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A Comparative Analysis in the Annual Rate of Change in US-born Non-Hispanic Black and US-born Non-Hispanic White Tuberculosis Cases, 1993-2011

By

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Master of Science in Public Health

Epidemiology

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Samford University

2011

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Abstract

A Comparative Analysis in the Annual Rate of Change in US-born Non-Hispanic Black and US-born Non-Hispanic White Tuberculosis Cases, 1993-2011

By Scott Cope

Background: Tuberculosis in the United States remains a major public health problem as prevention efforts have failed to reach previous goals of elimination. Despite this, annual CDC reports have shown US-born TB cases declining since 1993. In particular, US-born non-Hispanic black TB cases have declined dramatically since 2007.

Objective: The purpose of this study is to analyze the US-born non-Hispanic black TB case counts to determine if a) the sharper decline since 2007 is significant and b) if this decline is significantly different from the US-born white TB case count in the same time period. Case counts are analyzed here instead of incidence rates due to the amount of burden TB has on health program resources and its significant treatment time (~12 months).

Methods: Data collected from 1993-2011 as part of the National Tuberculosis Surveillance System (NTSS) was used to compare US-born black and white TB cases. Using JoinPoint 4.0.4 software and its spline/knot algorithm, graphs were generated to determine average annual percent change (APC) and SAS was incorporated to confirm the estimates that JoinPoint produced.

Results: From 1993 to 2011, there were 312,620 cases of reported TB in the United States, 53.5% (n=167,260) were US-born in origin. Of the US-born, black and white TB cases represented 45.92% (n=76,803) and 35.5% (n=59,374), respectively. JoinPoint's spline algorithm determined that there were two join points over the 19 year period in US-born black TB data (2002, 2007) and only one join point in US-born whites (2002). These join points delineated a significant change in the average APC and were affirmed through Poisson regression analysis in SAS. Relevant risk factors were also stratified in JoinPoint, searching for differences in trends of TB among US-born non-Hispanic blacks categorized at different levels of risk factors.

Conclusion: The decline in US-born black TB cases since 2007 was significant compared to previous years and to US-born white TB cases in the same time period. A few risk factors associated with TB shared a similar pattern with the average APC changes in US-born black TB cases including specific age groups, type of therapy, and place of therapy.

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Chapter I: Literature Review

Burden/Infection

Tuberculosis (TB) is one of the most common global infectious diseases and is often very deadly in developing countries[1]. Tuberculosis is a silent global epidemic affecting approximately one third of the population worldwide due to its active and latent forms, as well as the increased risk for coinfection with HIV[1]. Of the current 8.7 million individuals infected with TB, 1.4 million died, while 95% of these deaths occurred in developing countries[2]. The WHO and other public health partners set an ambitious goal for the global elimination of tuberculosis by 2050[3]. This means reducing the incidence rate of TB to less than 1 per 1,000,000 persons. More than twenty years ago, the United States shared this same desire to eliminate TB in the US by 2010[4]. However, because of the complex epidemiology and difficult treatment of TB as well as the economic, social, and public health factors that foster the propagation of tuberculosis, this disease has not yet been eliminated and the goals set by both the WHO and the United States are in essence beyond our reach[3,5].

Tuberculosis is a transmissible disease caused by the bacterium known as *Mycobacterium tuberculosis* that is inhaled through droplet nuclei. This allows TB to spread between individuals through the air. Four factors influence the probability of TB transmission. The first two are (1) susceptibility (immune status) of the exposed individual and (2) infectiousness of the person with TB disease. Patients who expel many tubercle bacilli are more infectious. (3) The environment in which the transmission occurs, and (4) the proximity, frequency, and duration of the exposure are the final two factors[6]. Pulmonary TB is the most common form of the bacteria and it primarily attacks the lungs, due to its preference to areas of

high oxygen tension. However, when TB infects other parts of the body such as the brain or kidneys, it is called extrapulmonary TB[1]. Individuals frequently exposed to infectious TB patients are at highest risk of becoming infected with tuberculosis[2, 6]. This is why contact investigation is the most common form of containing a tuberculosis outbreak and tracing the most infectious individuals. An infected individual in contact with numerous social groups is often considered the highest risk for spreading disease. Contact investigation involves gathering contact information of individuals who may have had frequent contact with the infected patient to determine if they are exhibiting symptoms of tuberculosis[7].

However, not everyone infected with the TB bacteria is symptomatic. There are two forms of tuberculosis including the active form known as active TB disease, which is contagious and capable of spreading to others; the other form is latent TB infection (LTBI), where the disease dwells in an individual without causing illness. Depending on the strength of their immune system a person's LTBI can develop into active TB disease later on in life. In fact, nearly 80% of all active tuberculosis cases in the United States are the result of reactivated LTBI[7]. Approximately one-tenth of those infected with M. tuberculosis will become ill with active TB in their lifetime[1]. Common symptoms for active TB disease include chest pain, coughing up blood or sputum, night sweats, fever, chills, weight loss, and fatigue[1, 7]. Since both LTBI and active TB should be treated, it is easier to utilize detection methods such as skin tests and chest x-rays, rather than looking for symptoms of active TB disease[6].

Detection/Treatment

There are two methods of detection used in the United States: the Mantoux tuberculin skin test (TST) and interferon-gamma release assays (IGRAs)[7]. TSTs are cheaper and more

widely used but their specificity can be affected by many environmental factors such as individuals from high-prevalence areas, those who have had a bacille Calmette-Guérin (BCG) vaccine, and incorrect interpretation of the TST[2, 6, 8]. Sensitivity may be reduced because of immunosuppression related to HIV infection and injection drug use[6, 9]. Those with risk factors are often encouraged to seek regular testing to ensure prevention of TB disease. Furthermore, healthcare employees, correctional facility employees, and unemployed individuals are at a higher risk for TB infection[6]. Those who test positive are given anti-TB drugs depending on the form of TB: Varying treatments of Isoniazid (INH) alone are given to patients with LTBI, while active TB patients are given a course of INH, rifampin (RIF), Pyrazinamide (PZA), and Ethambutol (EMB) over a period of 9-12 months[6, 8, 9]. A recently approved treatment regimen for LTBI has recommended 12 weekly treatments of INH-Rifapentine in order to decrease the length of treatment and hopefully increase adherence to treatment in LTBI patients [11]. Individuals not properly treated with these drug therapies, particularly those with active TB, will likely spread the disease. In previous years, antibiotic regimens for LTBI treatment lasted approximately 4-9 months[8], however, the adherence to such treatment was less than 50% [10].

Risk Factors/Ethnic Groups

Racial minorities and foreign-born persons are at an increased risk of TB transmission[12], however tuberculosis has numerous other risk factors that contribute to the increased risk of contraction. These include residence in correctional facilities, homelessness, residence in long-term care facilities, injecting/non-injecting drug use, and excessive alcohol use[12, 13]. Furthermore, individuals with HIV/AIDS are at a significantly increased risk of TB coinfection due to their suppressed immune systems[14]. In fact, TB is the leading cause of death among individuals infected with HIV[1]. Those infected with TB disease but not treated will

increase the number of active TB cases and add to the morbidity and mortality in the United States. Untreated tuberculosis may result in more TB outbreaks in a community and can contribute to population-based clusters: an untreated case is at risk to infect his/her family, professional circle, social circle, and other personal contacts[15].

The United States has reported tuberculosis cases on a national scale since 1953[12]. Throughout the last 19 years both the number of TB cases reported has decreased in the United States (Figure 1). In the U.S., a total of 10,528 cases of tuberculosis were reported in 2011, resulting in a national incidence rate of 3.4 cases per 100,000 persons in the United States[12]. This was a 6.4% decrease from the number of cases reported in 2010. Of these cases, 3,961 (38%) were attributed to U.S.-born persons, resulting in a case rate of 1.5 per 100,000 persons[2]. The TB incidence rate among foreign-born in the United States was much larger, approximately 17.3 per 100,000 persons[12]. Non-Hispanic Asians were the largest race/ethnicity with reported TB cases (30%), with Hispanics accounting for the second largest group (29%). In these two groups, a large majority are foreign-born cases, as exemplified by the top four countries of origin for foreign-born TB cases: Mexico, the Philippines, Vietnam, and India[12]. The next two largest groups with TB are Non-Hispanic Blacks (23%) and Non-Hispanic Whites (16%). Unlike the two previous groups, the majority of cases in these two ethnic groups are U.S.-born cases[12]. To further illustrate the contrast in U.S.-born and the foreign-born population, the rate of TB among foreign-born individuals is 17.3 cases per 100,000, while the U.S.-born incidence rate of TB is only 1.5 cases per 100,000 (Figure 2).

Drug Resistant TB

A growing world-wide problem is the development of drug resistant tuberculosis. While very few cases are reported in the United States, this is becoming an increasing problem in developing countries with poor therapy treatments. The WHO estimates that worldwide, 3.7% of new TB cases are estimated to have MDR TB[16]. In 2011, they estimated that there were 310,000 (range, 220,000 – 400,000) pulmonary MDR TB cases. In 2011, the United States reported 124 cases of MDR TB, with 85.5% of cases among the foreign-born[12].

Two forms of drug resistant TB exist: multi-drug resistant TB (MDR) and extensively drug resistant TB (XDR). MDR is resistant to at least isoniazid and rifampin, the two most common and most widely used TB treatment drugs[17]. INH and RIF are considered first-line drugs: they are the most effect drugs in combination therapy, have fewer side-effects, and are less expensive than most second-line drugs. An array of fluoroquinolones and injectable second-line drugs must be used to treat MDR TB. If improperly treated with these drugs, MDR TB can develop into XDR TB. XDR TB is resistant to INH, RIF, at least one member of the fluoroquinolone family, and at least one injectable second-line drug[17]. It is estimated that approximately 9% of all MDR cases are actually XDR TB[16]. Both descriptions of MDR and XDR TB above are the acquired form. That is, drug resistance develops over the course of treatment for regular TB[18]. Primary resistance is when a person with no previous TB treatment, becomes infected with a drug resistant strain[18]. Treatment for MDR and XDR TB is much the same, requiring two years of aggressive treatment and chemotherapy.

The Question

Since 1993, TB cases among both U.S.-born non-Hispanic blacks and non-Hispanic whites have been steadily decreasing. U.S.-born non-Hispanic blacks have had a higher burden of tuberculosis than U.S.-born non-Hispanic whites (henceforth, both subpopulations will not have the "non-Hispanic" moniker) and internal study at the CDC's TB surveillance department has shown the ratio between the two groups remaining steady for many years (Figure 3), despite the decrease in the number of cases in both groups[12]. However, starting in 2008, this ratio diminished dramatically, as the number of U.S.-born black TB cases has declined much faster than in previous years (Figure 3). However, the U.S.-born white TB cases have continued a steady decline in that same time period. This sharp decrease in US-born black TB cases adds more surprise to the already unexpected results of TB cases during "The Great Recession" period[19]. By most accounts, the Great Recession began in December 2007 and ended in June 2009, reaching a peak unemployment rate of 10% in October 2009[20]. This time period coincides with a larger decrease in TB cases across many ethnic categories, contrary to the accepted convention that increases in economic hardship will slow/reverse the rate of decline in tuberculosis cases in the United States[19]. The primary question of focus is to statistically determine how to a) characterize annual trends in TB case counts in US-born black and white subpopulations and whether there is a change in the rate of decline in US-born black TB cases. This characterization includes finding how often and when these changes occur, and b) further investigating these changes within and between the two subpopulations.

Analytic Method and Software

JoinPoint (version 4.0.4, National Cancer Institute, Bethesda, Maryland) is being used to characterize these annual trends of US-born black and white TB cases in conjunction with SAS (version 9.2, SAS Institute, Cary, North Carolina) to carry out Poisson regression analysis of the knots (changes in the annual rate of decline) that JoinPoint selects. Originally used by the National Cancer Institute for its Surveillance, Epidemiology and End Results (SEER) Program[21], JoinPoint takes trend data and tests the assumption of a linear slope. This has been useful to the National Cancer Institute in representing large amounts of data, stratified by various predictor variables and demographics. Using a frequentist approach, the JoinPoint procedure involves two steps. First, it fits a joinpoint regression model to the entire available data. Then, conditional on the projected joinpoints, it calculates the annual percent change (APC), average APC, and their standard errors. Starting at zero joinpoints (a straight line), the software uses comparability tests[22] to determine whether more joinpoints are statistically significant and need to be added to the trend data. This analysis utilizes Poisson regression modeling on with a logarithmic link function case counts of annual TB, choosing the best regression parameters with the smallest sum of squared error. Each model calculates annual percent change (APC); this selection is done using Monte Carlo Permutation method at a significance level of 0.05. This software is similar to the application of spline methods in epidemiology and which has been explored in other studies[23, 24]. There has also been precedent for the use of JoinPoint in TB surveillance[25].

This can be quite useful to the tuberculosis department at the CDC for two reasons. First, the National Tuberculosis Surveillance System (NTSS) studies a large amount of data. By collecting socio-demographic data and tracking medical treatment of each case, NTSS

holds more than 200 variables for each case. Having JoinPoint can more efficiently represent change in data for specific variables of interest. Secondly, NTSS is one of the few branches in the CDC that distributes up-to-date statistics in its annual report. Most branches report on data that has been time-delayed to insure data completeness and integrity. Tuberculosis reports with annual up-to-date statistics except for completion of treatment therapy as it takes approximately one year to complete treatment. This allows the TB department to report on trends that are currently happening and to advise health departments and the public of upcoming trends. Having JoinPoint would allow the CDC to better inform the public and scientists with an informative graph that is easy for both the user and the reader to understand. Therefore it is the purposes of this study to not only answer a question about the change in TB rates affecting US-born whites and blacks but to also assess the effectiveness of the JoinPoint software.

