born populations in DeKalb County from 2004 to 2015 (2) Determine refugee TB case contribution to total DeKalb County TB case burden (3) Examine possible trends in number of cases diagnosed ≤ 6 months of US entry, among refugee and other foreign-born persons screened overseas before and after implementation of 2007 expanded CDC Technical Instructions.

METHODS: Retrospective study on all new TB cases diagnosed in DeKalb County during 2004-2015. Due to the lack of data on refugee population estimates along with the dynamic nature of this population, three different annual incidence rates were calculated for refugees and other FB. Participant characteristics were compared using chi-square tests and univariate analyses to identify significant differences between groups. Logistic regression was used to model change in number of TB diagnoses ≤ 6 months of US entry against implementation status (pre vs. post) and immigration status (refugee vs. other-FB).

RESULTS: From 2004 to 2015, a total of 898 active TB cases were diagnosed in DeKalb County; 569 total foreign-born (144 refugees and 425 other foreign-born) and 329 US-

born. Age, race/ethnicity, TB verification type, HIV status, and previous TB diagnosis were found to have significant differences between groups ($p < 0.05$). Throughout the study period, the highest TB incidence rate was among refugees followed by other FB, and drastically lower rates among US-born. There were significantly more diagnoses ≤ 6 months of US entry among post vs pre-implementation, OR: 2.784 (95% CI: 1.683 – 4.606). Refugee vs. other-FB, OR: 5.103 (95% CI: 3.085 – 8.442). Majority of cases with prior B1 classification (83.6%) were diagnosed ≤ 6 of US entry, which is considered to be possible imported TB, While (90.9%) persons with Class B2, although few, were diagnosed ≤ 6 months of US entry, which suggests possible LTBI reactivation.

DISCUSSION: Although TB cases and rates have decreased in DeKalb County over the years, particularly among US-born persons, the foreign-born population remains disproportionately afflicted, with majority of county disease burden, over 70% in 2015. Refugee TB rates in DeKalb County are more comparable to rates in high TB incidence low and middle-income countries rather than US rates. Imported TB and LTBI activation may be major factors involved in the stagnation of progression towards TB elimination. Efforts need to refocus on LTBI identification and treatment to tackle the global issue of TB.

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CASES IN DEKALB COUNTY DURING 2004-2015

by

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Author's Statement Page

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Background:

Tuberculosis is an ancient disease, which remains to cause more mortality than any other bacterial disease worldwide. Genetic studies suggest the pathogenic bacteria causing TB, *Mycobacterium tuberculosis*, has been around for at least 15,000 years and evidence in mummies dates back to 2400-3400 B.C. (N. J. Health, 2016). In 1993, the World Health Organization (WHO) declared TB a global emergency (WHO, 2002). Twelve years later, WHO declared an emergency in Africa, where approximately 1,500 deaths from TB occurred every day (WHO, 2005). Although incidence has decreased overall, TB remains endemic in many countries, particularly in Southeast Asia, Africa, and Western Pacific regions.

Approximately 10 million persons develop TB annually, which leads to 1.5 million deaths that could have been prevented by early diagnosis and treatment (Alert). The majority of new cases of TB are from the large pool of persons with Latent TB Infection [11]. LTBI occurs when *M. tuberculosis*, is alive but dormant within an individual. About 5-10% of persons with LTBI develop TB disease, usually after 6-18 months, although for some it may take years or decades (CDC, 2011). Among high risk groups, this percentage greatly increases. LTBI is more difficult to identify than active TB due to lack of symptoms. Diagnosis is usually made based on a positive TST or IRGA, normal chest x-ray (CXR), and negative sputum and culture. Although persons are noninfectious, treatment is needed to prevent development of disease, especially among high risk groups, such as persons in high incidence countries.

Almost all cases and deaths (95%) occur in low and middle-income countries. Much of these areas have poor healthcare infrastructures, which hinder efforts to treat and prevent the spread of TB. Approximately 9.6 million persons developed TB disease worldwide in 2014, which of over 3 million, did not get the care or treatment needed (Alert). An untreated case of active TB has a case-fatality ratio of about 50% and can transmit infection to 10 -15 contacts annually until death or recovery (Kimbrough, Saliba, Dahab, Haskew, & Checchi). Untreated TB spreads even faster in crowded refugee camps and shelters (WHO, 2002). This population already faces increased risk of morbidity and mortality, as well as progression from LTBI to TB disease, therefore are disproportionately afflicted by TB.

According to the Refugee Act of 1980, a refugee is defined as any person who is outside his/her home country unable or unwilling to return to, and is unable or unwilling to avail himself or herself protection of that country because of persecution or a well-founded fear of persecution on account of race, religion, nationality, membership in a particular social group, or political opinion [19]. Many flee from their countries of nationality due to imprisonment, torture, loss of property, physical assault, extreme fear, rape, loss of livelihood, and other harsh circumstances. The refugee population requires particular attention, since there are more refugees worldwide today than in the past 20 years, where many are in conflict settings. In 2011, there were 10.4 million refugees which increased to approximately 15.1 million by mid-2015. The main factor of this significant increase has been the war in the Syrian Arab Republic. Other armed conflicts such as those in Afghanistan, Burundi, the Democratic Republic of the Congo, Mali, Somalia, South Sudan, Ukraine and others have also been a factor in this large increase in refugees worldwide. In addition, the number of refugees able to return home has trended downward. (UNHCR).

After fleeing country of nationality, many refugees live in crowded conditions in camps or urban areas in host countries for years before resettlement in a third country. More than 85% of refugees flee from and stay in high burden TB countries, which is a major risk factor for TB development. Overcrowding has been associated with increased transmission of pulmonary disease. Other factors contributing to increased risk of increased transmission as well as morbidity and mortality include malnutrition, disrupted health services, lack of TB medications, and comorbidities such as HIV, Hepatitis, vitamin D deficiency, and diabetes, along with lack of water,

sanitation, social services, and education. Mild malnutrition can even increase the risk of tuberculosis progression and case-fatality. Disruption of health services could lead to interruption of TB treatment along with drug shortages, which may result in relapse or promote drug resistance. Another issue is minimum laboratory standards for smear/culture microscopy and length of treatment or time for results or complete diagnosis. When crisis affected populations have a high prevalence of HIV, TB screening methods are less sensitive in these populations [20] According to WHO, approximately 36.9 million people were living with HIV worldwide at the end of 2014, with majority refugees in high HIV prevalence regions (AIDS, 2015).

A longitudinal study by Kimbrough et al (Kimbrough et al.) provided evidence of increased incidence of TB after displacement into refugee camps. Camp populations are very dynamic, with ongoing arrivals and departures, which increases the susceptible and infectious populations and also makes them more difficult to treat (WHO, 2002). For long-term Tibetan refugees, notifications remained high between 1994 and 1996 with up to 1100 per 100 000 persons. Among Burmese refugees in Thailand camps, TB notifications sharply increased during the first 3 years of establishment of camps, from 22 (per 100 000) in 1987 to 212 in 1991. During war period, notification increased dramatically and peaked in the year after the war period among Bhutanese refugees. Among Burundian and Rwandan refugees in Tanzania (1995-1999) the case fatality rate was 10.9% where directly-observed therapy (DOT) was already implemented (Kimbrough et al.) .

Immigrants and refugees are the only foreign-born groups that are required to undergo TB screening before US entry. Panel physicians are appointed by the department of state who conduct the medical evaluations following CDC TB Technical Instructions (TI). B1 classification is defined as persons with abnormal CXR but normal sputum/culture smears. B2 classification are defined as persons with identified LTBI CDC notifies the health departments of arriving immigrants and refugees and their overseas screening classification, who then complete the follow-up post-arrival examination. Cases diagnosed with TB disease within 6 months of migration with prior B1 classification from overseas screening are considered possible imported TB. Applicants with B1 classifications are allowed 3 months instead of the usual 6 months for travel clearance.

The risk of TB development has been found to be highest immediately after US entry and decreases overtime. The CDC technical instructions were expanded from 1991, and were implemented in different countries from 2007 to 2013 on a rolling basis. Major changes include required sputum culture in addition to sputum smears, DOT for treatment of cases, drug susceptibility testing, and CXR for all immunosuppressed individuals. The purpose of expanding the TI include increase identification of TB cases by 2 or 3, reduce TB importation, reduce number of drug resistant cases, improve TB control in US immigrants and refugees. Although some articles provided evidence of the expanded CDC TI There is a lack of data on TB rates among these populations and effects of implementation of the 2007 expanded CDC Technical Instructions on imported TB and LTBI reactivation.

Although majority of TB cases are in low and middle income countries, due to a highly globalized society along with the inherent nature of the infectious disease, worldwide efforts are required for control and prevention, to hopefully eventual elimination. Global trade and travel has dramatically increased over the years, which increases spread of TB. Even though TB is an inadmissible health condition, imported TB cases remain along with LTBI progression. The higher income countries still face a risk of increased numbers of TB if global efforts and more funding is put toward TB control and prevention. TB occurrence remains greatest among foreign-born populations, especially refugees and can surface years after migration.

On World TB Day 2016, CDC reported the number of US tuberculosis cases increased in 2015, the first time in 23 years (CDC, 2016). Twenty-nine (58%) states reported an increase in cases. Two-thirds of the TB cases were among foreign-born persons, which has consistently been

approximately 13 times the US-born rate (15.1 vs. 1.2 per 100 000). This has brought attention to the fact that TB elimination in the US requires increased efforts in screening and treating latent tuberculosis (LTBI) among high-risk groups, particularly refugees.

The US tuberculosis incidence rate slightly increased from 2014 to 2015 (2.9 to 3.0 per 100 000) by 0.9%. The TB incidence rate in Georgia decreased during this time period (3.3 to 3.2 per 100 000) by 5%; however, Georgia remains one of the states with the highest TB incidence rates in the US (ranked 8th). Georgia is one of the top states in the US for refugee arrivals. In 2004, it ranked 6th and in 2015 it tied for 4th (Resettlement, 2015). Approximately 90% of the refugees that resettled in GA in 2010 were in DeKalb County (G. D. o. C. Health, 2011).

Objectives: (1) Estimate and compare TB disease incidence rates among refugee, other foreign-born, and US-born populations in DeKalb County from 2004 to 2015. (2) Determine refugee TB case contribution to total DeKalb County TB case burden. (3) Examine possible trends in cases diagnosed within 6 months of US entry, among refugee and other foreign-born persons (with overseas screening) screened overseas before and after implementation of the 2007 revised CDC technical instructions. (4) Compare 1995-1999 DeKalb County TB rates and case burden from Hadzibegovic et al (2005) with the 2004-2015 estimated TB rates.

Methods:

Data

Retrospective study of all active TB cases diagnosed in DeKalb County from 2004 to 2015. The list of all TB cases was obtained from Georgia's State Electronic Notifiable Disease Surveillance System (SENDSS). The year 2004 was chosen due to lack of prior records in SENDSS. The list of all refugees screened at DeKalb County Board of Health (DCBOH) was obtained from the DCBOH database (InSight). Identification of 'refugee' cases was done by comparison of names and date of birth of refugees extracted from InSight with DeKalb County active TB cases in SENDSS. Non-refugees with a non-US country of origin were defined as 'other foreign-born' cases. 'Total foreign-born' consisted of refugee and other-foreign born cases. Cases of US-origin were defined as 'US-born'.

Data on age, sex, HIV status, race/ethnicity, disease site, verification type, country of origin, previous TB diagnosis, date of US entry, date of physician notification (diagnosis), and overseas TB classification were collected. Tuberculosis cases were defined as individuals with a TB clinical case definition (CDC), positive culture, positive smear/tissue, or a positive Nucleic Acid Amplification (NAA) result.

Data used for this study were extracted by authorized personnel at the DCBOH.

This study was determined to be non-human subjects research by GSU IRB.

Annual population estimates

(1) Population figures and estimates were used as denominators to calculate annual TB disease incidence rates among total county, refugee, other foreign-born, US-born, and total foreign-born. Number of new annual cases were divided by the annual population numbers and multiplied by 100 000 to calculate the estimated incidence rates per 100 000 persons.

Intercensal annual DeKalb County population estimates were used for years 2004 to 2009. 2010 Census data was used for 2010 population figures. The postcensal county population estimates were used for years 2011 to 2014. Intercensal, census, and postcensal population numbers and estimates were obtained through the US Census Bureau (Bureau, 2000,2010). This source did not have available postcensal 2015 DeKalb County population estimates. Therefore, the 2015

population projection was obtained from the Georgia Public Library Service (GPLS), the state agency for public libraries in Georgia (Service, 2015). The year of physician notification/diagnosis was used as the incidence year.

According to the 2010 census, DeKalb County foreign-born population was 16.3% of the total county population, which was constant for 2011-2014 postcensal estimates. The American Community Survey estimated the FB population was 16.2% between 2005 and 2009. Therefore, annual 'total foreign-born' population estimates were calculated by using 16.3% of the total DeKalb County population for each year. These annual FB population figures were subtracted from annual total county populations to calculate annual US-born population numbers.

Considering lack of data on refugee population estimates in DeKalb County, along with their dynamic nature, three different population estimates were calculated for refugees using 10%, 15%, and 20% of the annual total foreign-born population estimates. Due to total FB consisting of other FB and refugee, other FB population estimates equated 90%, 85%, and 80% of total FB population. A previous study done by Hadzibegovic et al (2005) (Hadzibegovic, Maloney, Cookson, & Oladele, 2005) used the 10% estimate to calculate annual refugee populations, based on the US Citizenship and Immigration Services' approximation of 10% foreign-born persons arriving in the US, with the intention of permanent residency, are refugees. Further evidence for the 10% approximation used for this study is from the US Department of Homeland Security, which stated in 2012, 10.2% of the total US legal permanent residents were refugees and 4.4% asylees (Randall Monger, 2013).

According to an analysis by the Pew Research Center, in recent years, refugees and asylees account for approximately 15% of all legal permanent residents in the US (Center, 2013). Therefore, 15% of total foreign-born population was also used for refugee annual population estimates, considering Georgia does not have high asylee application acceptance rates. The 20% approximation was used for more conservative annual population estimates and incidence rates, since Georgia is one of the top ten states for refugee arrivals and resettlement.

Overseas Evaluation Date Estimates Pre- and Post-implementation of Revised CDC TI

The study sample consisted of TB cases from countries of origin with > 3 TB cases diagnosed in DeKalb County from 2004 to 2015 and had available implementation dates.

Due to implementation of revised 2007 CDC Technical Instructions (TI) on a rolling basis from 2007 to 2013, different dates of implementation based on country and refugee status were considered (Table 1). The revised CDC technical instructions allow for persons to enter US within 6 months (180 days) of the overseas medical exam. Due to the lack of accessible overseas screening data for DeKalb County TB cases, estimated earliest possible overseas screening/medical evaluation dates were calculated by subtracting 180 days from the US entry date, for conservative estimates. This date of estimated overseas screening was used to determine persons screened overseas before and after the date of implementation for the specific countries. DeKalb cases with date of US entry (minus 180) before the country based implementation date were defined as 'pre-implementation'. DeKalb cases with date of US entry (minus 180) after the implementation date were defined as 'post-implementation'.

Refugees with country of origin as Nepal or Bhutan, were defined as 'Bhutanese refugees' and associated with refugee implementation date of Nepal, considering that Bhutanese refugees have been living in camps in Nepal for over 2 decades [27]. Refugees with country of origin as Burma or Malaysia were defined as Burmese refugees and associated with the Malaysia refugee implementation date. Burmese refugees have also lived in camps in Thailand for years, however, due to unknown host country for refugees with country of origin as 'Burma', Malaysia's implementation date was used for these individuals for more conservative estimates of overseas

screening dates. Refugees with countries of origin as Somalia, Ethiopia, and Sudan were associated with the refugee implementation date of Kenya. Countries with available implementation dates had different dates for refugees and all other applicants. Implementation dates were obtained from CDC [28].

Proportion of TB cases diagnosed ≤ 6 months of US entry with available overseas TB classifications were identified to determine for possible imported TB or LTBI reactivation. ‘Imported TB’ was defined as cases with B1 classifications diagnosed ≤ 6 months of US entry. ‘LTBI reactivation’ was defined as cases with B2 classifications diagnosed ≤ 6 months of US entry.

Table 1. Implementation Dates of Revised 2007 CDC Technical Instructions by Country and Applicant Type

Country	Applicants	Implementation Date
Ethiopia	All applicants Refugees: Eritreans	April 1, 2009 March 10, 2009
Somalia	All applicants	April 1, 2009
Burma	All applicants	August 1, 2013
Malaysia	All applicants Refugees: Burmese	November 1, 2011 January 1, 2009
Thailand	All applicants Refugees: Burmese Hmong	April 25, 2011 April 9, 2007
India	All applicants	October 1, 2010
Vietnam	All applicants	February 1, 2008
Mexico	All applicants	October 1, 2007
Guatemala	All applicants	May 2, 2011
Bangladesh	All applicants	June 15, 2011
Nepal	All applicants Refugees: Bhutanese	August 2, 2010 December 13, 2007
Kenya	Refugees: Ethiopians Somalis Sudanese	January 1, 2008
South Sudan	All applicants	July 9, 2011
Haiti	All applicants	September 26, 2009
Honduras	All applicants	June 1, 2012
China	All applicants	July 1, 2009
Philippines	All applicants	October 1, 2007
Jamaica	All applicants	May 1, 2013
Indonesia	All applicants	November 1, 2012

Analysis

Participant characteristics of refugee, other foreign-born, and US-born DeKalb County TB cases were compared using chi-square tests and univariate analyses to identify significant differences between groups.

Annual TB rates for each subgroup were calculated by dividing the annual incidence, new cases, by the corresponding subgroup population estimate. Case burden among refugee, other FB, and US-born were determined by annual percentages of total new DeKalb cases for each year.

To examine possible trends in foreign-born TB cases diagnosed ≤ 6 months of US entry before and after implementation of the revised CDC TI, logistic regression was used to model change in number of TB diagnoses ≤ 6 months of US entry against implementation status (pre vs. post) and immigration status (refugee vs. other-FB). Countries implemented the expanded CDC TI on a rolling basis from 2007 to 2013. Country of origin and refugee status was used to determine associated implementation date. 2004-2015 estimated TB incidence rates and case burden were compared with 1995-1999 data from Hadzibegovic et al. article to determine possible trends. All data was analyzed with SAS software, version 9.4 (SAS Institute, Cary, NC, USA).

Results:

Comparison of Refugee, Other FB, Total FB, and US-born TB Cases

From 2004 to 2015, a total of 898 active TB cases were diagnosed among DeKalb County residents, consisting of 569 total foreign-born cases, 144 refugees and 425 other foreign-born, and 329 US-born cases. Significant differences in many demographic characteristics were found among refugee, other FB, US origin, and total TB disease cases diagnosed in DeKalb County (Table 2). Age, race, TB verification, HIV status, and previous TB diagnosis were found to have significant p -values < 0.05 , considering the α -level was set to 0.05. The median (IQR) age for refugee, other FB, and US-born cases were 29 (19-45), 35 (27-46), and 45 (27-59) respectively. There were a total of 126 (14%) HIV positive individuals, including 13 (9%) refugees, 53 (12.5%) other FB, and 60 (18.2%) US-born. However, there were 95 missing values for HIV status, which may skew results and create bias. Most TB cases were verified with positive culture results 569 (63.4%), followed by 315 (35.1%) with clinical case definition, although verification with positive culture was slightly less than clinical case definition among refugees (48% vs 52%). Percentage of TB cases with previous TB diagnosis was 49 (5.5%), which only refugees had a higher proportion (9.7%). The greatest amount of total new cases/incidence were diagnosed in 2010 (Figure 1) with 96 (10.7%), and the least in 2015 57 (6.3%), with peaks in 2008 and 2012. Race was also found to be statistically significant, with the majority of cases Black (US-born 87.2%, other FB 40.0%) except among refugees where Asian (57.6%) was the majority, followed by Black (38.2%) and a small proportion of White (3.5%). The majority of cases were pulmonary only (73.6%), rather than pulmonary and extrapulmonary (2.8%) or extrapulmonary only (21.7%). Refugees had a higher percentage of individuals with only pulmonary (81.3%) than other FB (69.4%), or US-born (76.3%), although the differences were not found to be statistically significant.

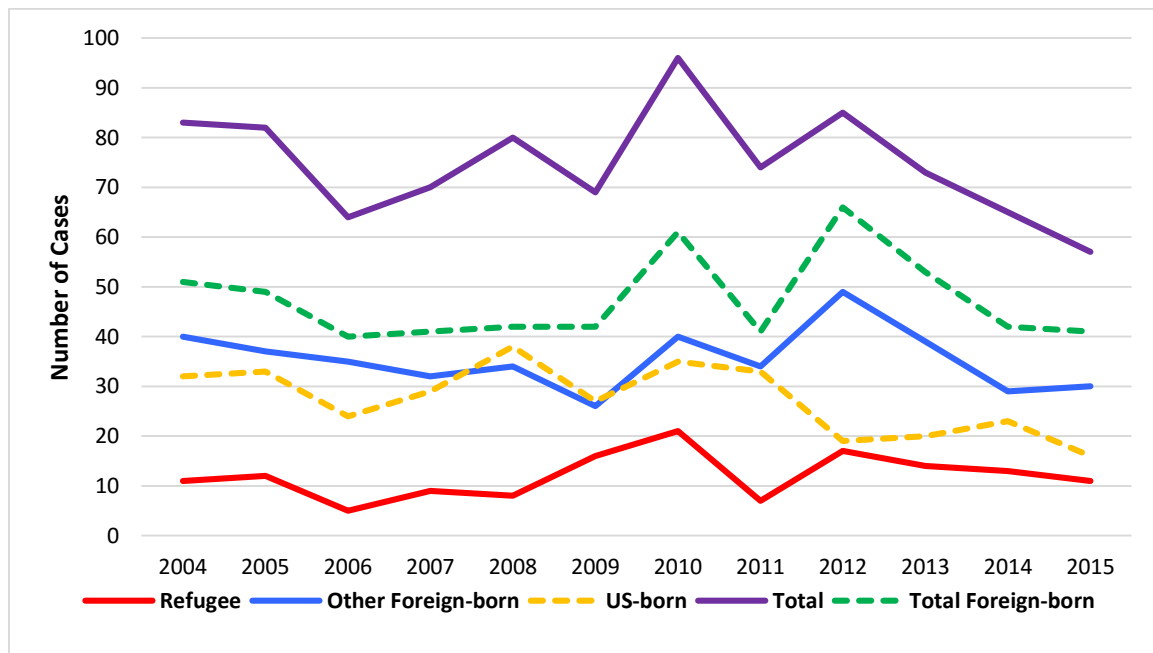


Figure 1. TB Incidence in DeKalb County (2004-2015)

Table 2. Characteristics of Refugee, Other FB, US Origin, and Total DeKalb County TB Cases (2004-2015)