Part II: Manuscript

Introduction

In 2011, the global incidence of active tuberculosis (TB) was approximately 8.7 million individuals[1]. Approximately one-third of the global population is infected with TB, whether it is the active form or latent tuberculosis infection (LTBI)[1]. In the United States, 10,521 new cases of tuberculosis were reported in 2011 across all 50 states, excluding territories[2]. Based upon the current U.S. population in 2011, the reported incidence rate was 3.4 per 100,000 individuals[11]. Of these TB cases, 3,961 (38%) were attributed to US-born cases; of these US-born cases, non-Hispanic blacks and non-Hispanic whites are the two racial groups with the largest portion of TB cases[12].

Since 1993, TB cases in the United States have been on the decline (Figure 1), particularly US-born TB cases (Figure 2). However, US-born non-Hispanic black TB cases have been disproportionately higher than US-born non-Hispanic white TB cases. (Henceforth, the "non-Hispanic" moniker will be dropped.) The rate ratio between the two ethnic groups has remained relatively stable over the past 19 years (Figure 3). However, since 2008, the annual number of US-black TB cases has declined at a considerably higher rate[12]. This has also lessened the rate ratio between US-born whites and blacks, as the current incidence rate is 0.6 per 100,000 and 4.3 per 100,000, respectively. During this same time period, "The Great Recession" occurred, as housing markets crashed, personal wealth decreased, and unemployment rose as high as 10%[20]. Contrary to most predictions, annual TB case counts declined at an even faster pace, particularly for US-born blacks[19].

This study aims to characterize US-born TB cases counts over the past 19 years in both non-Hispanic black and white subpopulations to statistically determine changes in the annual rate of decline in both groups, including how many changes there are and when they occur. Once these changes are defined, further analysis using Poisson regression with piecewise linear trends will analyze further trends within and between the US-born black and white subpopulations. Furthermore, common risk factors and variables of interest will be stratified by these annual changes in US-born black TB cases in order to have a better understanding of what variables may be affecting the rate of decline in the subpopulation.

Methods

Data was retrieved from the National Tuberculosis Surveillance System (NTSS), comprising of several reporting modules including the electronic Report of Verified Case of Tubeculosis (eRVCT), commercial off-the-shelf system modules, state-based surveillance systems, and CDC's own National Electronic Disease Surveillance System (NEDSS) module[27]. NTSS data included social, demographic, and clinical variables collected from patients using the Report of Verified Case of Tuberculosis (RVCT) form[26]. The forms are filled out by local nurses and public health officials and submitted online to NTSS where the CDC's Division of Tuberculosis Elimination (DTE) can access them. All 50 states including the territories use the RVCT as a standardized reporting method to allow the CDC to report annual TB trends.

JoinPoint (version 4.0.4, National Cancer Institute, Bethesda, Maryland) and SAS (version 9.2, SAS Institute, Cary, North Carolina) software will be used to analyze trend data, Poisson regressions, and to search for possible socio-economic characteristics that mirror the sharp decline in US-born black TB cases. The purpose of using JoinPoint software is twofold.

First, it characterizes temporal trend data, in this instance annual TB counts for US-born black and white subpopulations, and determines statistically significant changes in the average annual percent change (APC). Furthermore it provides a unique and simple visual representation of the TB trend data. Secondly, it was implemented in this study to allow SAS to build upon the changes demarcated by JoinPoint by formally characterizing the magnitude of differences in the slope of each subpopulation and whether they differ from zero. JoinPoint is relatively unknown and has not been used much outside of its original intent of displaying temporal cancer rates by the National Cancer Institute. Therefore, this study intends to accept its algorithm utilizing knot search[24] but and wants to expand upon that method by utilizing SAS in determining the order of magnitude in each subpopulation's slope.

Outcome/Predictor Variables

The outcome variable of interest is a reported case of verified TB in either the non-Hispanic black or non-Hispanic white US-born population between 1993 and 2011. For this study, only counts of TB were analyzed. While lacking a denominator to produce a rate is not ideal, there is precedence and reason for not collecting US-born population statistics for this study. The CDC TB surveillance program primarily uses case counts as a measure of program burden because of the significant resources needed to treat and cure tuberculosis over an extended period of time. Population increase/decrease is not as heavy a factor in TB surveillance because of the significant time resources required by nurses, doctors, and public health workers to provide treatment and directly observed therapy.

The CDC allows for five methods in which an event can be determined as a verified case of TB: nucleic acid amplification test (NAAT) positivity, lab culture positivity, acid-fast

bacilli test positivity (AFB), provider diagnosis, and clinical diagnosis[5]. A clinical diagnosis must be based upon evidence of TB infection (TST or IGRA test) and either show symptoms of active TB disease or show clinical evidence of current disease while being treated with at least 2 TB medications[12]. Provider diagnosis has been used much less in the last decade, as it does not require a confirmation of the case definition. Because the study spans the past nineteen years when current laboratory tests were not as readily available, there are a number of cases in the early 1990s that were given this definition. The main predictor variables were race and country of origin as collected by the RVCT form[26]. Country of origin was used to exclude all foreign-born TB cases and race was used to determine black and white race.

Data Analysis

Data analysis was done with JoinPoint 4.0.4 and SAS 9.2. Beginning with JoinPoint to determine the points of change in the data, two separate files of annual US-born black TB counts and annual US-born white TB counts were analyzed by using textfile inputs to calculate average annual percent change (APC) and to determine potential knots (join points) where the average APC changed. This was done for both US-born blacks and US-born whites over the past nineteen years. In each race category, JoinPoint selected a plausible number of join points where the annual percent change in the TB count most accurately defined the change over time. More or fewer knots could have been inserted, but would not have been necessarily significant. This option by JoinPoint allows for some human judgment in determining best fit, however, this study selected the optimum fit chosen by the software. These knots were used to appropriately categorize US-born black TB data and US-born white TB data by segments of time. Each knot delineates a shift in the temporal slope of the TB cases

based upon an optimization algorithm used for significance testing. For clarity, each section of the timeline demarcated by a knot will be referred to as a "segment."

Once JoinPoint has evaluated for different annual percent changes in the temporal trend data of each subpopulation, each segment representing a different average APC will be analyzed by SAS using a Poisson regression with piecewise linear trends. Using equation A below, the piecewise linear trends defined by JoinPoint allows for the calculation of each slope estimate for segments in both subpopulations during the first Poisson regression.

Equation A : $(1 - \exp(X)) * 100\%$ = average APC, where $X = coefficent\ estimate$

Stratified by race and running each subpopulation separate, the first Poisson regression analyzed each segment compared to the previous segment to determine if the average APC significantly differed from the previous time segment. Furthermore, all segments in the same race were simultaneously compared to determine significance of overall change. This was done for both US-born black and white subpopulations.

First Poisson Regression Hypotheses

$H_{01}: \beta_{i1} = \beta_{i2}$ $H_{02}: \beta_{i2} = \beta_{i3}$ $H_{03}: \beta_{i1} = \beta_{i2} = \beta_{i3}$

B = coefficient estimate

i = race category (0 = US-born white, 1 = US-born black)

j = time segment (1 = 1993-2002, 2 = 2002-2007, 3 = 2007-2011)

A second Poisson regression was created where a race variable was included to determine if the rate of change in the time segments of black TB cases differed with time segments of the white TB cases in the same time segment.

Second Poisson Regression Hypotheses

$H_{11}: \beta_{0j} = \beta_{1j}$ i = race category (0 = US-born white, 1 = US-born black)

j = time segment (1 = 1993-2002, 2 = 2002-2007, 3 = 2007-2011)

Since TB rates are declining for both blacks and whites, the logic behind this action is to determine if the rate of decline in black TB cases is significantly different from white TB cases. Finally all segments of both white and blacks were combined, respective to race, to determine if there is an overall significant change during the past 19 years of the study.

*This study has been approved by Emory University's IRB organization as not involving human test subjects and is therefore free from the specific mandates involving human subject testing.

Results

Since 1993, there have been 312,620 verified cases of tuberculosis in the United States. Of the 312,620 TB cases, 53.5% (n=167,260) were US-born in origin. Non –Hispanic blacks and non-Hispanic whites were the two largest US-born ethnic groups with reported TB cases spanning the past 19 years at 45.92% (n=76,803) and 35.50% (n=59,374), respectively. There were two knots (three segments) in the black TB case data that established 2002 and 2007 as the point in time in which the APC rate significantly differed (Figure 1). In white TB case data only 2002 was established by the JoinPoint algorithm as a significant knot (Figure 2); however 2007 is included in subsequent regression models, regardless of significance, to allow direct comparison between black and white TB case data. Selected population characteristics for all TB cases are shown in Tables 1-3. Each table represents the three time segments that were chosen by the JoinPoint software. Table 1 is a time period when total US-born TB cases

outnumbered total foreign-born TB cases in the United States. Tables 2 & 3 find US-born cases rapidly become a minority in TB cases in the United States.

Results of the first and second Poisson regression models in SAS are presented in Table 4. It presents the overall (1993-2011) average percent change in race categories as well as the average percent change within and between three time segments: 1993-2002, 2002-2007, and 2007-2011. This table only evaluates the change within the same race. In US-born black TB cases, the annual percent decline between the 1993-2002 segment and 2002-2007 segment was significantly different (magnitude =3.61%, $p< 0.01$) as well as the rate between the 2002-2007 and 2007-2011 segments (magnitude = -5.08%, $p< 0.01$). In US-born white TB cases, the annual percent decline between 1993-2002 segment and 2002-2007 segment was significantly different (magnitude = 3.24%, $p< 0.01$), however the rate between the 2002-2007 and 2007-2011 segment was not (magnitude = -1.31%, $p= 0.14$).

Table 4 further represents the results of the second Poisson regression evaluating the significance between the black and white subpopulation for the same time segment. The difference between the black TB APC and white TB APC for the 1993-2002 segment was insignificant ($p=0.10$) as was the 2002-2007 segment ($p=0.14$). However the average APCs between black and white TB case rates for the 2007-2011 time segment was significant ($p< 0.01$).

JoinPoint graphs of typical predictors and risk factors for TB were generated in JoinPoint for US-born blacks (Figures 8-36). The purpose was to see what factors/predictors shared a similar decline as the overall case count for US-born blacks. Association does not mean causation, but it would help those in public health surveillance in TB to know what

trends are developing in the fight to eliminate TB in US-born blacks. There were a few categories that mirrored the rate of decline in US-born blacks, particularly the sharp decrease since 2007. Factors that were affected by the recent sharp drop in US-born blacks included self-administered therapy (SAT) (Figure 18), directly observed therapy (DOT) (Figure 19), both DOT/SAT (Figure 17), Health Department Provider Type (Figure 20), as well as Private/Other Provider Type (Figure 21). Four figures had joinpoints close to 2002 and 2007, closely reflecting the overall US-born black TB JoinPoint graph (Figure 7). These included two age groups: 15-24 years of age (Figure 24) and 45-64 years of age (Figure 26). New York City TB counts (Figure 34) had three joinpoints, however two of them were in 2002 and 2007. Finally, the provider type category "Both" (Figure 22) which combines the two other categories "Health Department" and "Private/Other" also had three joinpoints, where two of the joinpoints were in 2001 and 2008.

Discussion

JoinPoint is not widely used outside of the SEER database by the National Cancer Institute but it could be a useful tool in the realm of non-cancer epidemiological analysis. The applications of this software are most beneficial for public health surveillance because of how often surveillance deals with temporal data. Having software that quickly determines the "joinpoints" or inflections in trend data samples would be beneficial to the user in his/her analysis and equally useful to the reader in understanding the underlying principles of the study. By having easy to understand graphical interpretation of the data, it will allow the reader to quickly understand the background of a study better. This will allow the author to use more word space explaining the nuances of his/her study question. One limitation, however, is the

inability to manipulate the graph and define a custom joinpoint. The software did not allow this study to add a joinpoint at 2007 for US-born whites in order to compare the average APC.

Using JoinPoint and SAS in conjunction with each other allowed this study characterize a significant change in the rate of decline in US-born blacks that is not seen among US-born whites. Since 2007, US-born black TB cases have decreased significantly in two ways: 1) compared to previous US-born black TB annual rates and 2) compared to US-born whites rates in the current time period. This has major implications for the future of TB in the United States and its focus. For the previous 19 years, there has been a disparity between US-born blacks and whites in the burden of tuberculosis. With US-born blacks reaching the levels of US-born whites, this will allow TB eliminations efforts to shift their efforts to foreign-born individuals with TB. Total US-born TB cases have been steadily decreasing while foreign-born TB case totals have remained relatively unchanged, accounting for a larger majority of total TB cases in the United States each year (Figure 4). In most states, foreign-born TB cases represent the majority; only the Southeastern states have majority US-born TB cases (Figure 5).

Strengths/Limitations

This study has the benefit of utilizing government-sponsored surveillance data that has been well reported at the state and federal level. However, there are several deficiencies regarding the study and the software used. California did not report HIV status with TB cases until 2011. Vermont was also another state to recently choose not to disclose/test for HIV status, however California is the state with the largest number of TB cases and this greatly affects the trend data for TB. Incidence rate was not included in this study due to reasons explained in the methods section. Though the Current Population Survey and the US Census

Bureau have collected data for race/ethnicity and country of origin, their definition for US-born non-Hispanic black has changed multiple times over the past 19 years and was not even included in 1993. Furthermore, only counts of TB were used in the analysis. The lack of a good source of US-born population over the past 19 years made it difficult to decide whether or not to include an analysis of incidence rate.

Data collections for US-born population statistics on an annual basis are hampered because there was no annual collection of US-born/foreign-born populations until 1994. There has been a decennial count of foreign-born in the U.S. since 1850; however this is only for every 10 years. Current Population Survey has begun to keep annual foreign-born counts, however only US-born populations could be derived from the data, not race/ethnicity. The definition for race/ethnicity has changed over the past 19 years, leading to uncertainty as to how best to bridge race categories across years. This is compounded by the definition change in many CDC departments of race/ethnicity in 2002, having implemented the new definition from the 2000 Decennial Census. Previous studies by the CDC have model trends without population statistics[25] and this study saw fit to limit the variable of interest to case counts.