Participant Characteristics	Refugee N= 144	Other FB N= 425	US Origin N= 329	Total N= 898	P-value
Age, years					
Median (IQR)	29 (19-45)	35 (27-46)	45 (27-59)	37 (26-52)	<0.0001
Age, n (%)					
0-5	11 (7.6)	2 (0.5)	31 (9.4)	44 (4.8)	<0.0001
6-14	11 (7.6)	11 (2.6)	16 (4.9)	38 (4.2)	
15-24	38 (26.4)	59 (13.9)	23 (7.0)	120 (13.4)	
25-44	48 (33.3)	233 (54.8)	94 (28.6)	375 (41.8)	
45-64	21 (14.6)	87 (20.5)	121 (36.8)	229 (25.5)	
≥ 65	15 (10.4)	32 (7.5)	44 (13.4)	91 (10.1)	
Missing	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.1)	
Sex, n (%)					
Male	92 (63.9)	259 (60.9)	204 (62.0)	555 (61.8)	0.8868
Female	52 (36.1)	163 (38.4)	124 (37.7)	339 (37.8)	
Missing	0 (0.0)	3 (0.7)	1 (0.3)	4 (0.4)	
HIV Status, n (%)					
Positive	13 (9.0)	53 (12.5)	60 (18.2)	126 (14.0)	0.0090
Negative	123 (85.4)	322 (75.8)	232 (70.5)	677 (75.4)	
Missing	8 (5.6)	50 (11.7)	37 (11.3)	95 (10.6)	
Race, n (%)					
Asian	83 (57.6)	120 (28.2)	5 (1.5)	208 (23.2)	<0.0001
Black	55 (38.2)	170 (40.0)	287 (87.2)	512 (57.0)	
White	5 (3.5)	121 (28.5)	37 (11.2)	163 (18.2)	
Missing	1 (0.7)	14 (3.3)	0 (0.0)	15 (1.7)	
TB Verification, n (%)					
Clinical Case Definition	75 (52.0)	121 (28.5)	119 (36.2)	315 (35.1)	<0.0001
Positive Culture	69 (48.0)	297 (69.9)	203 (61.7)	569 (63.4)	
NAA Positive Case	0 (0.0)	5 (1.2)	6 (1.8)	11 (1.2)	
Positive Smear/Tissue	0 (0.0)	2 (0.5)	1 (0.3)	3 (0.3)	
Disease Site, n (%)					
Pulmonary	117 (81.3)	295 (69.4)	251 (76.3)	663 (73.8)	0.0979
Pulmonary & Extrapulmonary	2 (1.4)	16 (3.8)	7 (2.1)	25 (2.8)	
Extrapulmonary	24 (16.6)	101 (23.8)	70 (21.3)	195 (21.7)	
Missing	1 (0.7)	13 (3.0)	1 (0.3)	15 (1.7)	
Previous TB Diagnosis, n (%)					
Yes	14 (9.7)	23 (5.4)	12 (3.6)	49 (5.5)	0.0317
No	129 (89.6)	383 (90.1)	311 (94.5)	823 (91.6)	
Missing	1 (0.7)	17 (4.0)	15 (4.6)	33 (3.7)	
Year of diagnosis, n (%)					
2004	11 (13.3)	40 (48.2)	32 (38.6)	83 (9.2)	0.0674
2005	12 (14.6)	37 (45.1)	33 (40.2)	82 (9.1)	
2006	5 (7.8)	35 (54.7)	24 (37.5)	64 (7.1)	
2007	9 (12.9)	32 (45.7)	29 (41.4)	70 (7.8)	
2008	8 (10.0)	34 (42.5)	38 (47.5)	80 (8.9)	
2009	16 (23.2)	26 (37.7)	27 (39.1)	69 (7.7)	
2010	21 (21.9)	40 (41.7)	35 (36.5)	96 (10.7)	
2011	7 (9.5)	34 (46.0)	33 (44.6)	74 (8.2)	
2012	17 (20.0)	49 (57.7)	19 (22.4)	85 (9.5)	
2013	14 (19.2)	39 (53.4)	20 (27.4)	73 (8.1)	
2014	13 (20.0)	29 (44.6)	23 (35.4)	65 (7.2)	
2015	11 (19.3)	30 (52.6)	16 (28.1)	57 (6.3)	

Annual TB Incidence Rates

Annual TB incidence rates were calculated among total DeKalb, US-born, total FB, refugee, and other FB from 2004 to 2015 (Table 3). For refugee and other FB, 3 different annual incidence rates were calculated due to the lack of data on refugee population numbers. Refugee population estimates equate to 10%, 15%, and 20% of the total FB population, therefore, other FB equate to 90%, 85%, and 80% of the total foreign born population. With the 10% estimate, throughout 2004-2015, refugees had the highest TB incidence rate, with a large peak in 2010 (186.2 per 100 000), followed by total FB (54.1), other FB (39.4), total DeKalb (13.9), and US-born (6.0) respectively (Figure 2). Total DeKalb and US-born rates declined throughout and stayed relatively low. Other FB and total FB incidence rates peaked in 2012 (47.2, 57.2, refugee: 147.2 per 100 000) but declined overall, with some fluctuations but not as extreme as the refugee incidence rate. With the 15% estimate (Figure 3), refugees remained the highest rates compared to other groups, including total and other FB, except for in 2006 when their rate (36.5, 37.6) was greater than the refugee rate (30.4). When refugee population equated to 20% and other FB to 80% of total FB population (Figure 4), refugees remained to have the highest TB incidence rates, except in 2011 where it was less than other FB and total FB (37.4, 36.0 vs. 30.8), slightly less in 2008 (38.3, 37.8 vs. 36.0), and much lower in 2006 (39.9, 36.5 vs. 22.8). Other FB rates closely followed the pattern of total FB incidence rates, although the total FB was higher during the refugee incidence peak years, due to total foreign born consisted of refugee and other FB. Overall, the refugee incidence rate declined from 2014 to 2015 by approximately 15.7% and declined for the last three years of the study period. US-born incidence rate peaked in 2008 (6.6 per 100 000) but remained relatively constant/steady and decreased to 2.6 per 100 000 persons in 2015, lower than any other subgroup rate, despite consisting of the majority of the county population.

In 2010, the incidence rate among White Americans was 2.1 per 100 000, while among Black Americans was 9.9 per 100 000. For total US-born, the TB incidence rate was 6.0 in 2010.

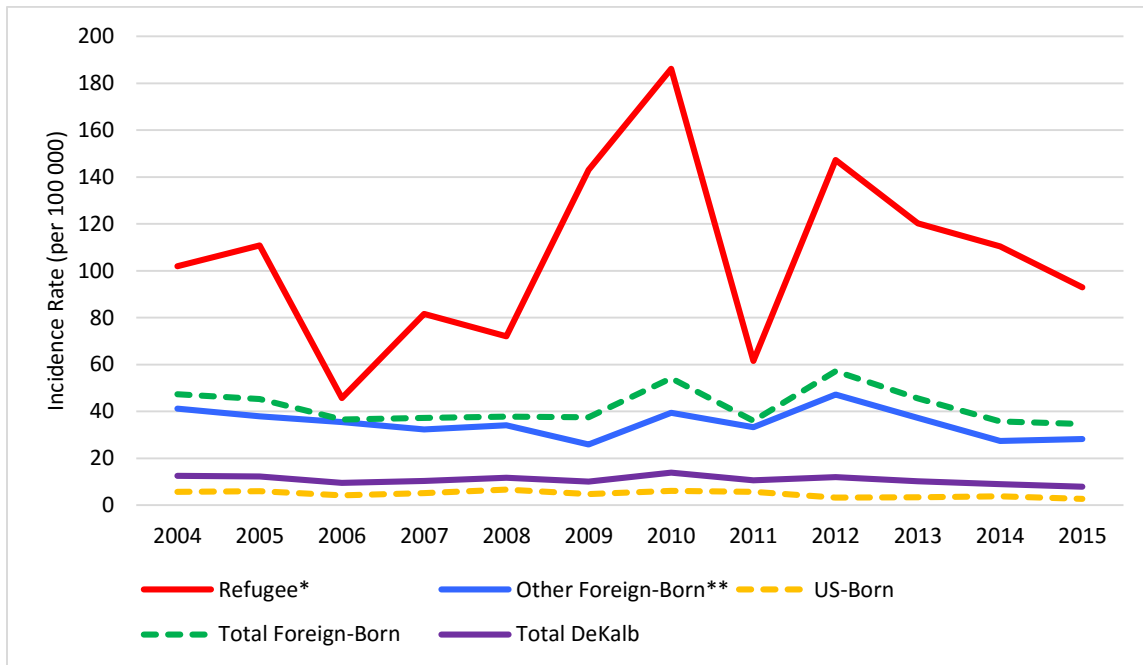


Figure 2. TB Incidence Rates Among Total DeKalb County, US-born, Total FB, Refugee, and Other FB Populations in DeKalb County (2004-2015); where *Refugee annual population is 10% and **other FB annual population is 90% of annual total FB population.

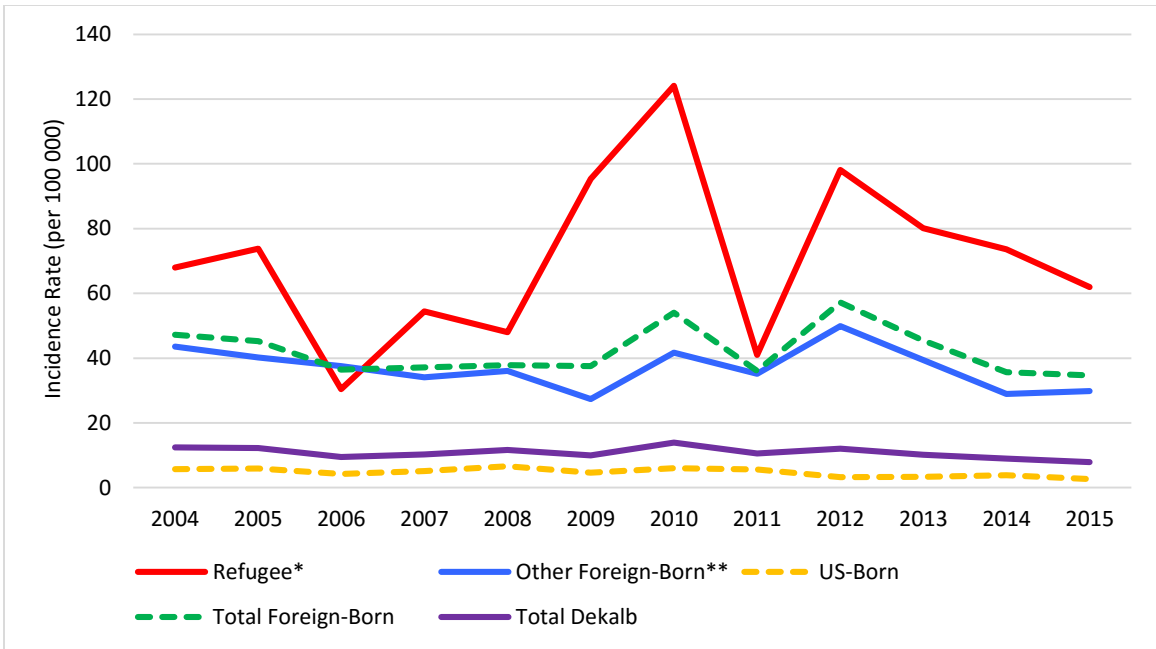


Figure 3. TB Incidence Rates Among Total DeKalb County, US-born, Total FB, Refugee, and Other FB Populations in DeKalb County (2004-2015); where *Refugee annual population is 15% and **other FB annual population is 85% of annual total FB population.