JoinPoint Software, while very useful, is a niche analysis tool. Its best strength is dealing with large amounts of temporal data with many time points to determine trends. Having only a handful of time points would severely limit the usefulness of this software. Many scientific studies do not encompass long follow-up times and would not benefit from this software; however government surveillance agencies would value this software in its ability to effectually display trend data for those particular agencies' variables of interest. While spline mechanics and graphing could be done in SAS, it would take a high level of skill and

understanding that the typical scientist does not have. Instead, JoinPoint is already available in making the most out of temporal trend data.

Chapter III: Broader Perspective

Study Critique

There are two issues from this study that need to be expounded upon: 1) the usefulness of JoinPoint software in scientific research and 2) the implications of this study regarding US-born TB cases in blacks and whites. JoinPoint analysis can be very useful in providing visual representation and applying knot/spline technology. It can take simple temporal data and straightforwardly translate it into a graph that provides answers about significant changes. It provides the user with a number of options regarding model selection methods, permutation test options, and various comparison methods to fit the user's need. This software will be most useful to users with data over a long period of time and with a lot of variables of interest. Spline technology is specifically geared for data collection over an extended period of time; it is difficult to discern a significant trend with only a handful of time intervals collected. With these preconditions, it makes it unlikely that it will see a large incorporation into many scientific studies. However, it could be useful to government surveillance programs that have years of data collected. These surveillance programs would benefit in displaying useful graphs that would better inform the public of the work they do and the new trends that are developing in their surveillance purview.

Regarding the recent significant decline of US-born black TB cases in the United States, there are many possible reasons but no definite answer. This could be just the eventuality of decreasing US-born cases in the United States; white TB cases are very low and cannot easily decrease significantly while US-born black TB cases are still high enough to see a sharp decline in rates. Public health departments and state surveillance programs doing a

better job could be the reason, however I suggest that it may be more attributable to the information-saturated culture we are continuing to live in. With online health forums and websites dedicated to explaining your symptoms, it may be more likely that people are more educated and can easily spot symptoms that are alarming. Furthermore, older generations are more likely to have been exposed to TB and carry LTBI simply because it was more common in the early 20th century. As they pass away, we are reaching a new era where TB infection is not as common, thus, developing active TB from LTBI is also becoming less common.

TB Relationship with Economy

What makes this sharp decline in US-born black TB cases so intriguing is the time period in which it has occurred. During that same time frame, the housing market crashed and unemployment climbed as high as 10%. In actuality, this unemployment rate for blacks was higher than 16%[20]. With a housing market crash, families and friends usually tighten their personal space and share housing together in order to save costs. This is prime development for TB disease as it is easily spread within close social contact in enclosed spaces. But instead the case rate of US-born blacks declined dramatically. It is difficult to pinpoint a reason for this counterintuitive result. Instead we can now consider the possibilities of what might occur once the economy begins to turn around and thrive.

Personal wealth usually helps drive disease down and this is most often the case with tuberculosis, as lower socio-economic groups are more likely to be infected. Once the housing market recovers and unemployment in the US black community begins to rebound, it will be interesting to see if the decline in TB cases declines even sharper or remains insusceptible to

personal wealth. Regardless, collection and examination of future TB data will provide a better picture of the consistent trends in the decline of US-born black TB cases.

Refocusing on Foreign-born TB

The implications of this study represent a shift in the way the United States must deal with the problem of tuberculosis. The two largest US-born groups, blacks and whites, have rapidly declining TB rates. This translates into a shift in focus toward foreign-born tuberculosis, where foreign-born TB cases have represented the majority of cases in the United States since the early 2000s and still have a significantly high incidence rate[12]. Foreign-born is defined as someone who was not born in the United States or its associated jurisdictions, and does not have any U.S.-born parents[28]. In U.S.-born persons, there were a total of 4,378 cases in 2010 for a rate of 1.6 cases per 100,000 population. In contrast, 6,707 cases of foreign-born TB resulted in a rate of 18.1 cases per 100,000 population. Until 2009, TB cases among foreign-born cases from 1993-2008 remained relatively stable between 7,000 and 8,000 cases annually[28].

Many issues surround the problem of high incidence rates of tuberculosis in foreign-born immigrants when compared with domestic citizens. While immigration is still a polarizing issue in American politics today, it should not overshadow the truth that many immigrants are coming to America with latent tuberculosis infection (LTBI) or active tuberculosis. Four states have more than 500 total cases annually and also have a majority of the foreign-born tuberculosis cases: California, Florida, New York, and Texas[12]. These states have a high immigration rate, whether it is seaports, airports, or contact with other border countries.

Of foreign-born cases, Mexico has the largest number of emigrants with tuberculosis who come to the United States at more than 1,500 cases annually[12]. Two of the four states previously mentioned, California and Texas share a land border with Mexico. Therefore many Mexican immigrants, legal and illegal, settle in these two states close to their home country[29]. More concerted efforts should be made both in Mexico and in the United States to combat tuberculosis. In the United States, public health clinics with a focus on Hispanic populations should be placed close to the land border with Mexico. While many immigrants may fear such a government-instituted establishment, focus should be made to reach out to these communities and offer services. In Mexico, there needs to be better protocol for documenting potential TB contacts and making sure they are not infectious. One of the goals of CDC's TB group is to eliminate tuberculosis on a global scale, as it will reduce the cost of treating tuberculosis domestically. Efforts to curb TB in Mexico would be productive for the United States.

When considering that many other cases of TB and LTBI may travel through airports, it would be good to increase the response time of TB tests in order to make them standard for new foreign-born immigrants. The current tuberculin skin test (TST) takes 48 to 72 hours and requires two visits by the patient in order to confirm diagnosis[30]. New IGRA tests reduce the time it takes to detect tuberculosis and would be a great improvement over TST[31]; this is mainly because of the human-factor concerning a lack adherence to following up with a professional after the initial TST visit. In fact, TSTs may even hinder the IGRA test and its ability to detect true positive cases[31]. Furthermore, the TST's very poor specificity[29], especially for immigrants, warrants a better method of testing.

One concern raised may also be foreign-born children in school. Often contacts with TB are limited to households or family, but a child attending school who is at risk to develop

TB represents a danger to other children as well[32]. This is another reason why an IGRA test may become very useful; along with immunizations, this could be very useful in creating an early detection system for other contacts for TB. A positive test by a child will lead us to other contacts for TB outside of the education system.

On a larger scale, new drugs must be introduced to the foreign-born cases in an effective manner in order to avoid possible escalation of drug-resistant TB they may have obtained from their home country. More TB drugs means better options and while there are a few drugs that are coming soon[33] we must be sure to utilize these drugs in a way that will limit drug-resistance. LTBI testing should be a priority among foreign-born immigrants outside of contact investigations and recent immigration status in order to better detect dormant TB[34]. While a majority of TB cases in America are foreign-born, there are many more that have LTBI and go undetected. There is good news for treatment for LTBI as there has recently been a 12 week regimen instead of the previous regimen that required a minimum of 6 months treatment[35]. Many foreign-born TB cases are actually immigrants who have lived in the United States for more than 5 years[12, 36]. Eighty percent of TB cases in the United States are the result of reactivation of LTBI[37]. This statistics only reinforces the idea that testing for LTBI among immigrants must go beyond the scope of recent immigration status in order to eradicate it.

In a 5 year scope, heavy emphasis must be placed on detection of LTBI in foreign-born residents in the United States. There are a number of reasons for this, namely to best utilize resources at the federal and state level. States make annual requests for resources in order to better facilitate their operations and laboratories. Performance will usually be a key factor in determining allocation. Some of the implementations to be made would be to ask states to begin the process of transitioning to IGRA tests in the major metropolitan areas where there is

a higher incidence of cases. Furthermore, encouraging states to begin testing children in the larger cities via IGRA tests would help avoid outbreaks in the education system. Anyone who tests positive for LTBI should be informed of the new 12-week regimen that only requires a weekly visit from a healthcare provider. Finally, encouraging states to increase the cultural training of public health professionals in these large cities would help them succeed in reaching out to nested communities within the city to better increase detection of TB. States that perform well on these merits would receive better funding if their specific requests are for these efforts.

Having had a personal experience with surveillance and detection of TB, one of the problems is the reporting of cases on a state-to-federal level. Many states prefer to use their own TB-reporting system apart from CDC's NEDDS system. There are many similarities, but sometimes variables or values are not reported in a correct fashion. This creates errors for CDC's system and makes reporting difficult. Given the incredible increase of technology today, I think it would benefit not only federal and state levels to begin a new reporting system, but also the local health care providers as well. With the rise of smartphones and access to internet in many places, a reporting system that enables local healthcare providers ease of access on their phone or computer when reporting TB cases would make surveillance much easier. Working outside of the office with homeless, immigrants, and other high-risk groups may limit access to a computer console; having a phone with reporting capabilities would be very useful for local providers. Secondly, overhauling the reporting system into a universal program accepted by state and federal authorities would make reporting easier for those at the CDC.

Conclusion

This study found that US-born black TB cases significantly dropped between 2007 and 2011. Furthermore, this decline was significantly different from US-born white TB cases, as they experienced no significant decline in that same time frame. A handful of risk factors associated with TB were found to share this same decline in US-born blacks including two age groups (15-24 & 45-64), all three completion of therapy types (directly observed, self-administered, both), and where they received treatment (public health department, private facility, both/other).

Future studies should focus on evaluating the effect of the economy on TB cases in US-born blacks. More specifically, it would be interesting to see any change in US-born black cases when unemployment and the housing market are better. The counterintuitive drop in TB cases among US-born blacks suggests that personal wealth may be playing less of a role than imagine and this decline is insulated from its effects. If the US economy recovers, it would be interesting to see if this decline in US-born black TB cases decreases even more.

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Tables & Figures

Table 1: Univariate associations of demographic/risk factors for TB cases in US-born non-Hispanic blacks and US-born non-Hispanic whites, 1993-2002

		US-Born Black TB Cases			US-Born White TB Cases		
	Total Cases	N	% of Total	% of US-born	N	% of Total	% of US-born
Total	196091	55347	28.23	46.95	48486	21.91	36.45
Sex							
Male	123899	36343	29.33	46.93	28989	23.40	37.44
Female	72185	19003	26.33	46.99	13973	19.36	34.55
Age Group (years)							
0-14	12415	3785	30.49	40.68	1280	10.31	13.76
15-24	16435	2900	17.65	52.42	937	5.70	16.94
25-44	70150	22412	31.95	58.48	9992	14.24	26.07
45-64	52277	16661	31.87	49.17	12659	24.21	37.36
65+	44776	9578	21.39	31.09	18079	40.38	58.69
DOT Status (missing = 8884)							
Directly Observed Therapy	77009	25456	33.06	51.73	15887	20.63	32.29
Self-Administered Therapy	64572	13730	21.26	37.79	16601	25.71	45.69
Both	42760	12482	29.19	51.77	7098	16.60	29.44
Provider Type							
Health Department	87011	24041	27.63	51.69	14643	16.83	31.48
Private/Other	50808	12488	24.58	39.96	12886	25.36	41.24
Both	48376	15309	31.65	46.89	12439	25.71	38.10
Homeless Status							
Yes	11698	4970	42.49	51.67	3388	28.96	35.23
No	169903	45002	26.49	45.57	37209	21.90	37.68
Unknown	14146	5247	37.09	56.69	2279	16.11	24.62
Non-Injecting Drug Use							
Yes	12440	7301	58.69	67.40	2213	17.79	20.43
No	151180	36322	24.03	42.76	33665	22.27	39.63
Unknown	31896	11532	36.16	53.24	6910	21.66	31.90
Excessive Alcohol Use							
Yes	26521	12143	45.78	55.35	6957	26.23	31.71
No	138476	31976	23.09	42.74	29131	21.04	38.93
Unknown	30483	11012	36.13	53.33	6696	21.97	32.43
States with 5000+ Total US-born Cases							
Georgia	6878	4151	60.35	72.94	1380	20.06	24.25
Illinois	9182	3977	43.31	61.13	1532	16.68	23.55
Florida	13692	5051	36.89	53.94	3700	27.02	39.51

New York City	18819	6237	33.14	61.48	1320	7.01	13.01
Texas	19373	4774	24.64	37.22	3891	20.08	30.34
California	40211	4036	10.03	31.96	4110	10.22	32.55

Table 2: Univariate associations of demographic/risk factors for TB cases in US-born non-Hispanic blacks and US-born non-Hispanic whites, 2002-2007

		US-Born Black TB Cases			US-Born White TB Cases		
	Total Cases	N	% of Total	% of US-born	N	% of Total	% of US-born
Total	85462	17388	20.35	45.22	13002	15.21	33.82
Sex							
Male	52464	11024	21.01	44.81	8760	16.70	35.61
Female	32985	6362	19.29	45.97	4238	12.85	30.62
Age Group (years)							
0-14	5240	1206	23.02	31.85	355	6.77	9.38
15-24	9327	1203	12.90	47.07	380	4.07	14.87
25-44	29043	5227	18.00	54.12	2543	8.76	26.33
45-64	24856	6714	27.01	50.41	4800	19.31	36.04
65+	16993	3038	17.88	17.47	4924	28.98	53.94
DOT Status (missing = 1396)							
Directly Observed Therapy	46889	10429	22.24	46.96	6994	14.92	31.49
Self-Administered Therapy	11174	1610	14.41	37.55	1900	17.00	44.31
Both	24151	4529	18.75	44.91	3391	14.04	33.63
Provider Type							
Health Department	48283	9744	20.18	47.97	6258	12.96	30.81
Private/Other	16104	2821	17.52	39.64	2652	16.47	37.26
Both	18363	4058	22.10	43.54	3433	18.70	36.83
Homeless Status							
Yes	5097	1932	37.90	50.40	1324	25.98	34.54
No	79551	15299	19.23	44.60	11608	14.59	33.84
Unknown	750	133	17.73	50.00	57	7.6	21.43
Non-Injecting Drug Use							
Yes	6224	3117	50.08	63.15	1141	18.33	23.12
No	77122	13809	17.91	42.51	11544	14.97	35.53
Unknown	2030	436	21.48	44.67	295	14.53	30.23
Excessive Alcohol Use							
Yes	11623	4180	35.96	50.81	2715	23.36	33.00
No	71912	12763	17.75	43.57	10005	13.91	34.16
Unknown	1890	436	23.07	11.62	274	14.50	30.04
States with 5000+ Total							

US-born Cases							
Georgia	3089	1438	46.55	72.63	414	13.40	20.91
Illinois	3550	1094	30.82	60.58	387	10.90	21.43
Florida	6312	1775	28.12	51.52	1324	20.98	38.43
New York City	6079	1060	17.44	57.11	253	4.16	13.63
Texas	9381	1845	19.67	36.88	1344	14.33	26.86
California	17782	1075	6.05	25.84	1220	6.86	29.32

Table 3: Univariate associations of demographic/risk factors for TB cases in US-born non-Hispanic blacks and US-born non-Hispanic whites, 2007-2011

		US-Born Black TB Cases			US-Born White TB Cases		
	Total Cases	N	% of Total	% of US-born	N	% of Total	% of US-born
Total	59400	9927	16.71	41.90	7740	13.03	32.67
Sex							
Male	36278	6390	17.61	42.09	5268	14.52	34.70
Female	23103	3536	15.31	41.56	2470	10.69	29.03
Age Group (years)							
0-14	3421	648	18.94	24.93	208	6.08	8.00
15-24	6534	758	11.60	39.29	267	4.08	13.84
25-44	19484	2629	13.49	49.10	1374	7.05	25.66
45-64	18119	4125	22.77	48.13	3211	17.72	37.47
65+	11828	1767	14.94	33.72	2680	22.66	51.15
DOT Status (missing = 6826)							
Directly Observed Therapy	30589	5977	19.54	45.07	4044	13.22	30.50
Self-Administered Therapy	5215	512	9.82	32.04	731	14.02	45.74
Both	16450	2319	14.10	38.73	2008	12.21	33.53
Provider Type Missing = 7266							
Health Department	35048	6137	17.51	43.95	4347	12.40	31.13
Private/Other	11039	1552	14.06	36.34	1561	14.14	36.55
Both	5938	1028	17.31	41.27	832	14.01	33.40
Homeless Status							
Yes	3197	1190	37.22	52.19	722	22.58	31.67
No	55743	8663	15.54	40.74	6984	12.53	32.84
Unknown	403	65	16.13	55.08	21	5.21	17.80
Non-Injecting Drug Use							
Yes	4220	1900	45.02	58.32	813	19.27	24.95
No	53937	7868	14.59	39.34	6803	12.61	34.02
Unknown	1179	147	12.47	36.75	108	9.16	27.00

Excessive Alcohol Use							
Yes	7214	2258	31.30	47.26	1598	22.15	33.44
No	51161	7518	14.69	40.52	6026	11.78	32.48
Unknown	964	142	14.73	43.03	99	10.27	30.00
States with 5000+ Total US-born Cases							
Georgia	2119	841	39.69	69.73	277	13.07	22.97
Illinois	2135	484	22.67	58.10	219	10.26	26.29
Florida	4355	1094	25.12	48.75	857	19.68	38.19
New York City	3953	474	11.99	51.86	139	3.52	15.21
Texas	7216	1185	16.42	34.23	932	12.92	26.92
California	12538	646	5.15	22.52	780	6.22	27.20

Table 4: Significance testing by JoinPoint & SAS for a Poisson regression of time segments within/between US-born non-Hispanic black and non-Hispanic white subpopulations

	Model coefficient (95% CI)			APC (95% CI)	
	White	Black	P-value*	White	Black
1993-2011	-0.0917 (-0.0933, -0.0901)	-0.0905 (-0.0919, -0.0891)	0.26	-8.76% (-8.91%, -8.62%)	-8.65% (-8.78%, -8.52%)
1993-2002	-0.1043 (-0.1075, -0.1012)	-0.1008 (-0.1036, -0.0981)	0.10	-9.90% (-10.19%, -9.62%)	-9.59% (-9.84%, -9.34%)
2002-2007	-0.0689 (-0.0762, -0.0617)	-0.0617 (-0.0680, -0.0554)	0.14	-6.66% (-7.34%, -5.98%)	-5.98% (-6.57%, -5.39%)
2007-2011	-0.0831 (-0.0966, -0.0696)†	-0.1172 (-0.1292, -0.1052)	0.0002	-7.97%† (-9.20%, -6.72%)	-11.06% (-12.12%, -9.99%)

* P-value for difference between white and black subpopulations

† All slopes change significantly ($p < 0.05$) between durations except this change. JoinPoint did not qualify the 2007-2011 segment in US-born whites ($p = 0.14$), but it is included for comparison to the US-born black grouping

Figure 1: Total reported TB cases in the United States, 1982-2011

(Citation: CDC, Reported Tuberculosis in the United States, 2011)

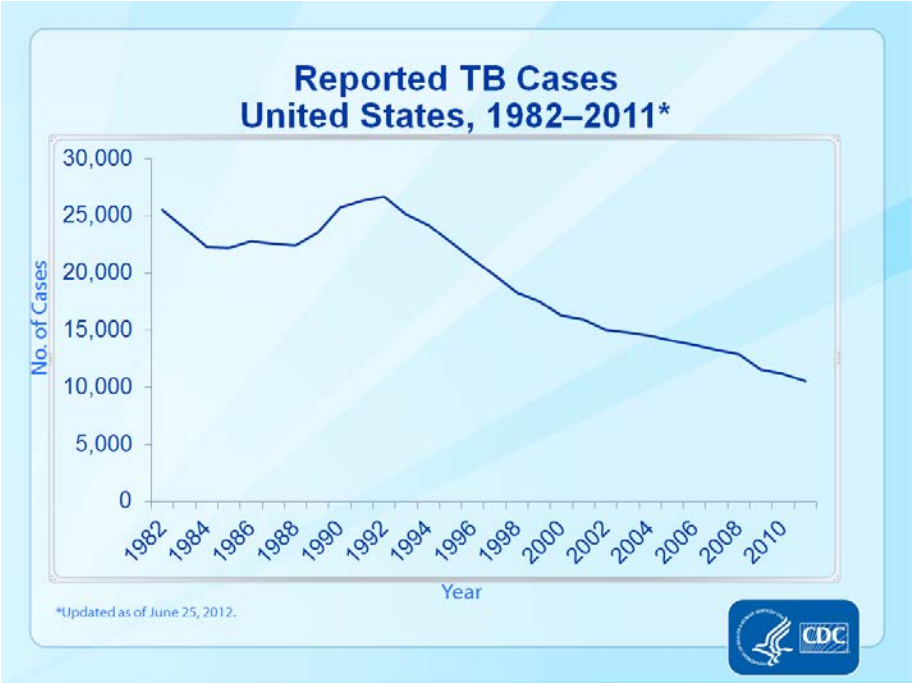


Figure 2: TB case rates in US-born vs. foreign-born persons, United States, 1993-2011 (presented in a logarithmic scale)

(Citation: CDC, Reported Tuberculosis in the United States, 2011)

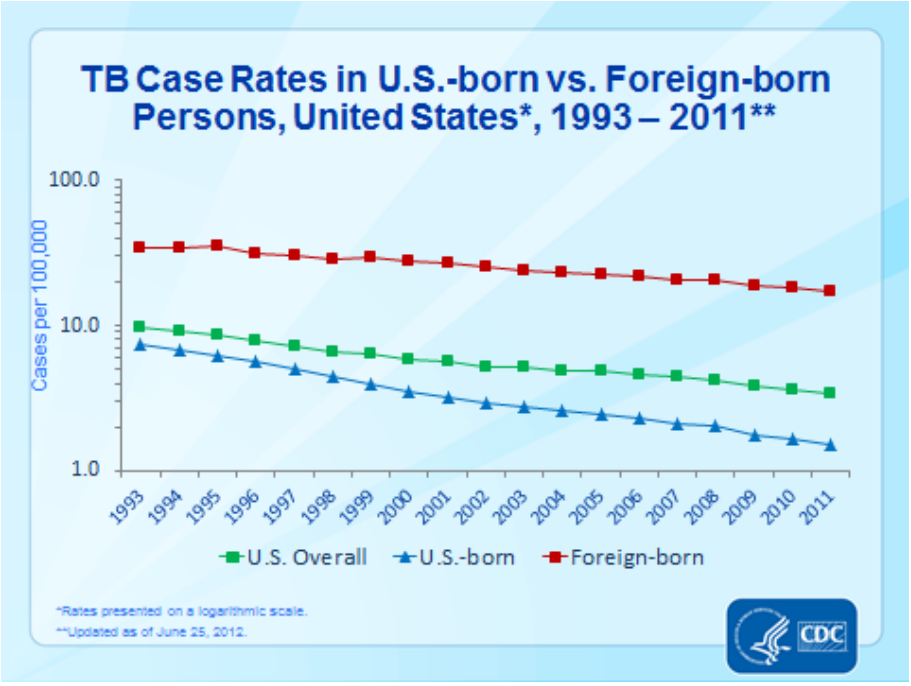


Figure 3:Ratio between US-born non-Hispanic black and US-born non-Hispanic white TB cases, 1993-2011

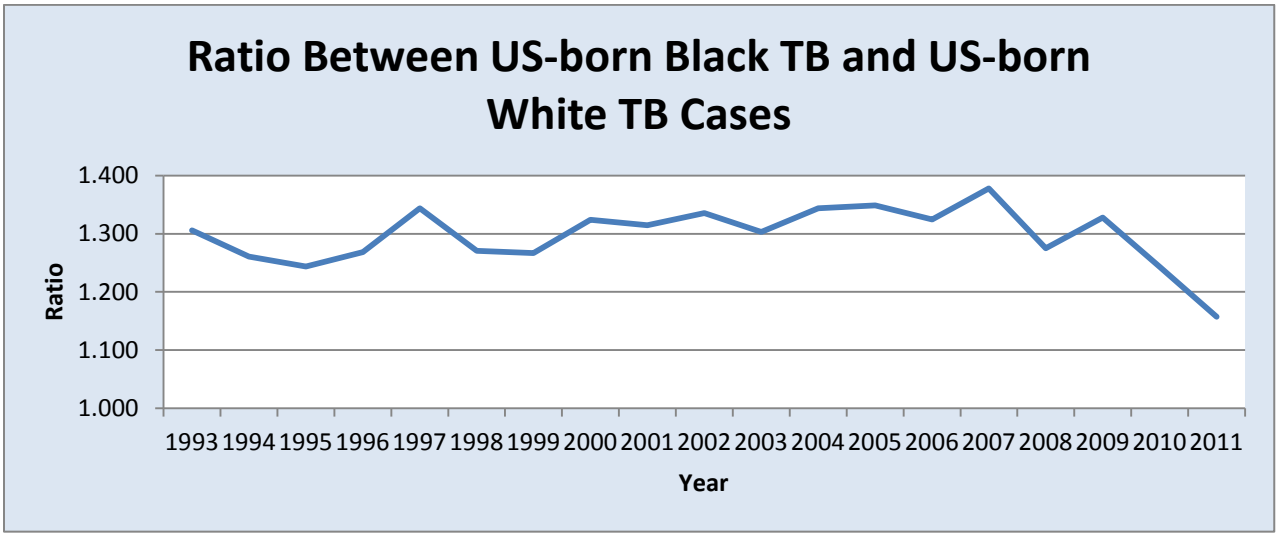


Figure 4: US-born vs. foreign-born TB cases in the United States, 1993-2011

(Citation: CDC, Reported Tuberculosis in the United States, 2011)

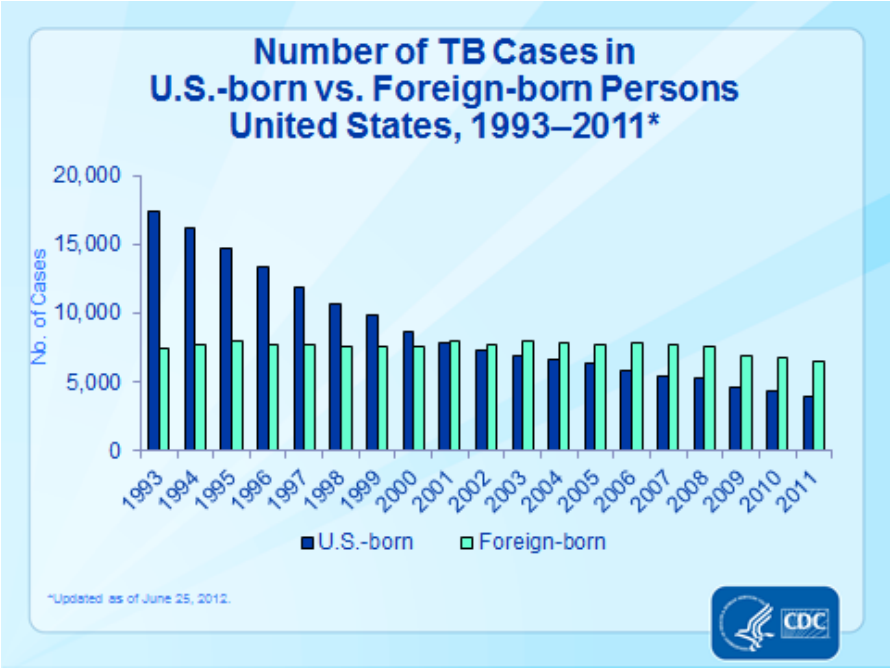


Figure 5: State-based percentage of TB cases among foreign-born persons, United States

(Citation: CDC, Reported Tuberculosis in the United States, 2011)