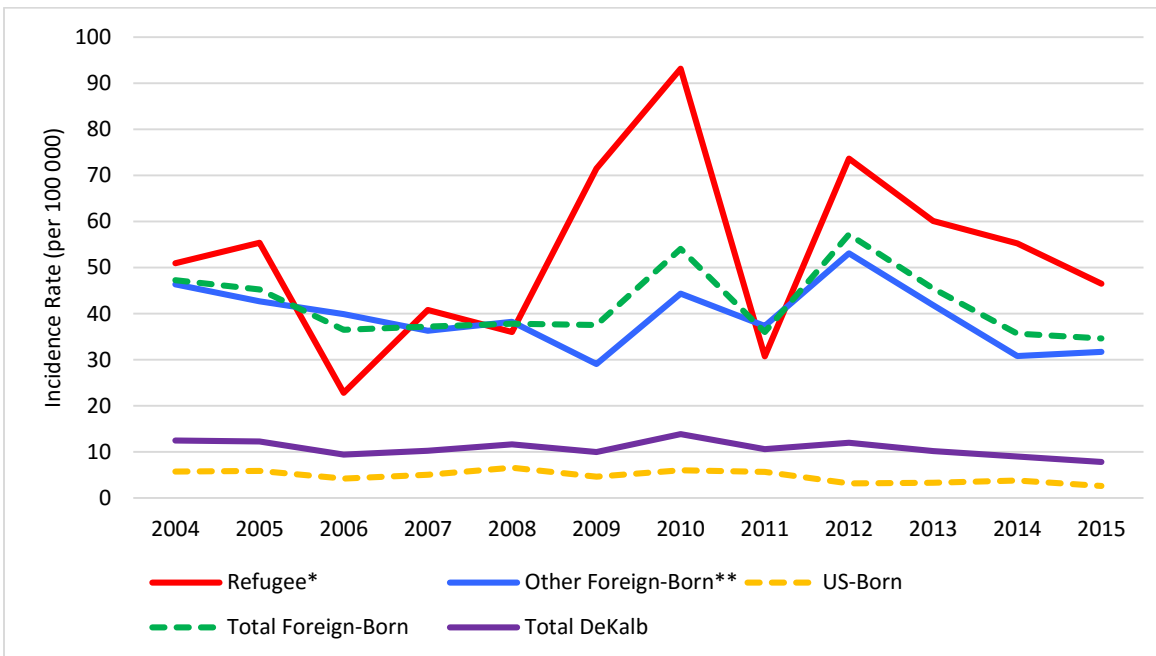


Figure 4. TB Incidence Rates Among Total DeKalb County, US-born, Total FB, Refugee, and Other FB Populations in DeKalb County (2004-2015); where *Refugee annual population is 20% and **other FB annual population is 80% of annual total FB population.

Table 3. Tuberculosis Disease Incidence Rates among Refugee, Other Foreign-born, Total Foreign-born, US-born, and Total County Populations in DeKalb County (2004-2015)

	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
No. Cases												
DeKalb	83	82	64	70	80	69	96	74	85	73	65	57
US-born	32	33	24	29	38	27	35	33	19	20	23	16
Total FB	51	49	40	41	42	42	61	41	66	53	42	41
Other FB	40	12	35	32	34	26	40	34	49	14	29	30
Refugee	11	37	5	9	8	16	21	7	17	39	13	11
Population												
DeKalb	666 204	668 998	676 687	680 962	685 646	690 658	691 893	697 953	708 304	714 935	722 161	726 171
US-born	558 279	560 620	567 064	570 646	574 571	578 771	579 114	584 187	592 851	598 401	604 449	607 805
Total FB	107 925	108 378	109 623	110 316	111 075	111 887	112 779	113 766	115 453	116 534	117 712	118 366
Other FB^a												
90%	97 132	97 540	98 661	99 284	99 967	100 698	101 501	102 389	103 908	104 881	105 941	106 529
85%	91 736	92 121	93 180	93 769	94 414	95 104	95 862	96 701	98 135	99 054	100 055	100 611
80%	86 340	86 702	87 698	88 253	88 860	89 510	90 223	91 013	92 362	93 227	94 170	94 693
Refugee^b												
10%	10 793	10 838	10 962	11 032	11 108	11 189	11 278	11 377	11 545	11 653	11 771	11 837
15%	16 189	16 257	16 443	16 547	16 661	16 783	16 917	17 065	17 318	17 480	17 657	17 755
20%	21 585	21 676	21 925	22 063	22 215	22 377	22 556	22 753	23 091	23 307	23 542	23 673
Incidence Rate^c												
DeKalb	12.5	12.3	9.5	10.3	11.7	10.0	13.9	10.6	12.0	10.2	9.0	7.8
US-Born	5.7	5.9	4.2	5.1	6.6	4.7	6.0	5.6	3.2	3.3	3.8	2.6
Total FB	47.3	45.2	36.5	37.2	37.8	37.5	54.1	36.0	57.2	45.5	35.7	34.6
Other FB^d												
90%	41.2	37.9	35.5	32.2	34.0	25.8	39.4	33.2	47.2	37.2	27.4	28.2
85%	43.6	40.2	37.6	34.1	36.0	27.3	41.7	35.2	49.9	39.4	29.0	29.8
80%	46.3	42.7	39.9	36.3	38.3	29.0	44.3	37.4	53.1	41.8	30.8	31.7
Refugee^e												
10%	101.9	110.7	45.6	81.6	72.0	143.0	186.2	61.5	147.2	120.1	110.4	92.9
15%	67.9	73.8	30.4	54.4	48.0	95.3	124.1	41.0	98.2	80.1	73.6	62.0
20%	51.0	55.4	22.8	40.8	36.0	71.5	93.1	30.8	73.6	60.1	55.2	46.5

^aOther foreign-born annual population numbers equal 90%, 85%, and 80% of the annual total foreign-born population.

^bRefugee annual population numbers equal 10%, 15%, and 20% of the annual total foreign-born population.

^cTuberculosis disease incidence rates (per 100 000 persons).

^dOther foreign-born annual TB incidence rates calculated with ^a90%, 85%, and 80% of the annual total foreign-born population numbers.

^eRefugee annual incidence rates calculated with ^b10%, 15%, and 20% of the annual total foreign-born population.

Pre- vs. Post-implementation

The study sample consisted of 449 TB cases from the following countries of origin; Ethiopia, Somalia, Burma, India, Vietnam, Mexico, Guatemala, Bangladesh, Bhutan, Honduras, Sudan, China, Haiti, Jamaica, Indonesia, and Philippines (Table 4). Refugee cases originated from Ethiopia, Somalia, Burma, Bhutan, Sudan, and Vietnam with one case. Thailand was not included, considering refugees in Thailand may be Hmong or Burmese. Individuals screened overseas pre-implementation and diagnosed after US entry consisted of 326 TB cases, 46 (14.1%) refugees and 280 (85.9%) other foreign-born. Individuals screened overseas post-implementation and diagnosed after US entry included 123 TB cases, 72 (58.5%) refugees and 51 (41.5%) other foreign-born (Figure 6). There was a 56.5% increase of refugee TB cases screened overseas pre-implementation to post-implementation, while other FB decreased by 81.8%. Refugee cases screened overseas pre-implementation mostly consisted of Burmese (32.6%) and Somali (32.6%) refugees, followed by those from Ethiopia (19.6%), Sudan (10.9%), and both Bhutan and Vietnam with one case (2.0%). Bhutanese refugees mostly entered the US post-implementation. Other FB cases screened overseas pre-implementation consisted of all of the countries of origin included in the sample except Bhutan. The highest percentages were among Mexico (22.5%) and Ethiopia (21.8%), followed by India (10.7%) and Vietnam (10.7%) with 30 cases each, Guatemala (9.3%), Somalia (6.8%), and Burma (5.4%). Refugees screened overseas post-implementation consisted of mostly Bhutanese (55.6%) and Burmese (29.2%), followed by those from Ethiopia (8.3%), Somalia (5.6%), and Sudan with one case (1.6%). Other FB cases screened overseas post-implementation consisted of mostly Ethiopian (56.9%), followed by Mexican (13.7%), and Vietnam (7.8%).

More than half were men among pre and post-implementation cases. More refugee cases were between the ages of 0-5 (pre: 4.3% vs. 0.3%, post: 6.9% vs. 2.0%) compared to other FB. Number of cases between 0-5 years of age increased among refugees post- compared to pre-implementation (5 vs 2). Most other FB cases were between ages 25-44, although decreased (61.4% to 51.0%). The median years of age of refugee TB cases screened overseas pre-implementation was 23.8 (IQR 19.1-35.6), while for other FB it was 34.8 years of age (IQR 27.2-44.8). The median age of TB diagnosis among other FB was 32.8 (IQR 23.6-41.4), while refugees were slightly older 34.3 (IQR 20.4-47.7) among post-implementation cases.

The majority of cases were verified by positive culture results, with the exception of refugees post-implementation with majority clinical case definition (59.7%). Verification by positive cultures decreased among refugees and other FB cases with prior history of TB diagnosis consisted of 10.9% refugees and 6.8% other FB pre-implementation, while 12.5% of refugees and no other FB screened post-implementation. HIV positive status seems to be more prevalent among other FB cases, however, there are a total of 7 missing values for refugees, and 36 among other FB to be able to make comparisons on HIV comorbidity. Pulmonary TB increased pre to post implementation for both groups, although remained higher percentage among refugees compared to other FB (83.8% vs 80.4%). Extrapulmonary prevalence decreased among both groups.

Median time from US entry to TB diagnoses decreased pre- to post-implementation among refugees (6.4 vs 2.3 months) and other FB (75.1 vs 15.9 months), although refugees were diagnosed more quickly. Diagnoses \leq 6 months from US arrival increased among refugees from 22 to 53, with a 140.9% increase pre- to post implementation. The number of other FB cases diagnosed \leq 6 months decreased by 62.2%, although the percentage increased (45, 16.1% to 17, 33.3%). Refugees diagnosed \leq 1 month increased from 7 (15.2%) to 18 (25.0%) and those diagnosed 2-3 months from US entry also increased from 9 (19.6%) to 21 (29.2%), pre- to post-implementation.