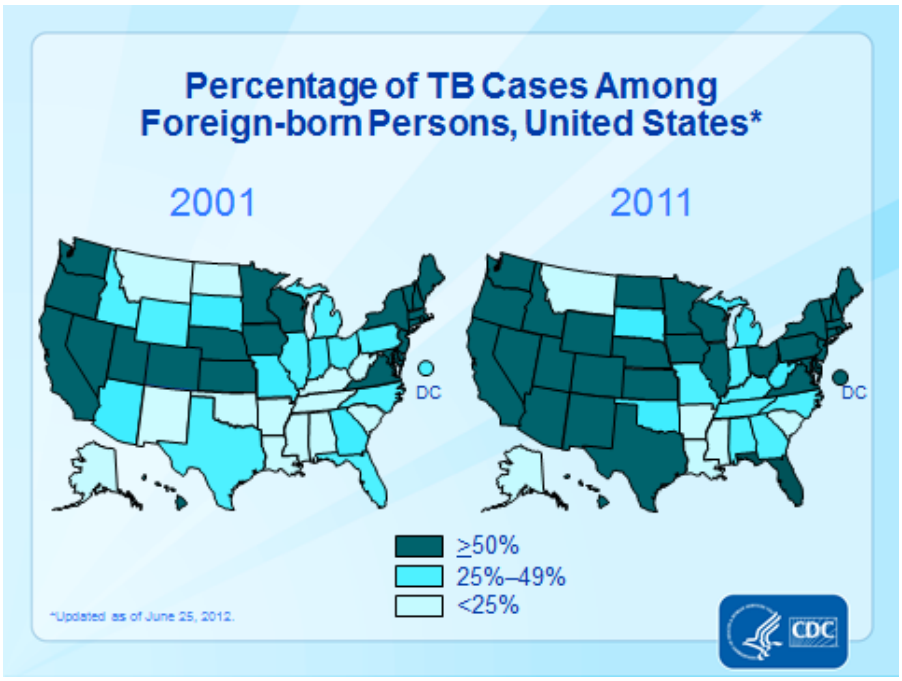


Figure 6: US-born non-Hispanic white TB case average annual percent change (APC)

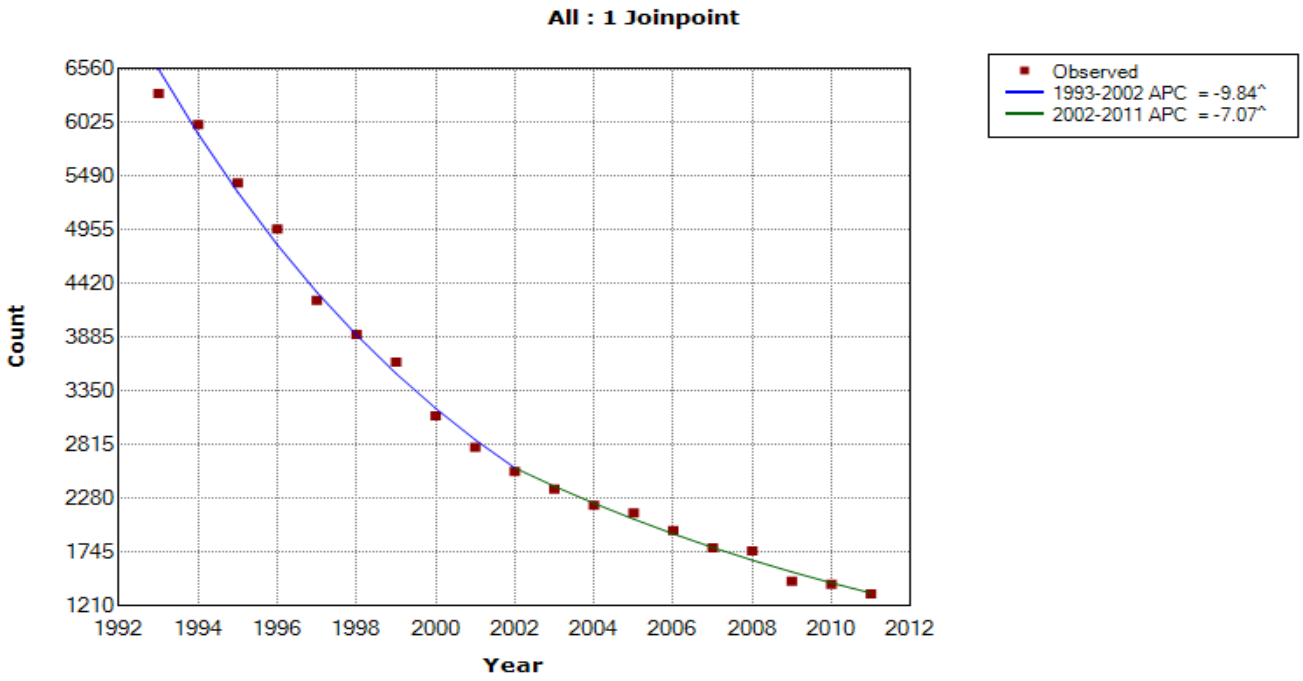
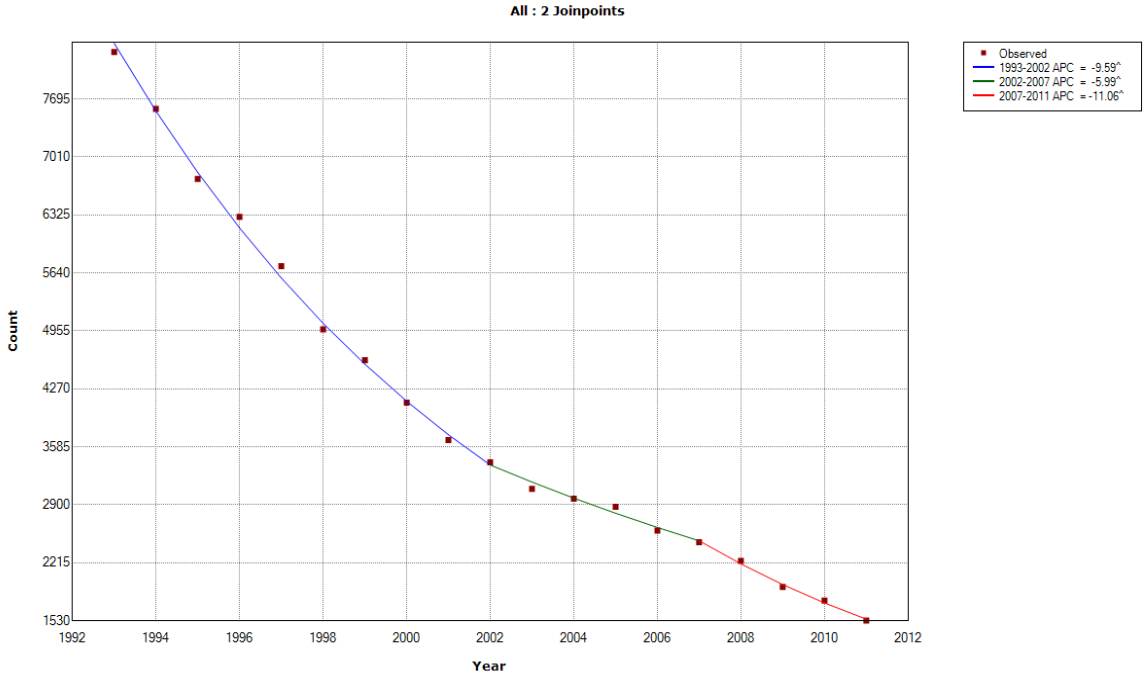


Figure 7: US-born non-Hispanic black TB case average annual percent change (APC)



Figures 8-10: JoinPoint models of annual US-born Black TB cases stratified on Non-Injectable Drug Use.

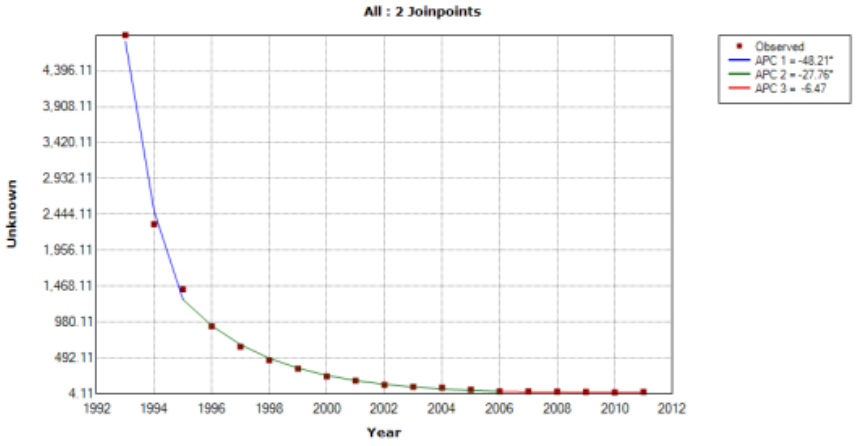


Figure 8: Unknown

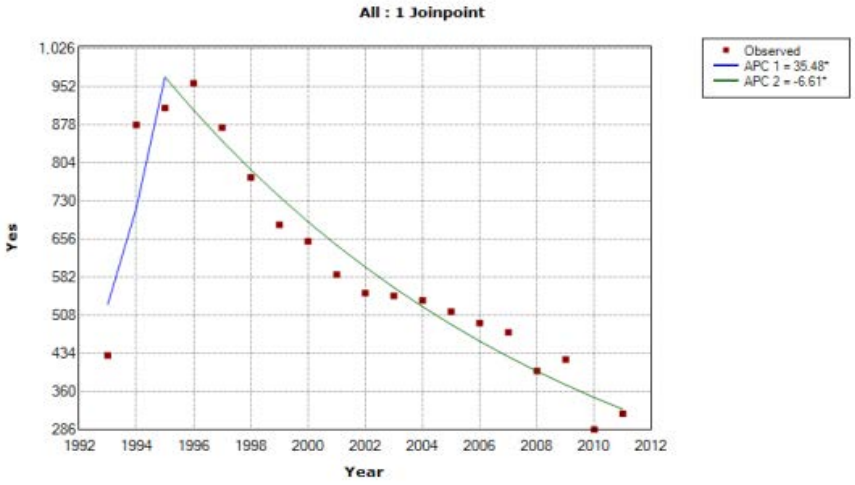


Figure 9: Positive

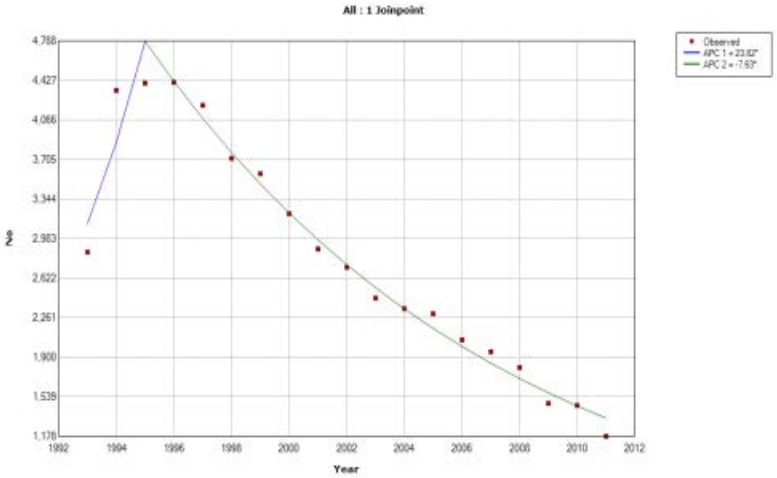


Figure 10: Negative

Figures 11-13: JoinPoint models of annual US-born Black TB cases stratified on Homelessness

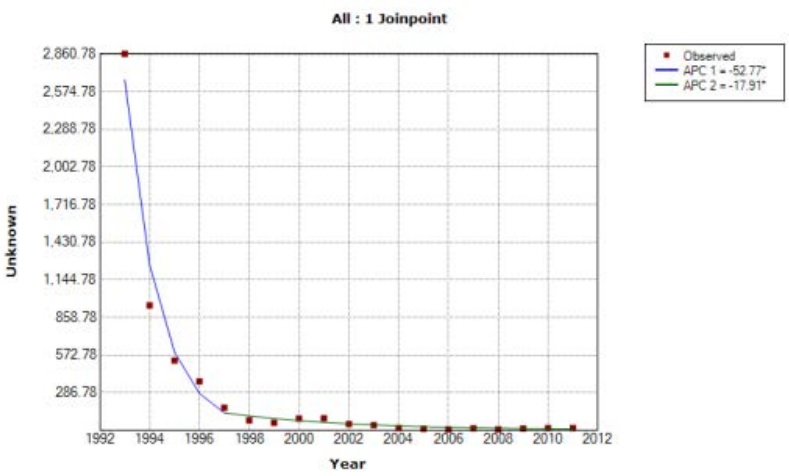


Figure 11: Unknown

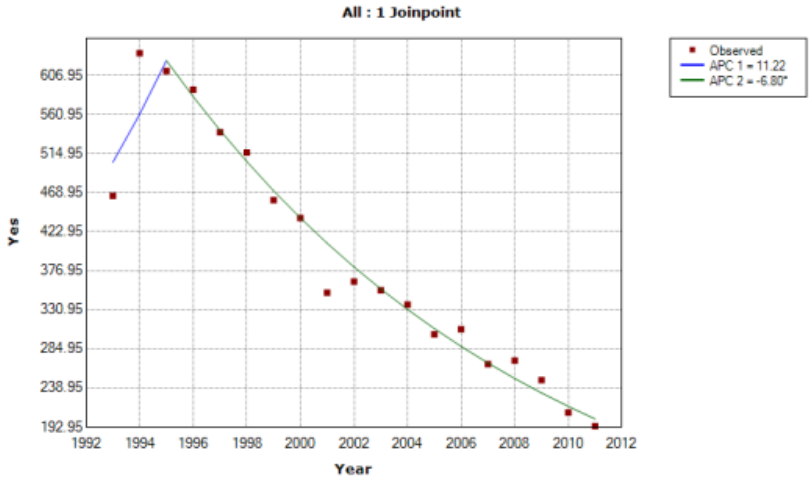


Figure 12: Positive

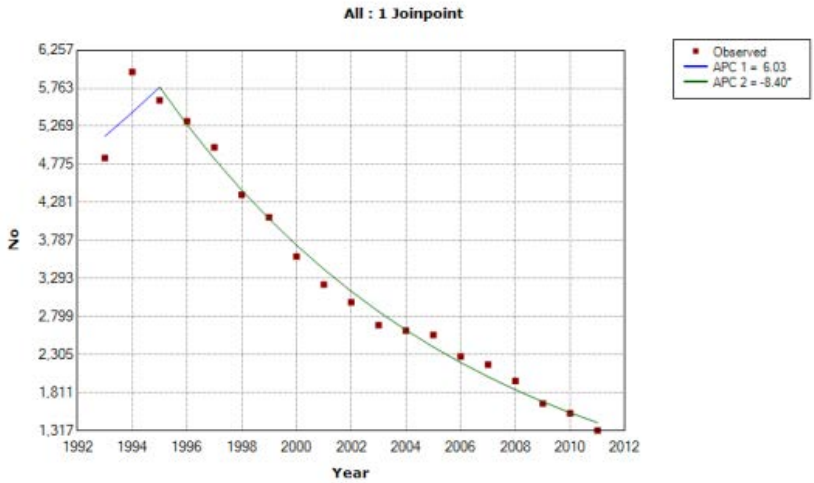


Figure 13: Negative

Figures 14-16: JoinPoint models of annual US-born Black TB cases stratified on Excessive Alcohol Use

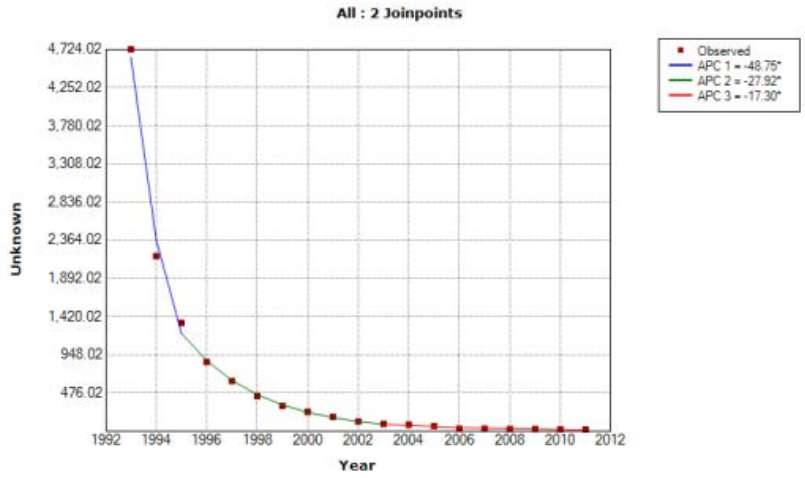


Figure 14: Unknown

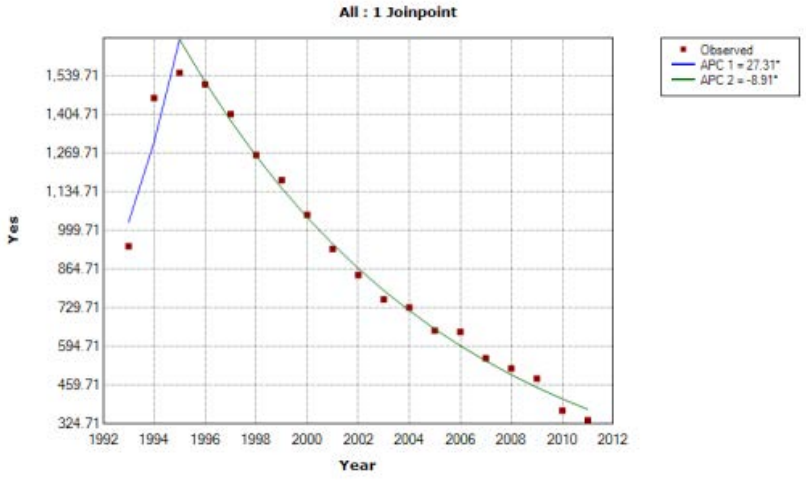


Figure 15: Positive

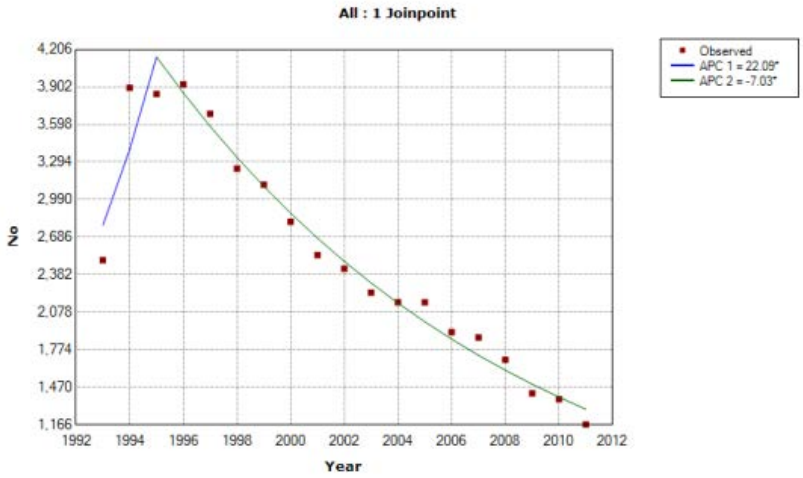


Figure 16: Negative

Figures 17-19: JoinPoint models of annual US-born Black TB cases stratified on DOT Status (Directly Observed Therapy (DOT), Self-Administered Therapy (SAT), or Both)

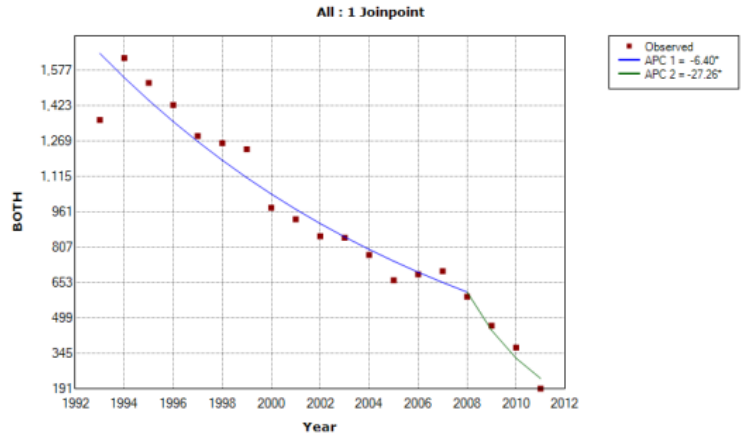


Figure 17: Both

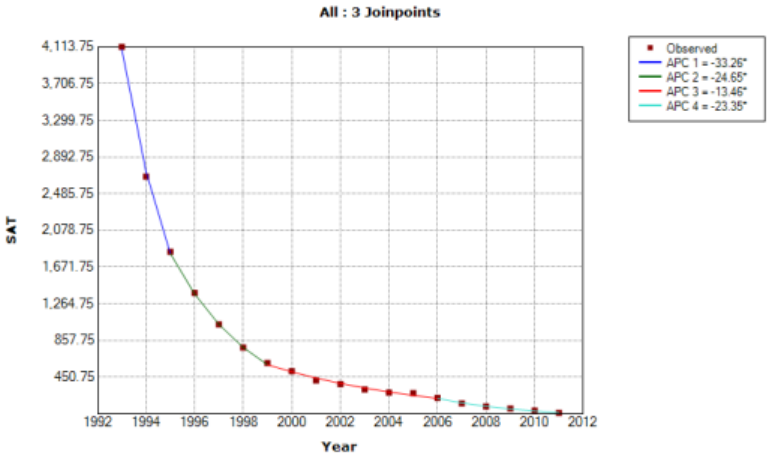


Figure 18: SAT

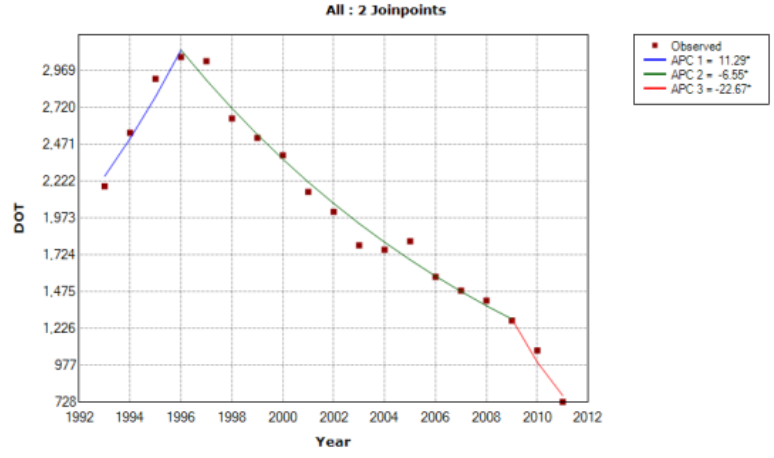


Figure 19: DOT

Figures 20-22: JoinPoint models of annual US-born Black TB cases stratified on Health Provider Type

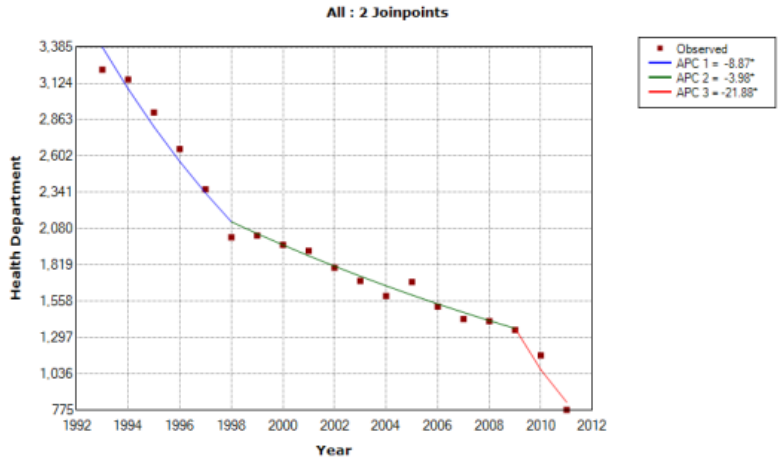


Figure 20: Health Department

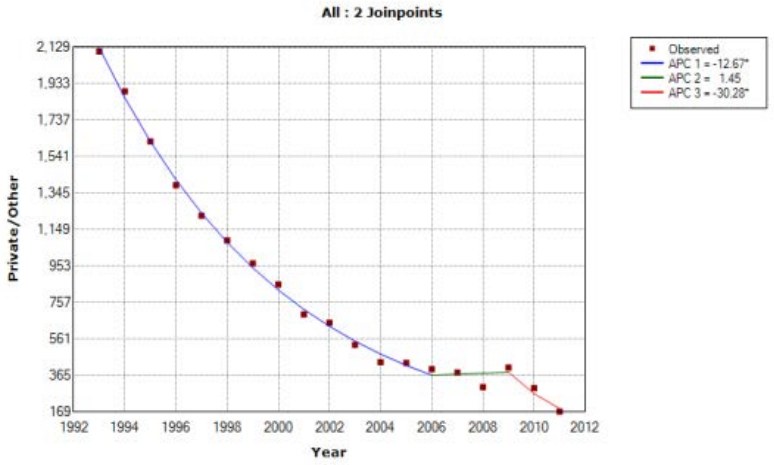


Figure 21: Private/Other

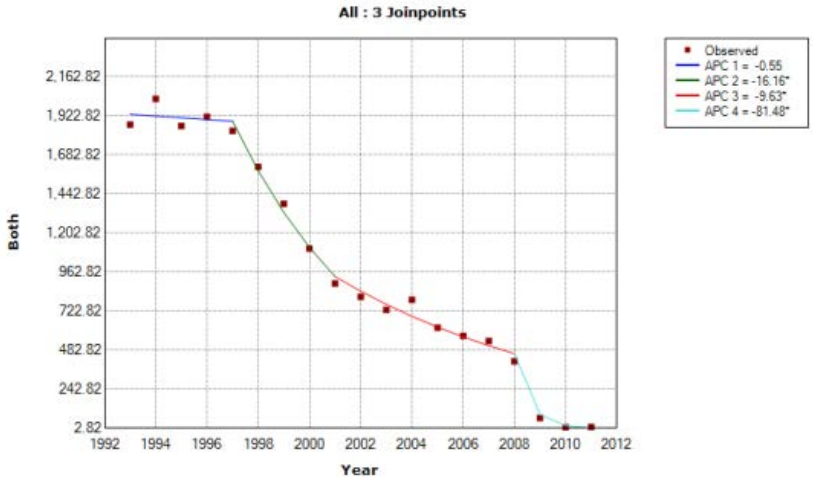


Figure 22: Both (Health Dept. & Private/Other)

Figures 23-27: JoinPoint models of annual US-born Black TB cases stratified on Age Groups