Table 4. Characteristics of Refugee and Other FB DeKalb County TB Cases (2004-2015) Pre- and Post-Implementation of Revised 2007 CDC Technical Instructions

Characteristics	Pre-implementation N=326		Post-implementation N=123	
	Refugee N=46 (14.1)	Other-FB N=280 (85.9)	Refugee N=72 (58.5)	Other-FB N=51 (41.5)
Country of Origin, n (%)				
Ethiopia	9 (19.6)	61 (21.8)	6 (8.3)	29 (56.9)
Somalia	15 (32.6)	19 (6.8)	4 (5.6)	2 (3.9)
Burma	15 (32.6)	15 (5.4)	21 (29.2)	1 (2.0)
India	0 (0.0)	30 (10.7)	0 (0.0)	3 (5.9)
Vietnam	1 (2.2)	30 (10.7)	0 (0.0)	4 (7.8)
Mexico	0 (0.0)	63 (22.5)	0 (0.0)	7 (13.7)
Guatemala	0 (0.0)	26 (9.3)	0 (0.0)	0 (0.0)
Bangladesh	0 (0.0)	9 (3.2)	0 (0.0)	1 (2.0)
Bhutan	1 (2.2)	0 (0.0)	40 (55.6)	0 (0.0)
Honduras	0 (0.0)	8 (2.9)	0 (0.0)	0 (0.0)
Sudan	5 (10.9)	1 (0.4)	1 (1.4)	0 (0.0)
China	0 (0.0)	4 (1.4)	0 (0.0)	1 (2.0)
Haiti	0 (0.0)	4 (1.4)	0 (0.0)	2 (3.9)
Jamaica	0 (0.0)	4 (1.4)	0 (0.0)	0 (0.0)
Indonesia	0 (0.0)	3 (1.1)	0 (0.0)	0 (0.0)
Philippines	0 (0.0)	3 (1.1)	0 (0.0)	1 (2.0)
Gender, n (%)				
Male	27 (58.7)	175 (62.5)	47 (65.3)	29 (56.9)
Female	19 (41.3)	103 (36.8)	25 (34.7)	22 (43.1)
Missing	0 (0.0)	2 (0.7)	0 (0.0)	0 (0.0)
Age, years				
Median (IQR)	23.8 (19.1-35.6)	34.8 (27.2-44.8)	34.4 (20.4-47.7)	32.8 (23.6-41.4)
Age, n (%)				
0-5	2 (4.3)	1 (0.3)	5 (6.9)	1 (2.0)
6-14	4 (8.7)	4 (1.4)	5 (6.9)	2 (3.9)
15-24	19 (41.3)	34 (12.1)	14 (19.4)	11 (21.6)
25-44	14 (30.4)	172 (61.4)	27 (37.5)	26 (51.0)
45-64	5 (10.9)	49 (17.5)	10 (13.9)	9 (17.6)
≥ 65	2 (4.3)	20 (7.1)	11 (15.3)	2 (3.9)
Time from US entry to TB Diagnosis, months				
Median (IQR)	6.4 (1.5-54.5)	75.1 (38.3-160.9)	2.3 (1.0-6.6)	15.9 (3.3-33.9)
Time from US entry to TB Diagnosis, months, n (%)				
0-1	7 (15.2)	3 (1.1)	18 (25.0)	7 (13.7)
2-3	9 (19.6)	8 (2.9)	21 (29.2)	5 (9.8)
4-6	5 (10.9)	10 (3.6)	14 (19.4)	5 (9.8)
7-12	6 (13.0)	9 (3.2)	7 (9.7)	4 (7.8)
13-24 (Year 2)	3 (6.5)	13 (4.6)	4 (5.6)	15 (29.4)
≥ 25 (Year 3)	15 (32.6)	213 (76.1)	8 (11.1)	15 (29.4)
Time from US entry to TB Diagnosis, months, n (%)				
0-6	22 (47.8)	45 (16.1)	53 (73.6)	17 (33.3)
>6	24 (52.2)	235 (83.9)	19 (26.4)	34 (66.7)
Disease Site, n (%)				
Pulmonary	33 (71.7)	192 (68.6)	60 (83.3)	41 (80.4)
Pulmonary and Extra	0 (0.0)	12 (4.3)	1 (1.4)	3 (5.9)
Extrapulmonary	13 (28.3)	72 (25.7)	10 (13.9)	6 (11.8)
Missing	0 (0.0)	4 (1.4)	1 (1.4)	1 (2.0)
TB Verification, n (%)				
Clinical Case Definition	18 (39.1)	80 (28.6)	43 (59.7)	21 (41.2)
Positive Culture	28 (60.9)	195 (69.6)	29 (40.3)	29 (56.8)
NAA Positive Case	0 (0.0)	3 (1.1)	0 (0.0)	1 (2.0)
Positive Smear/Tissue	0 (0.0)	2 (0.7)	0 (0.0)	0 (0.0)
Previous TB Diagnosis, n (%)				
Yes	5 (10.9)	19 (6.8)	9 (12.5)	0 (0.0)
No	41 (89.1)	252 (90.0)	62 (86.1)	51 (100.0)
Missing	0 (0.0)	9 (3.2)	1 (1.4)	0 (0.0)
HIV Status, n (%)				
Positive	4 (8.7)	28 (10.0)	4 (5.6)	10 (19.6)
Negative	40 (87.0)	218 (77.9)	63 (87.5)	39 (76.5)
Missing	2 (4.3)	34 (12.1)	5 (6.9)	2 (3.9)

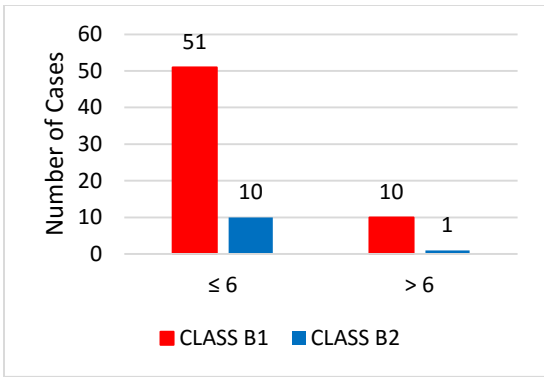


Figure 14. Immigrants and Refugees diagnosed ≤6 and > 6 months of US entry with B1 or B2 Classification

Table 5. TB Cases diagnosed ≤6 and > 6 months of US entry with B1 or B2 Classification

	Time	Class B1	Class B2
Pre-implementation	≤ 6	11	5
	> 6	5	0
Post-implementation	≤ 6	31	2
	> 6	5	0
Refugee	≤ 6	36	6
	> 6	9	0
Other FB	≤ 6	28	5
	> 6	7	0

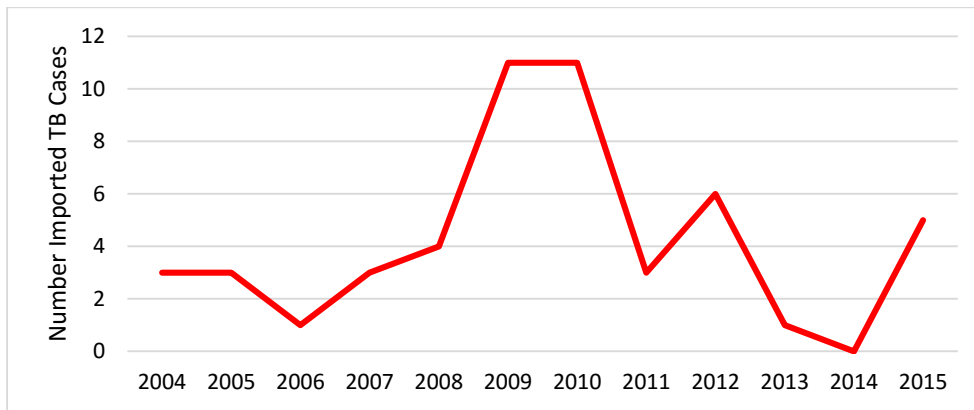


Figure 15. Number of Imported TB cases in DeKalb County diagnosed during 2004-2015

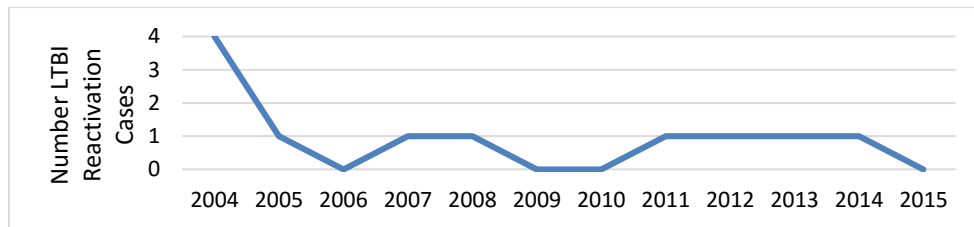


Figure 16. Number of LTBI Reactivation cases in DeKalb County diagnosed during 2004-2015

TB classifications from pre-immigration TB screening consisted of 72 out of 569 foreign-born TB cases in DeKalb County from 2004 to 2015, where 51 of 61 (83.6%) persons with B1 classification were diagnosed within ≤ 6 of US entry (Figure 14), which is considered to be imported TB (Walter et al., 2014). Among cases with prior class B2 TB, 10 of 11 (90.9%) were diagnosed ≤ 6 months of US entry, which is considered LTBI reactivation. More imported TB cases occurred post-implementation compared to pre-implementation (31 vs 11, 73.8%) (Table 5), with the assumption that all Burmese refugee cases departed from Malaysia rather than Thailand. The number of imported TB cases was greater among refugees than other FB (36 vs 28). Largest number of imported TB cases were diagnosed in 2009 and 2010, with 11 cases in both years, which declined to 3 in 2011, followed by an increase to 6 cases (Figure 15). Although the number of cases decreased to zero in 2014, it again increased to 5 cases in 2015. In 2004, the highest number of LTBI reactivation cases were diagnosed, followed by a decrease to 1 case, which was consistent in each year, except in 2006, 2009, 2010, and 2015 where there were no cases (Figure 16).

Out the sample of 449 TB cases (Table 4), 52 (11.6%) cases had prior B1 classification, 35 (67.3%) were from countries of origin Bhutan (20, 38.5%) and Burma (15, 28.8%). Among Bhutanese cases with Class B1, 17 of 20 (85%) were diagnosed ≤ 6 of US entry (Table 6), thus considered imported TB. Among Burmese cases with prior B1 classification, 13 of 15 (86.7%) were diagnosed ≤ 6 months of US arrival. The majority of class B1 diagnosed ≤ 6 months was also the case for Ethiopia (3 of 5), Vietnam (3 of 5), and Somalia (3 of 3). The majority of these cases in Ethiopia occurred post-implementation. Due to unknown host country and suspected refugee status of Burmese cases, refugee status and host country implementation date were varied to examine possible imported TB cases pre- vs post-implementation (Table 7). Most conservative estimates involved association of Burmese refugees with Malaysia refugee implementation date (1.5 years after Thailand implementation date) and other FB Burmese with all applicants Burma implementation date, which resulted in 4 of 6 (66.7%) imported TB pre-implementation and 9 of 9 (100%) imported TB among those screened post-implementation. In all scenarios over 92% cases among those screened post-implementation were considered to have imported TB, which ranged from 9-12 cases, and were greater than those screened pre-implementation (1-4). All B2 class persons (6) were diagnosed ≤ 6 months, which is considered LTBI reactivation.

Table 6. TB Cases diagnosed ≤ 6 and > 6 months from US entry with prior B1 or B2 Classification Pre and Post-Implementation of 2007 Expanded CDC TI by Country of Origin

TB Classification	Class B1				Class B2			
	Pre		Post		Pre		Post	
Country of Origin	≤ 6	> 6	≤ 6	> 6	≤ 6	> 6	≤ 6	> 6
Bhutan	0	0	17	3	0	0	2	0
Burma	4	2	9	0	1	0	0	0
Ethiopia	0	1	3	1	1	0	0	0
Vietnam	2	1	1	1	0	0	0	0
Somalia	3	0	0	0	2	0	0	0

Table 7. Cases with Burmese origin diagnosed ≤ 6 and > 6 months from US entry with prior B1 classification pre- and post-implementation of 2007 CDC Technical Instructions

2007 CDC TI Implementation	Pre		Post	
	≤ 6	> 6	≤ 6	> 6
Burmese Refugee – Malaysia ^a	4	2	9	0
Burmese Refugee – Thailand ^a	2	1	11	1
All Burmese- Malaysia ^c	3	2	10	0
All Burmese- Thailand ^d	1	1	12	1

^aBurmese refugees with Malaysia implementation date and Burmese other FB with Burma implementation date

^bBurmese refugees with Thailand implementation date and Burmese other FB with Burma implementation date

^cAll Burmese cases assumed to have refugee status with Malaysia implementation date

^dAll Burmese cases assumed to have refugee status with Thailand implementation date

Logistic regression I

Logistic regression was used to model change in number of TB diagnoses ≤ 6 months of US entry against implementation status (pre vs. post) and immigration status (refugee vs. other-FB). Country was not included in the model due to few TB cases in most countries.

Model:

$$\text{Logit}(P(\text{TB diagnosis} \leq 6 \text{ months of US entry})) \\ = -1.6679 + 1.6299_{STATUS} + 1.0240_{IMPLEMENTATION}$$

The *p*-value for both immigration status (*STATUS*) and the revised CDC Technical Instructions implementation (*IMPLEMENTATION*) were significant (<0.0001), since the α -level was set to 0.05.

Odds Ratios:

Immigration status (refugee vs. other-foreign born): 5.103 (95% CI: 3.085 – 8.442). The odds of TB diagnosis within 6 months of US entry among refugees is 5.103 times the odds of TB diagnosis within 6 months of US entry among other foreign-born controlling for implementation of revised CDC technical instructions.

CDC revised TB technical instructions implementation (pre vs. post): 2.784 (95% CI: 1.683 – 4.606). The odds of TB diagnosis within 6 months of US entry among those screened overseas after implementation is 2.784 times the odds of TB diagnosis within 6 months of US entry among those screened overseas before implementation controlling for immigration status (refugee vs other FB).

Logistic regression II (assuming Burmese other FB are refugees due to dates of entry consistent with time of Burmese refugee arrivals in GA)

Model:

$$\begin{aligned} & \text{Logit}(P(\text{TB diagnosis} \leq 6 \text{ months of US entry})) \\ & = -1.6639 + 1.4944_{STATUS} + 0.8919_{IMPLEMENTATION} \end{aligned}$$

The *p*-value for both immigration status (<0.0001) and the revised CDC Technical Instructions implementation (0.0004) were significant.

Odds Ratios:

Immigration status (refugee vs. other-foreign born): 4.457 (95% CI: 2.740 – 7.250).

CDC revised TB Technical Instructions implementation (pre vs. post): 2.440 (95% CI: 1.490 – 3.994). The odds ratios only slightly changed when all Burmese cases were defined as refugee cases.

Comparison of (1995-1999) and (2004-2015) TB Incidence Rates and Case Burden

The incidence rates from 1995 to 1999 were obtained from Hadzibegovic et al (2005). These rates were compared with the 2004 to 2015 estimated incidence rates. The US-born rate decreased drastically from 1995 (13.3 per 100 000) to 2015 (2.6). From 1999 to 2004 the US-born rate decreased by 46.2% (10.6 vs. 5.7 per 100 000), nearly half, while other FB (44.7 vs. 41.2) and refugee (122.9 vs. 101.9) which then peaked in 2009 and 2012. Foreign-born rates fluctuated from 1995 to 1999, as well as during 2004-2015. The total county and US-born rates declined and never reached the same rates in 2004-2015 as those during 1995-1999. Data for 2000-2003 was not available due to no prior records in SENDSS and lack of access to patient charts. The total number of cases in DeKalb County has been overall decreasing since 1999, with some fluctuations (Figure 8).

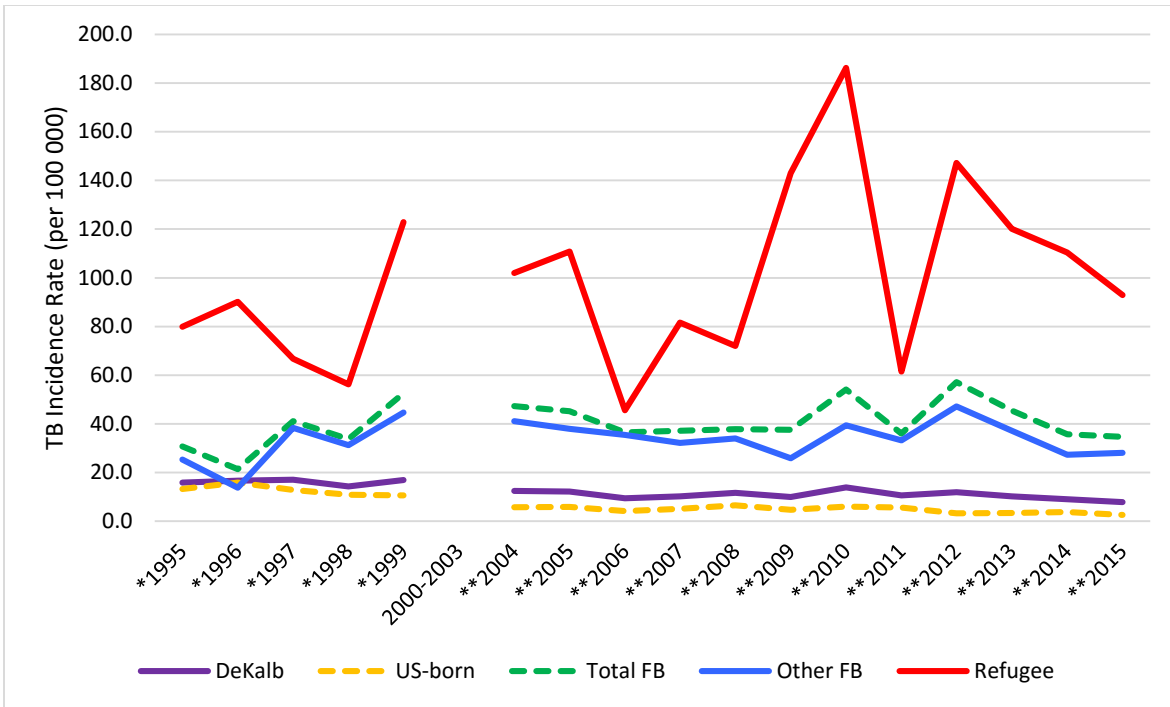


Figure 6. TB Incidence Rates among Total County, US-born, Total Foreign-born, Refugee, and Other Foreign-born populations in DeKalb County

*(1995-1999) rates obtained from Hadzibegovic et al. (2005)

** (2004-2015) rates from this study

Table 4. TB Incidence Rates Among County Total, US-born, Total Foreign-born, Refugee and Other Foreign-born populations in DeKalb County (1995-1999)* (2004-2015)**

	1995	1996	1997	1998	*1999	2000-2003	**2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
DeKalb	15.9	16.7	17.0	14.3	16.9		12.5	12.3	9.5	10.3	11.7	10.0	13.9	10.6	12.0	10.2	9.0	7.8
US-born	13.3	15.9	12.8	10.9	10.6		5.7	5.9	4.2	5.1	6.6	4.7	6.0	5.6	3.2	3.3	3.8	2.6
Total FB	30.8	21.4	41.1	33.7	52.5		47.3	45.2	36.5	37.2	37.8	37.5	54.1	36.0	57.2	45.5	35.7	34.6
Other FB	25.4	13.8	38.3	31.2	44.7		41.2	37.9	35.5	32.2	34.0	25.8	39.4	33.2	47.2	37.2	27.4	28.2
Refugee	79.9	90.1	66.7	56.2	122.9		101.9	110.7	45.6	81.6	72.0	143.0	186.2	61.5	147.2	120.1	110.4	92.9

*(1995-1999) TB Incidence Rates obtained from Hadzibegovic et al. (2005)

** (2004-2015) TB incidence rates estimated from this study

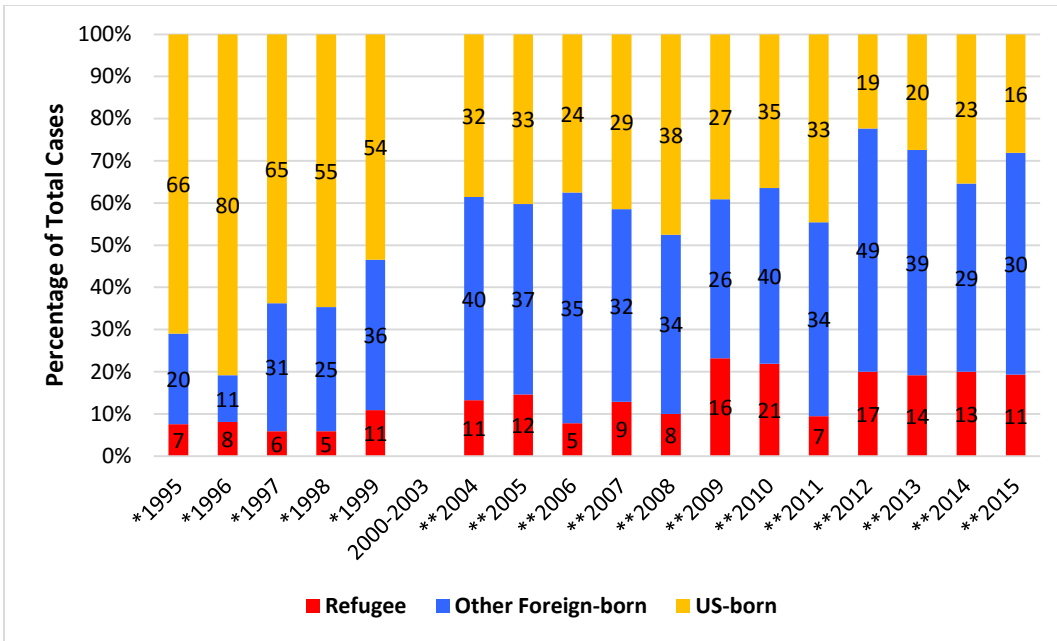


Figure 7. DeKalb County TB Case Burden among Refugee, Other-FB, and US-born
 *(1995-1999) rates obtained from Hadzibegovic et al. (2005)
 ** (2004-2015) rates from this study

During 1995-1999, US-born cases comprised more than half of new annual TB cases in DeKalb County with a peak in 1996 with 80 cases (80.8%) (Figure 7). During 2004-2015, US-born cases were less than half of annual total cases, with the least in 2015 (28.1%). Refugee cases were relatively few during 1995-1999 where the largest case burden of 10.1% of number of total county cases in 1999, however, refugee cases increased with fluctuations, with the highest burden in 2009 (23.2%) and decreased in 2015 (19.3%). Other foreign-born cases increased during 2004-2015 compared to 1995-1999, which peaked in 2012 with 49 cases (57.6%). The total number of new cases has decreased since 1995-1999, although population increased annually.

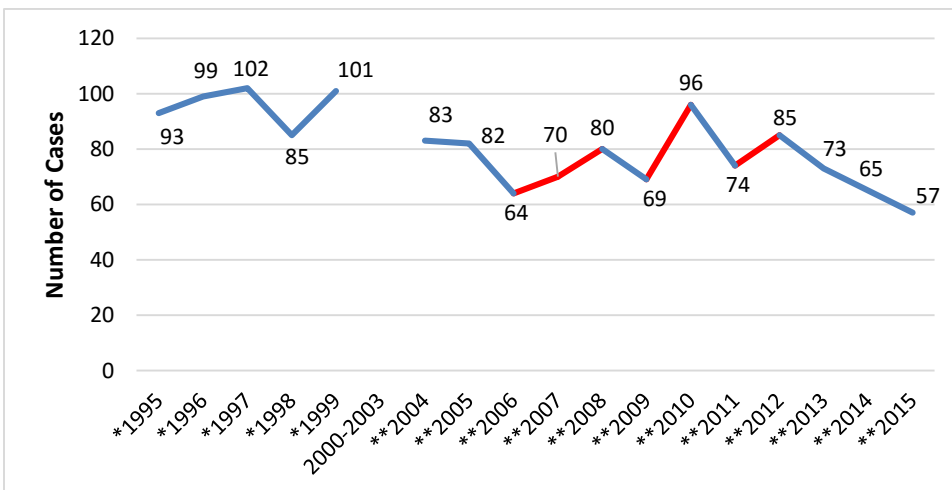


Figure 8. Total TB incidence (number of new cases) in DeKalb County
 *(1995-1999) rates obtained from Hadzibegovic et al. (2005)
 ** (2004-2015) rates from this study

Discussion:

Although TB cases and rates have decreased in DeKalb County over the last decade, particularly among US-born persons, the foreign-born population faces the majority of the county disease burden, which was 72% in 2015, compared to 66.2% among total US cases. Total foreign-born annual incidence rates decreased overall, however fluctuated throughout the years, sometimes drastically, especially among refugees. Refugee rates in DeKalb County are more comparable to rates in high TB incidence low and middle-income countries rather than to other US rates, which was also concluded by a previous study in DeKalb County (Hadzibegovic et al., 2005). Contributing factors may include large proportion of other FB and refugees diagnosed ≤ 6 months of US entry, which suggests possible imported TB or LTBI activation. Identification of imported TB and LTBI reactivation cases in DeKalb County during 2004-2015, suggests a high proportion of cases that may have been able to be prevented before US arrival.