Figure 23: Age 0-14

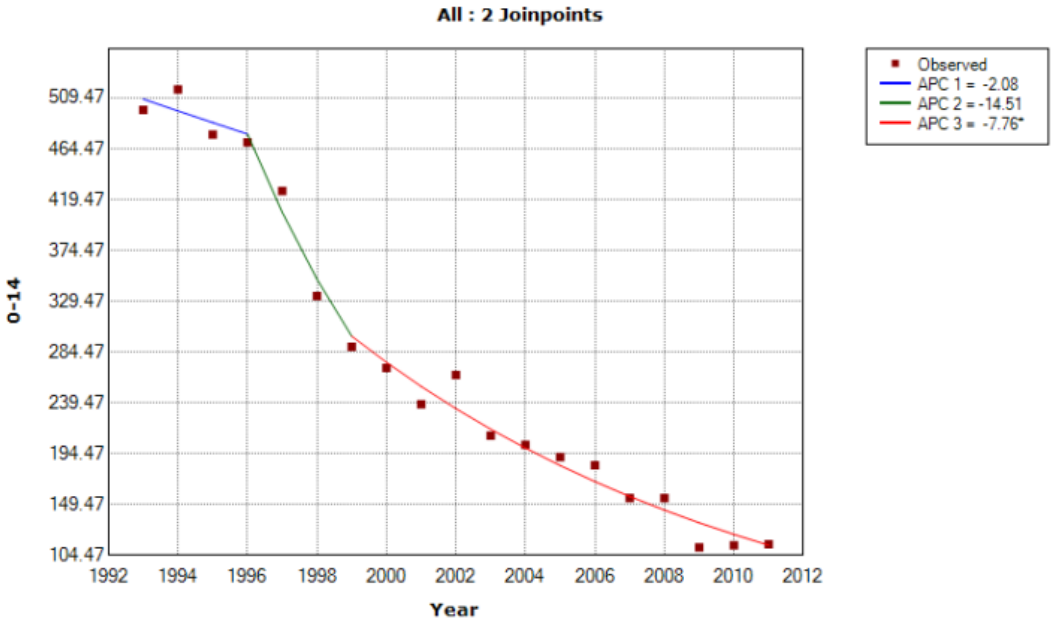


Figure 24: Age 15-24

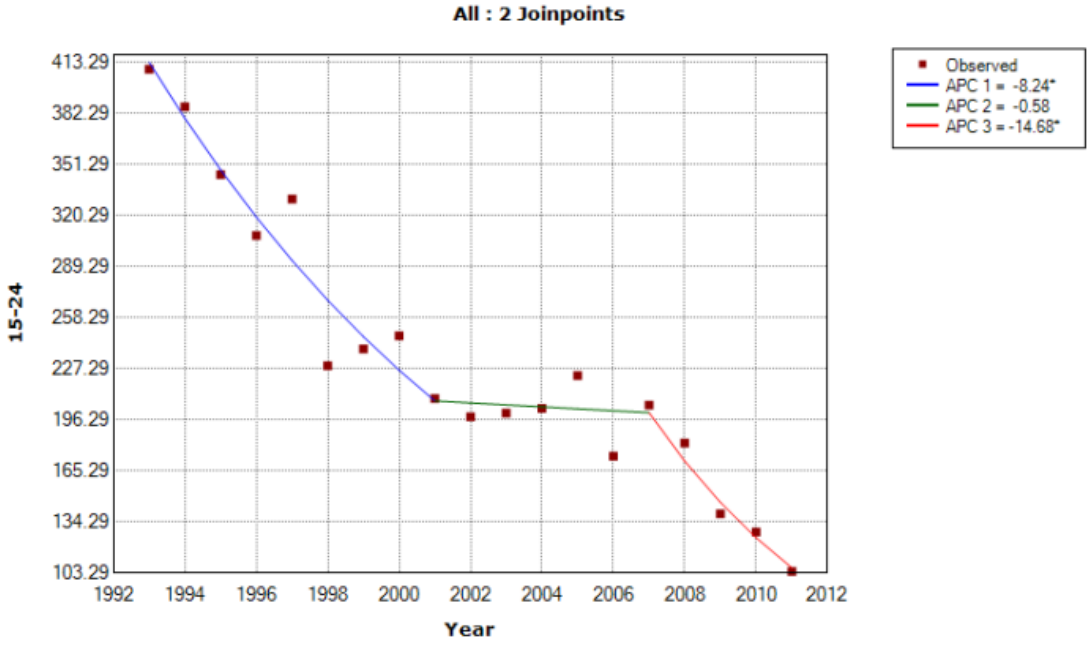


Figure 25: Age 25-44

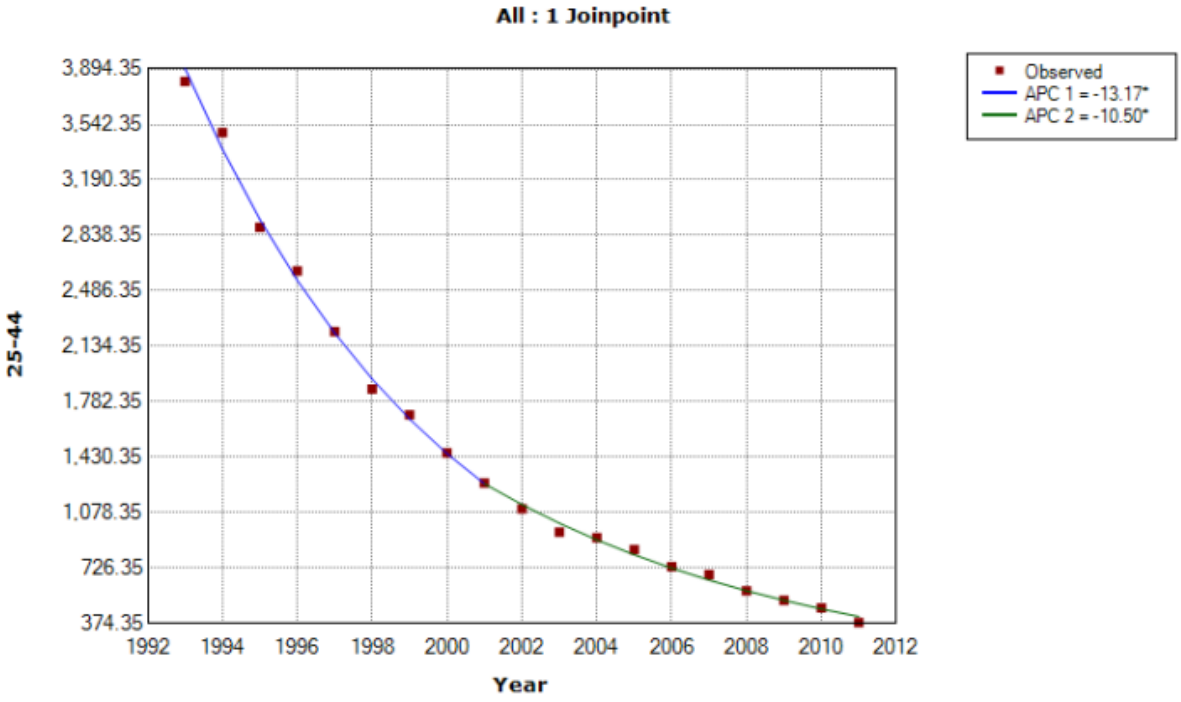


Figure 26: Age 45-64

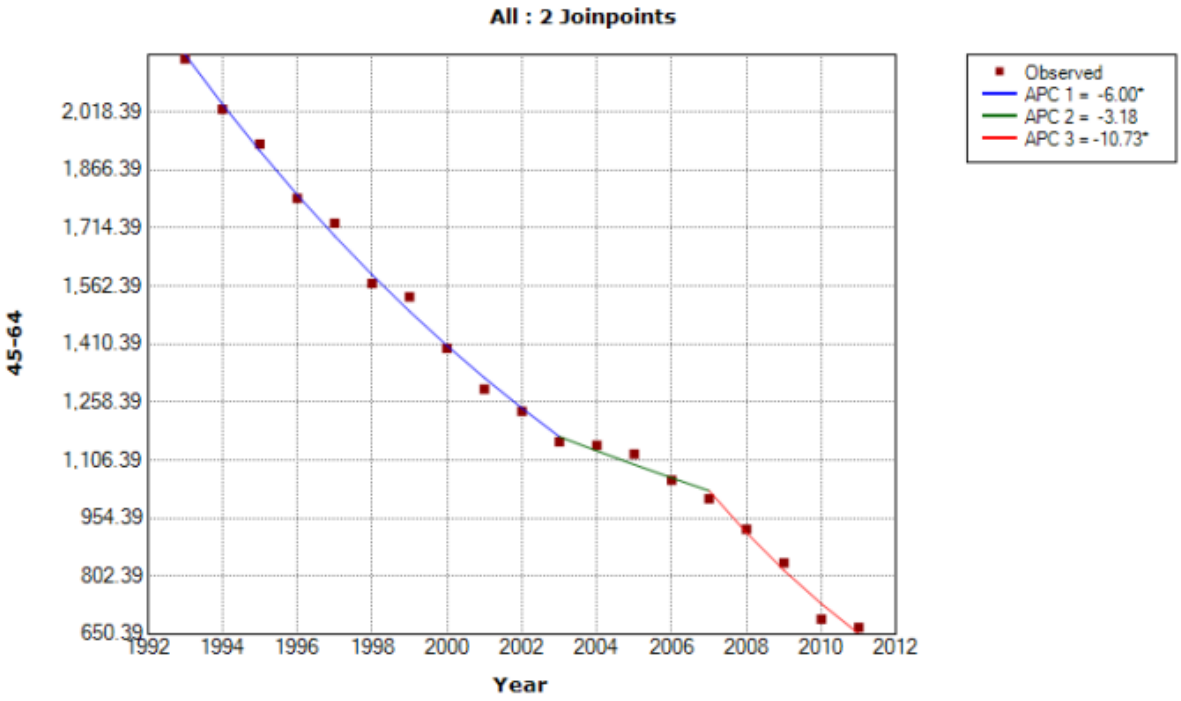
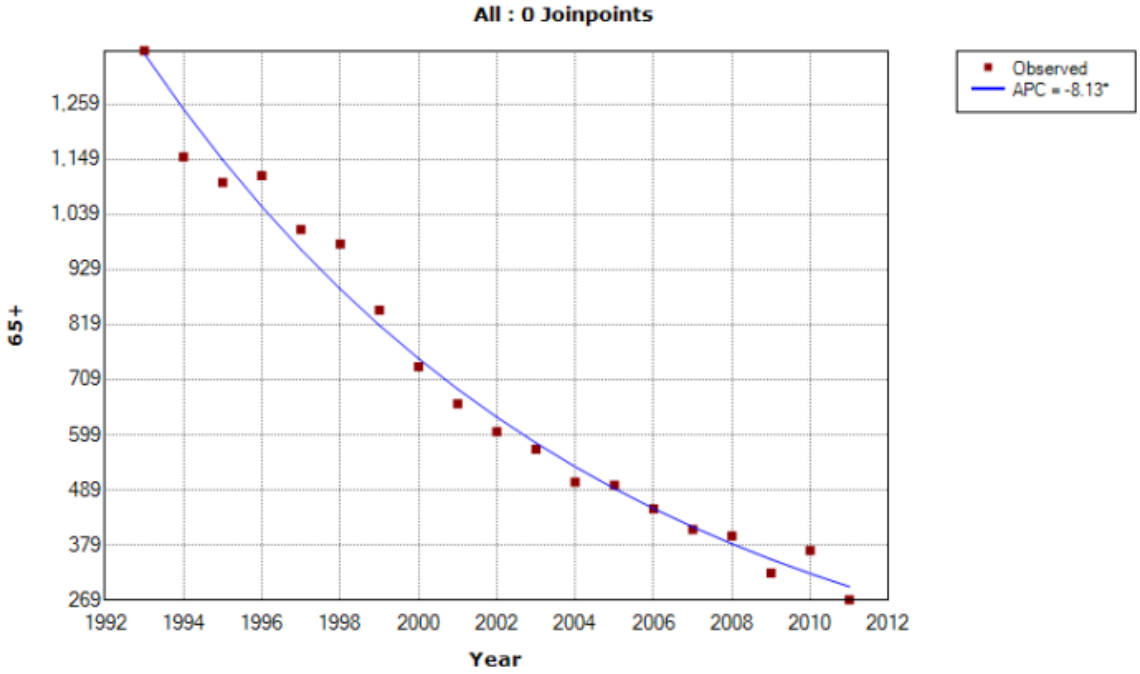


Figure 27: Age 65+



Figures 28-30: JoinPoint models of annual US-born Black TB cases stratified on HIV status, excluding California* (HIV Positive, HIV Negative, Other**)

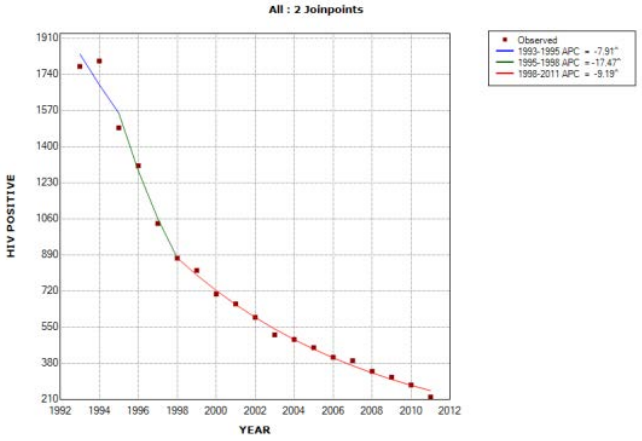


Figure 28: HIV Positive

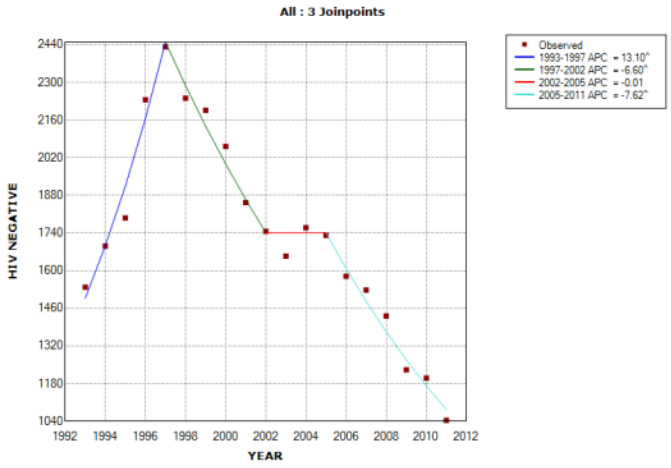


Figure 29: HIV Negative

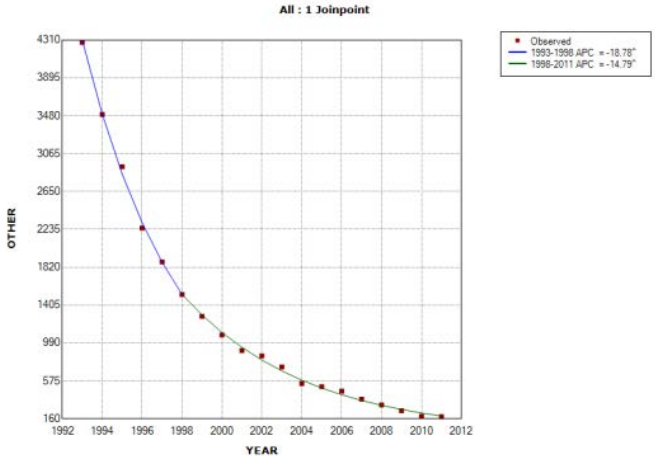


Figure 30: Other

*California did not start fully reporting HIV cases until 2011.
** Other for HIV Status includes Unknown, Indeterminate, Not Done, Test Not Offered, Refused, and Test Date Unknown