Majority of Class B1 cases (83.6%) and Class B2 cases (90.9%) were diagnosed ≤ 6 months of US entry. These high proportions of TB importation and LTBI reactivation occurred among mostly refugees (56.3%). Over half (57.4%) of persons with B1 classification were from countries of origin Bhutan (20) and Burma (15), both among the top 5 countries of origin among TB cases in DeKalb County, and the highest number of refugee arrivals in GA during 2004-2015 (Figure 12). All Bhutanese refugees were screened overseas post-implementation, which included 17 out of 20 (85%) with imported TB. Therefore, investigation into the large proportion of importation of TB is important, especially due to this occurrence post-implementation of expanded 2007 CDC TI, as well as the fact that all Bhutanese refugees are screened 6 months pre-arrival and those with Class B1 were screened 3 weeks before departure to the US (Quarantine, 2014).

Majority of B1 cases of Burmese origin (85.7%) imported TB, including 9-12 cases post-implementation. All class B2 cases (Table 6) were considered to have developed TB due to LTBI reactivation, since all were diagnosed ≤ 6 months. This further provides evidence for the need to focus TB elimination efforts toward prevention as well as treatment, along with improving screening or implementation of expanded CDC TI, especially among refugees. Also, studies have suggested overseas treatment of applicants with culture-negative active TB or inactive pulmonary TB to reduce imported TB. The huge influx of refugees in GA diagnosed within 6 months can greatly affect TB incidence in populations. Bhutanese and Burmese refugees accounted for 90% all refugee arrivals from countries with highest contribution to TB case burden in DeKalb County during 2004-2015, with peaks during higher incidence years.

Proportions of cases diagnosed ≤ 6 months without overseas TB classification were also identified pre vs post-implementation. The greatest number of refugee TB cases diagnosed ≤ 6 months of US entry were from Bhutan, Burma, Ethiopia, and Somalia (Figure 10). Ethiopian and Somali refugee cases diagnosed ≤ 6 months reduced after implementation except for 4 cases from Somalia and Ethiopia during 2012-2013, although it is unknown if implementation was causally associated due to lack of overseas screening results. The decrease may be due to relatively low number of refugee arrivals from Ethiopia and Somalia. The only year other countries had a greater percentage diagnosed ≤ 6 months than Burma, Bhutan, and Ethiopia was 2011. Other FB cases from Ethiopia had a higher proportion of cases diagnosed ≤ 6 months than Ethiopian refugee cases. The large proportion of TB cases diagnosed ≤ 6 months particularly among refugees suggests a possible high burden of imported TB or reactivation of LTBI. In 2010, Ethiopian, Bhutanese, and Burmese cases accounted for nearly 50% of all foreign-born TB cases in DeKalb County, which may have been a major factor in spike in county TB incidence in 2010 (Figure 8).

Burmese refugee cases diagnosed ≤ 6 months peaked in 2007 (4, 100%), the second year of Burmese refugee arrivals in Georgia (Figure 11), and 2013 with 4 cases (50%), although in the first

year, 2006, there were very few GA refugee arrivals. Burmese refugees diagnosed ≤ 6 months decreased in 2008-2009, after implementation in Thailand for Burmese refugees. An increase in 2010 occurred (3), corresponding with a large increase in Burmese refugee arrivals, despite implementation in Malaysia in 2009, and prior implementation in Thailand in 2007, and again increased during 2011-2014, but decreased from 2014-2015 by 2 cases, which may be associated with a decrease of approximately 200 Burmese refugee arrivals in GA. Bhutanese refugee cases diagnosed ≤ 6 months began in 2008 (2), the first year of Bhutanese refugee arrivals in Georgia, increased in 2009 (6, 75%), peaked in 2010 (7, 77.8%), again increased in 2012 (5, 71.4%), decreased until remaining at 2 cases during 2014 (50.0%), and 2015 (33.3%), the first years the percentage of Bhutanese cases diagnosed ≤ 6 months were below 70%. Bhutanese and Burmese refugee cases were the only cases in 2015 diagnosed ≤ 6 months of US entry among the highest TB incidence refugee countries of origin in DeKalb County, 4 cases of which were found to be due to imported TB (Figure 15).

Large numbers of Burmese and Bhutanese refugee arrivals in GA (Figure 12) and large percentage of cases diagnosed ≤ 6 months of US entry, along with the identified imported TB cases, may have contributed to the increase in county TB cases in 2007-2008, 2010, and 2012 (Figure 8). As large increases in annual population numbers among Bhutanese and Burmese refugee arrivals in GA, increases in TB cases among these countries seem to be associated along with the drastic increases of total county diagnosed cases, as well as total county incidence rates, although particularly refugee incidence rates, since considering that majority are diagnosed ≤ 6 months and are refugees. In 2011, there was a large drop in refugee incidence rate which corresponds with the drop in Bhutanese and Burmese refugee TB cases.

A few limitations of this study should be addressed. The greatest percentage, 20% of total FB population, was used for more conservative annual refugee population and incidence estimates. Therefore, it is likely the incidence rates for refugees was underestimated. Another contributing factor to this underestimation may be lack of identification of all refugee cases. The list of refugees in InSight only include refugees seen at DeKalb County Board of Health. Therefore, refugees that moved to DeKalb County after post-arrival screening elsewhere, such as other counties or states, would be defined as 'other FB' rather than 'refugee', which SENDSS does not differentiate. This may be the case for Burmese persons defined as other FB, since dates of entry of these individuals coincide with the dates refugees arrived in Georgia. However, odds ratios only slightly changed but remained significant when all cases from Burma were assumed to be refugees. DeKalb County resettles the most refugees than other counties in GA, with 90% refugees in 2010 (G. D. o. C. Health, 2011). Number of refugees screened annually in DeKalb County remained above 75% of total refugee arrivals in GA throughout fiscal years 2004-2014. In some years, the percentage reached nearly 100% if not more, which may suggest that many refugees move to DeKalb, shortly after arrival in another county or state (Table 8).

To estimate overseas medical evaluation dates, 180 days were subtracted from US entry dates, which were used to determine cases screened overseas pre vs post-implementation. This was done due to inaccessible data on overseas medical evaluation results, TB classification, and dates. When 360 days instead of 180 days were subtracted, considering the 1991 CDC TI implementation allowed applicants up to a year to enter US after medical evaluation results overseas, the odds ratios slightly decreased, however remained to be statistically significant for both predictor variables (implementation, status). Data on overseas evaluation results, TB classification, evaluation date, and host country would provide data for more accurate comparisons of pre vs post-implementation cases. This is also the case for the assumptions made by associating Burmese refugees with Malaysia implementation dates for refugees, since it was 1.5 years after the Thailand implementation dates for refugees, due to refugee host countries unknown. These

refugees also originate from high TB incidence/prevalence countries and live in host countries often with high numbers as well, and sometimes even higher such as Bhutanese living in Nepal. Another limitation is that undocumented and temporary visa holders are not differentiated from immigrants who were required to undergo overseas TB screening. Therefore, including them in analyses of cases diagnosed within 6 months of US arrival, may produce skewed results.

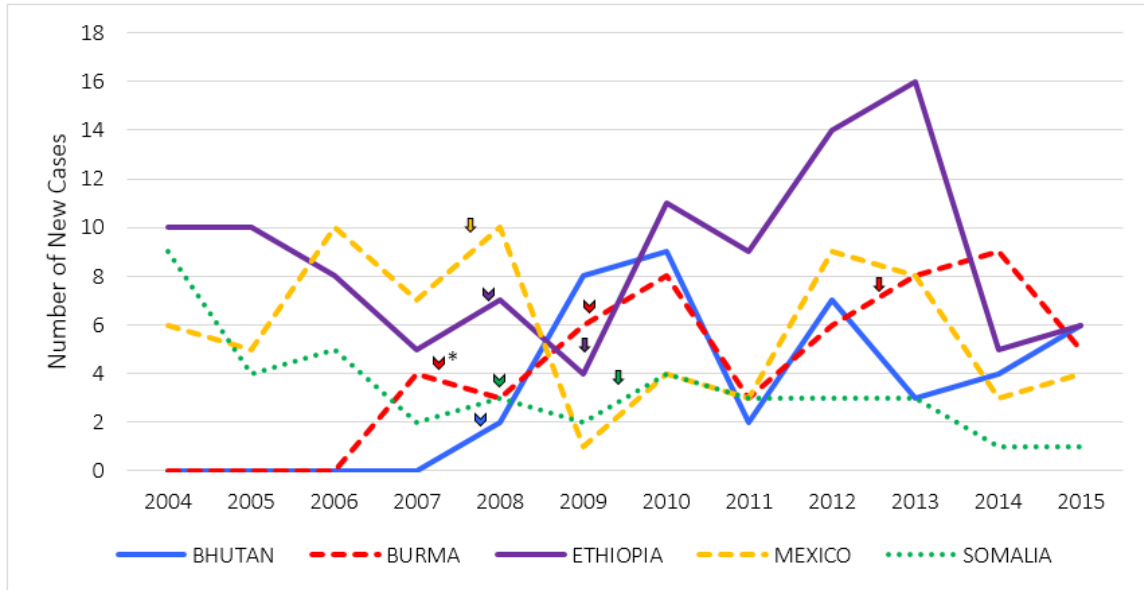


Figure 9. Number of Total Foreign-born TB Cases by Top 5 Countries of Origin in DeKalb County (2004-2015)

↙ Revised 2007 CDC Technical Instructions Implementation for Refugees
 ↓ Revised 2007 CDC Technical Instructions Implementation for All Applicants
 * Implementation Date for Burmese refugees in Thailand

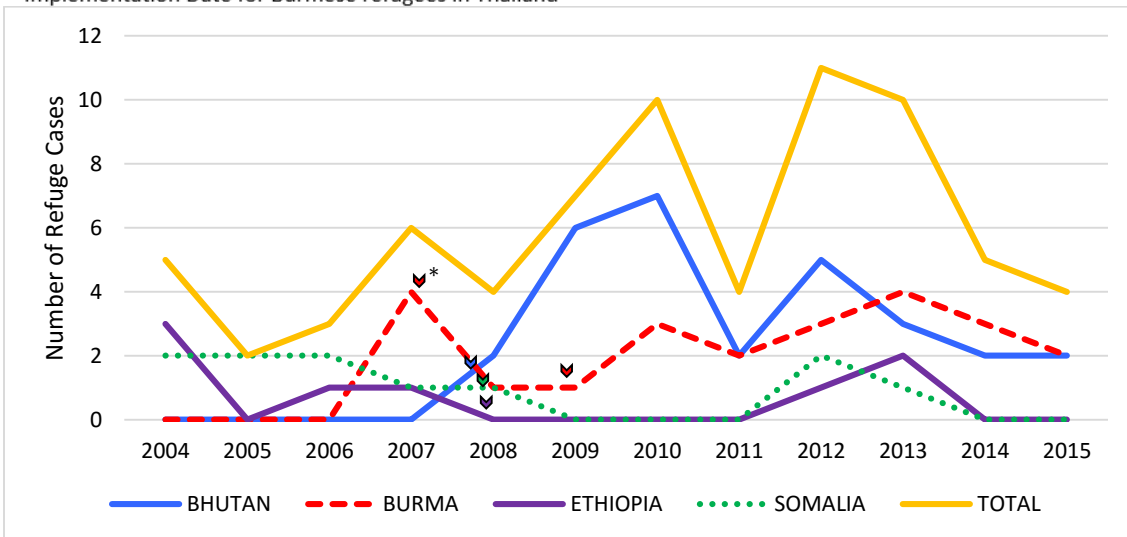


Figure 11. Number of Bhutanese, Burmese, Ethiopian, and Somali TB Cases Diagnosed Within 6 Months of US Entry in DeKalb County (2004-2015)

↙ Revised 2007 CDC Technical Instructions Implementation for Refugees
 ↓ Revised 2007 CDC Technical Instructions Implementation for All Applicants
 * Implementation Date for Burmese refugees in Thailand

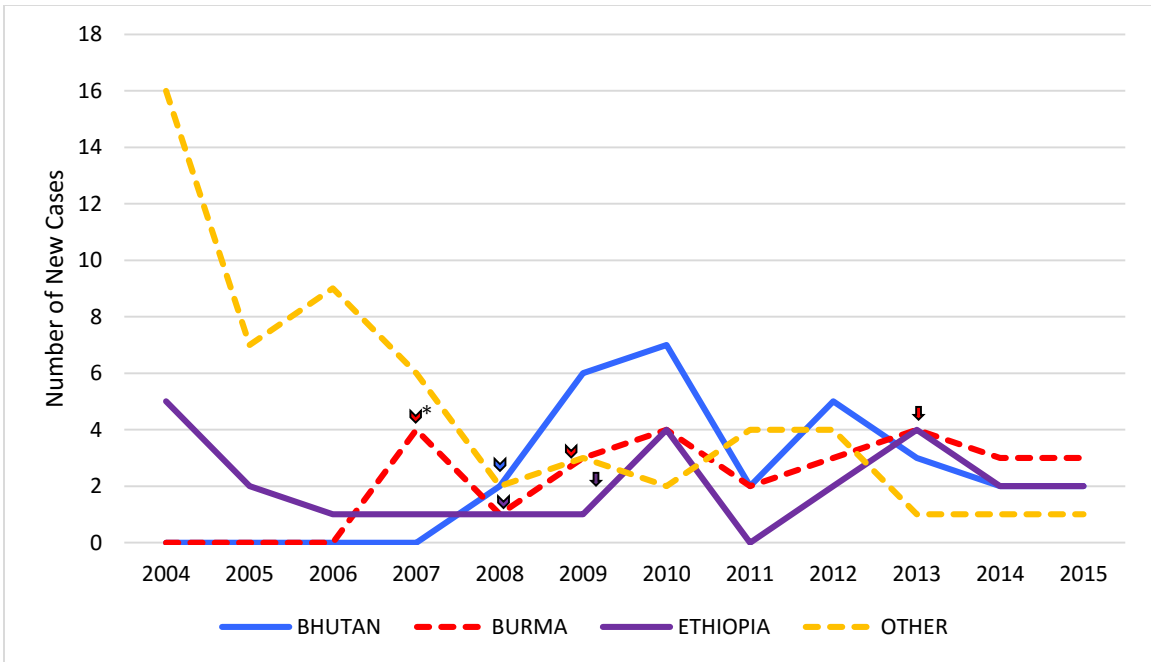


Figure 10. Number of Bhutanese, Burmese, Ethiopian, and other TB Cases in DeKalb County diagnosed within 6 months of US Entry (2004-2015).

- ↘ Revised 2007 CDC Technical Instructions Implementation for Refugees
- ↓ Revised 2007 CDC Technical Instructions Implementation for All Applicants
- * Implementation Date for Burmese refugees in Thailand

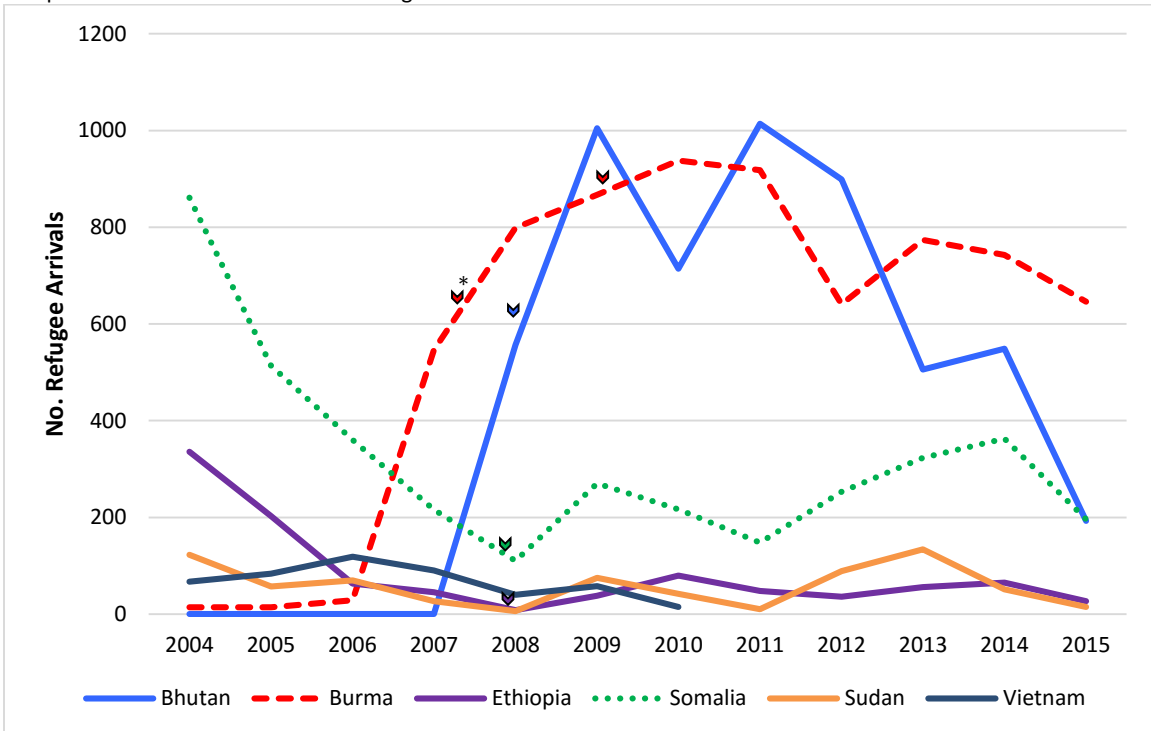


Figure 12. Number of Refugee Arrivals in GA (FY 2004-2015) from Selected Countries of Origin

- ↘ Revised 2007 CDC Technical Instructions Implementation for Refugees
- ↓ Revised 2007 CDC Technical Instructions Implementation for All Applicants
- * Implementation Date for Burmese refugees in Malaysia

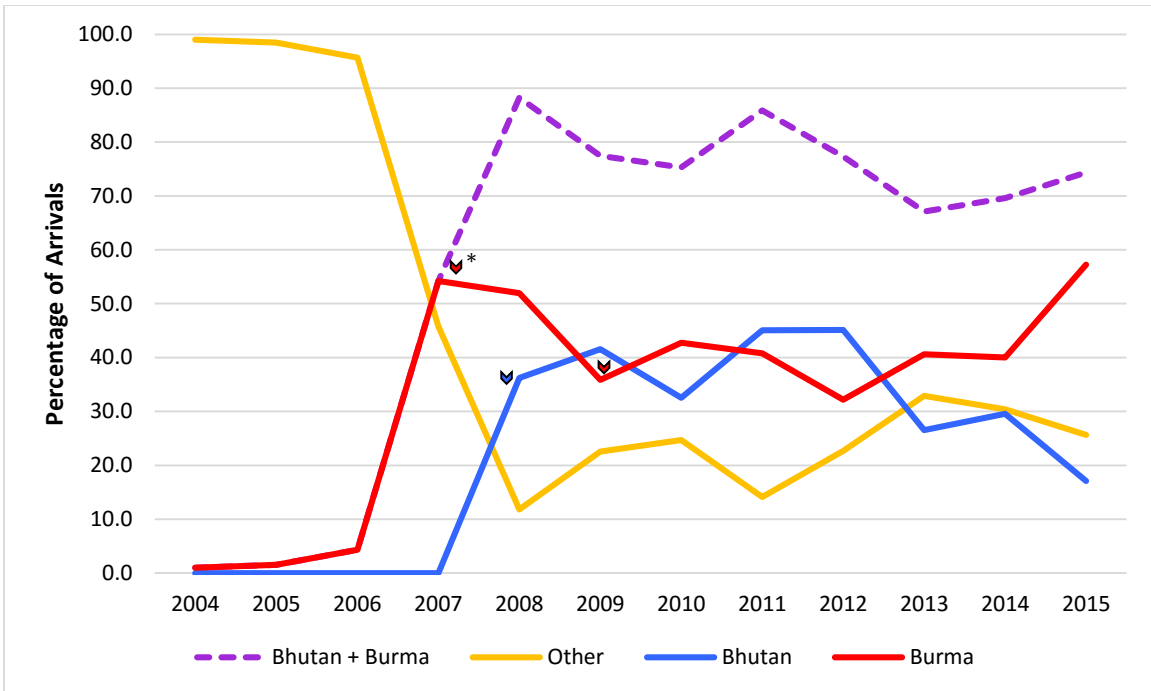


Figure 13. Percentage of Bhutanese, Burmese, and Other** Refugee Arrivals in GA (2004 - 2015)

**Other refugee countries of origin include Eritrea, Ethiopia, Somalia, Sudan, and Vietnam.

↘ Revised 2007 CDC Technical Instructions Implementation for Refugees

↓ Revised 2007 CDC Technical Instructions Implementation for All Applicants

* Implementation Date for Burmese refugees in Malaysia

Table 8. GA Refugee Arrivals

Fiscal Year	GA Total	DeKalb Screened	LPR GA Refugee/Asylee
2004	2165	1408	1736
2005	1860	1265	3621
2006	1457	1305	4174
2007	1624	1213	2805
2008	2340	1718	3338
2009	3275	2959	3945
2010	3230	3248	3498
2011	2635	2584	4031
2012	2513	2516	4156
2013	2706	2466	3078
2014	2699	2446	
2015	1860		

Conclusion:

Although TB cases and rates have decreased in DeKalb County over the years, particularly among US-born persons, the foreign-born population remains disproportionately afflicted, with majority of county disease burden, over 70% in 2015. Refugee TB rates in DeKalb County are more comparable to rates in high TB incidence low and middle-income countries rather than US rates. Imported TB and LTBI activation may be major factors involved in the stagnation of progression towards TB elimination.

TB elimination in the US and other 'developed' countries cannot be achieved without the realization that TB is a global issue and efforts should be refocused on LTBI identification and treatment as well as the prior focus of detection and treatment of active TB. Merely screening those that are entering the country with the intention to stay permanently will not eliminate TB or the importation of TB. Due to an increasingly globalized society with many war torn and crises affected populations, TB prevention along and conflict prevention efforts must be considered. With the increase in number of cases for the first time since WHO first declared TB a global emergency in 1993, refocus on those disproportionately afflicted must be also focused on.

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