Figures 31-36: JoinPoint models of annual US-born Black TB cases stratified on States and Cities with over 5,000 cumulative cases (1993-2011)

Figure 31: Georgia TB Cases

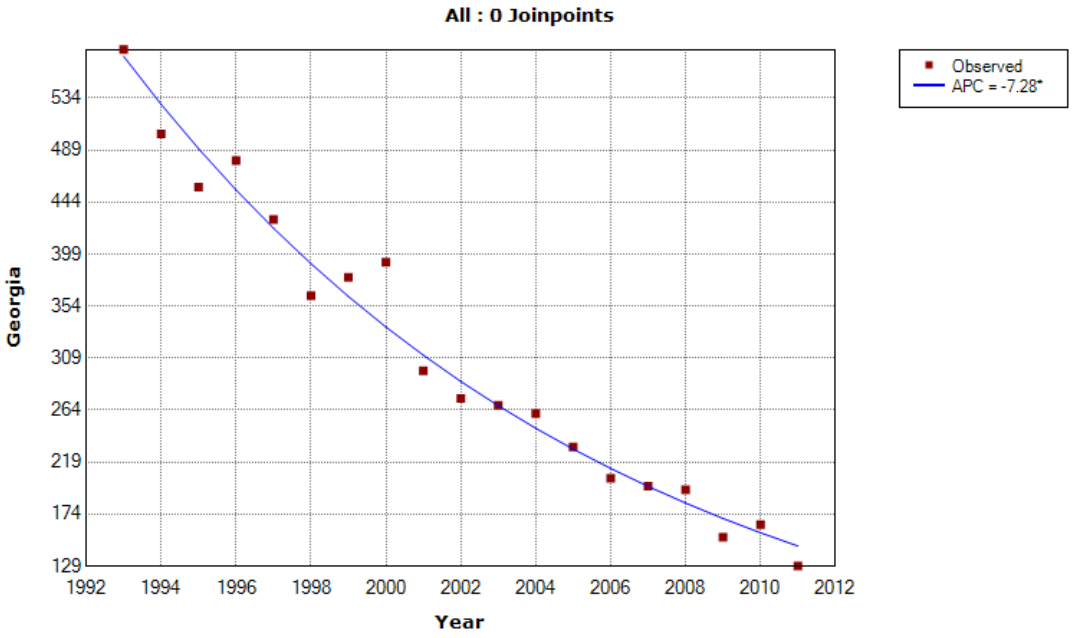


Figure 32: Florida TB Cases

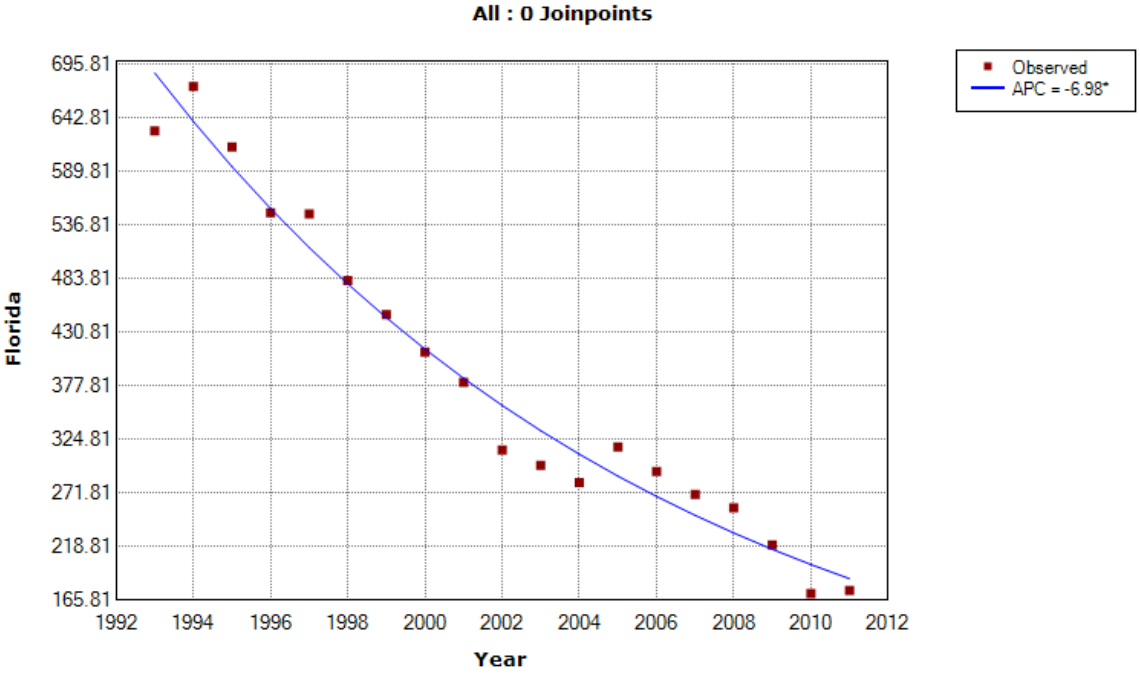


Figure 33: California TB Cases

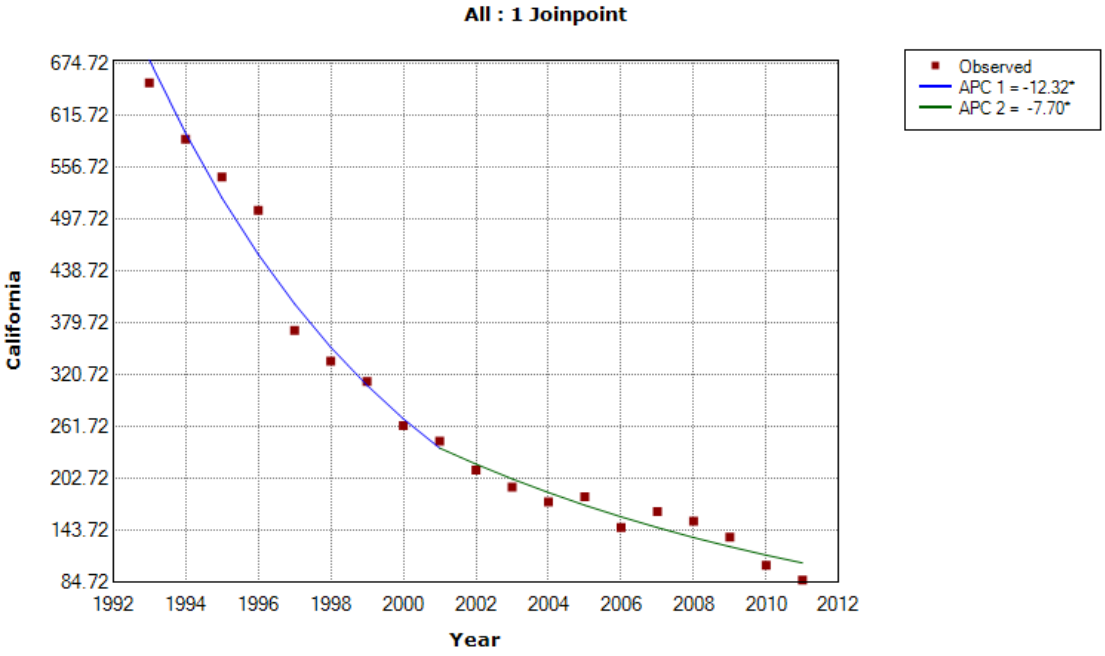


Figure 34: New York City TB Cases

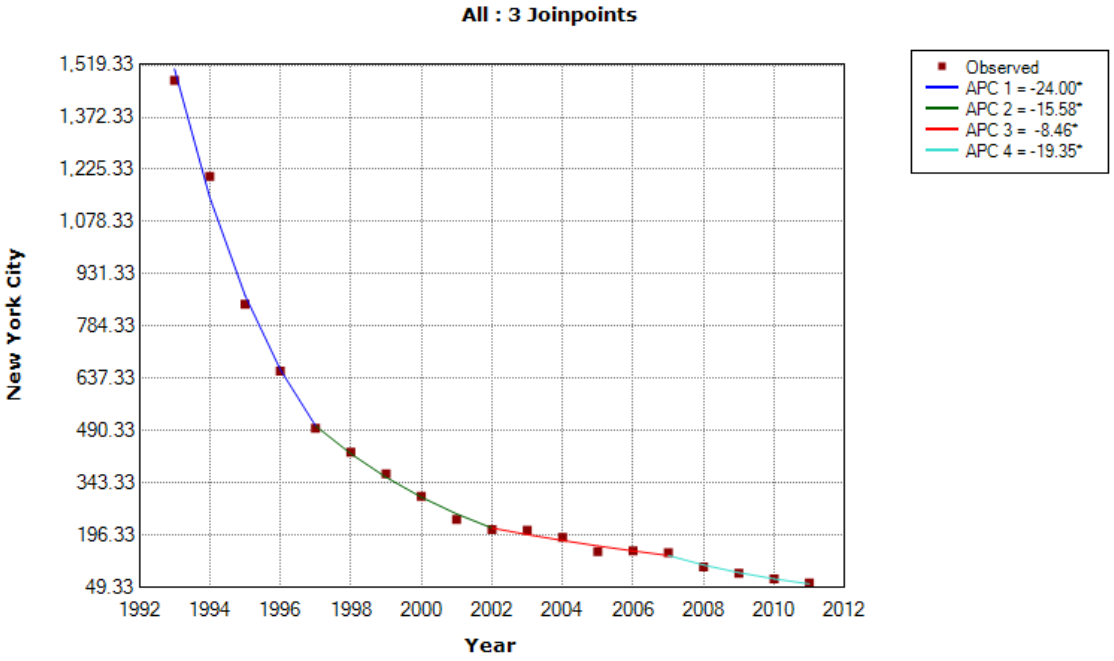


Figure 35: Illinois TB Cases

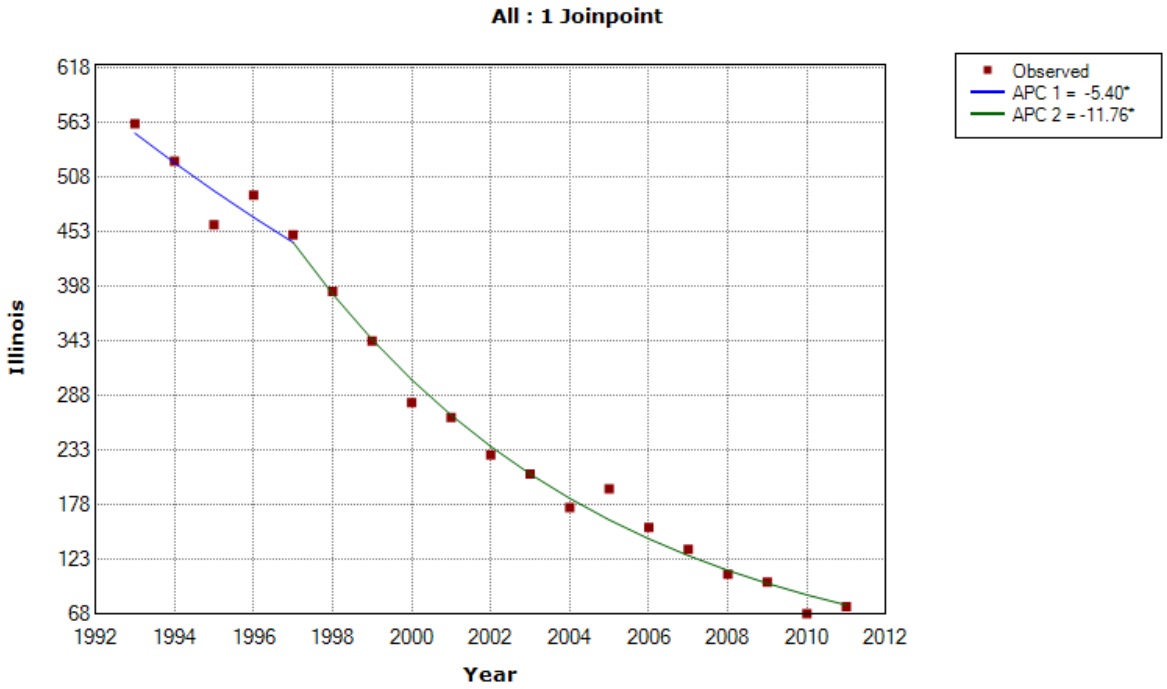


Figure 36: Texas TB Cases