2020 Annual Tuberculosis Report
Fresno County

Fresno County Department of Public Health (FCDPH)
Tuberculosis Control Program

2020 Annual Tuberculosis Report Fresno County
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3HP – Once-weekly Isoniazid-Rifapentine for 12 Weeks
AFB – Acid-Fast Bacilli
CDC – Centers of Disease Control and Prevention
CDPH – California Department of Public Health
DOT – Direct Observed Therapy
Dx – Diagnosis
EMB – Ethambutol
ETH – Ethionamide
FCDPH – Fresno County Department of Public Health
HIV – Human Immunodeficiency Virus
INH – Isoniazid
LTBI – Latent Tuberculosis Infection
MDR-TB – Multi-Drug-Resistant Tuberculosis
MOX – Moxifloxacin
NHPI – Native Hawaiian Pacific Islander
NTIP – National Tuberculosis Indicators Project
PZA – Pyrazinamide
RIB – Rifabutin
RIF – Rifampin
RIP – Rifapentine
Rx – Prescription
SM – Streptomycin
TB – Tuberculosis
TNF-Alpha – Tumor Necrosis Factor Alpha
WHO – World Health Organization
XDR-TB – Extensively Drug-Resistant Tuberculosis

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Tuberculosis Burden Summary

Globally[1,2]

In 2019, the World Health Organization (WHO) published updated estimates of global deaths by cause, and out of all causes of death, Tuberculosis (TB) ranked as thirteenth. During that same year, TB was the leading cause of death due to infectious disease. When final data is available for 2020, the WHO anticipates that TB will rank as the second leading cause of death due to infectious disease behind COVID19. Provisional estimates for the number of TB deaths in 2020 are 1.3 million (range, 1.2 – 1.4), an increase from 2019. This is the first annual increase in TB deaths since 2005, and is a result of decreased TB care during the COVID19 pandemic. During 2020, an estimated 9.9 million people (range, 8.9 – 11) became sick with TB, resulting in an incident of 127 cases (range, 114 – 140) per 100k population. These numbers represent a small decline in TB disease burden when compared to 2019.

Tuberculosis is a leading killer of people who are HIV-infected, and in 2020 around 214,000 (range, 187,000 – 242,000) people with HIV died from TB. Despite this high number, there is a 69% reduction in HIV deaths from 2000-2019. During the same time span, the deaths among HIV – negative people dropped by 31%. Unfortunately, this trend was reversed for both TB and HIV–TB patients in 2020 due to the COVID19 pandemic.

Worldwide, most TB cases are in adults (89%) that are male (56%). Two thirds of TB cases originate from eight countries: India, China, Indonesia, the Philippines, Pakistan, Nigeria, Bangladesh, and South Africa.

The WHO asserts that multidrug-resistant TB (MDR–TB) is of great public health concern. For the last 10 years, the proportion of new TB cases that are MDR–TB is estimated to be 3 to 4%. That estimate for previously treated TB cases is 18 to 21%. In 2020, there were 465,000 (range, 400,000 – 535,000) new TB cases with resistance to Rifampicin, of which 78% had MDR–TB. In 2019, 12,350 XDR–TB cases were reported globally.

Nationally[3,4,5]

A total of 7163 TB cases (an incidence of 2.2 cases per 100,000 people) were reported in the United States in 2020. Compared to 2019, in 2020 the incidence decreased by 18.5% and the number of cases decreased by 19.6%. In 2020, California, Texas, New York, and Florida accounted for about half of all TB cases reported.

Minority populations continue to have the highest incidence of TB in the United States. The 2020 foreign-born TB incidence per 100,000 population for Native Hawaiians/Pacific Islanders, Asians, Blacks, Hispanics/Latinos, American Indians/Alaska Natives, and Whites is 32.5, 21.7, 15.3, 8.0, 2.5, and 2.8 respectively. The 2020 incidence per 100,000 population for native-born TB cases who are Native Hawaiians/Pacific

Islanders, Asians, Blacks, Hispanics/Latinos, American Indians/Alaska Natives, and White is 6.2, 1.3, 2.0, 1.2, 3.2 and 0.3 respectively.

Foreign-born people represent 71% of all TB cases in 2020 and the top 5 countries of birth for foreign-born TB cases are Mexico, the Philippines, India, Vietnam, and China. In addition to being foreign-born, other top risk factors for TB infection include HIV, substance abuse, diabetes, kidney disease, organ transplantation, homelessness, and institutionalization (prisons, shelters, nursing homes).

There were 56 MDR-TB cases in 2020, and the number of MDR-TB cases decreased by 36 when compared to 2019. There was one XDR-TB case in 2020.

California[6,7]

In 2020, a total of 1703 new TB cases were reported compared to 2114 cases in 2019. California reported 29.5% of the nation's TB cases in 2020. The California TB incidence during 2020 is 4.3 per 100,000 people, a decrease of 18.9% compared to 2019. TB cases are reported in 42 (68.8%) of California's 61 local health jurisdictions.

Like the United States as a whole, minority populations continue to have the highest incidence of TB in California. The incidence of TB per 100,000 population for Whites, Blacks, Hispanics, Native Hawaiian/Pacific Islanders, and Asians is 0.8, 3.5, 4.0, 8.2, and 14.3 respectively.

Foreign-born people represent 84% of all TB cases and well over half of these cases were born in Mexico, the Philippines, Vietnam, China, and India. Social and behavioral risk factors identified in California TB cases include injection drug use, non-injection drug use, alcohol use, homelessness, long-term care facility residency, and jail residency. Medical risk factors identified in California TB cases include diabetes, TNF-alpha antagonist therapy, end-stage renal disease, HIV, other immunosuppressive conditions, and post-organ transplant.

It is estimated that 2 million Californians have a latent TB infection (LTBI) and are at risk of developing active TB if not properly diagnosed and treated. Many people with LTBI are unaware of their infection. Latent TB treatment is critical because an estimated 85% of active TB cases develop from LTBI.

In California, MDR-TB has remained a small proportion of TB cases (1-2%) during 1993-2020 despite the growth of MDR-TB cases throughout the world. A total of 11 (1.0%) MDR-TB cases are reported in California during 2020. No Extensively Drug Resistant (XDR-TB) cases are reported in California during 2020, and 25 XDR-TB cases are reported from 1993-2020.

Fresno County

A total of 36 TB cases (an incidence of 3.6 cases per 100,000 people) were reported in Fresno County during 2020. Compared to 2019, in 2020 the incidence decreased by 5.2% and the number of cases decreased by 5.3%.

In 2020, most TB cases occurred in older adults (average age 50.7 years old), and more TB cases were male than female (66.7% vs. 33.3%). Over half of TB cases were not employed when they received their diagnosis.

Racial and ethnic disparities continue to exist among populations with TB disease in Fresno County. During 2020, the incidence of TB for Asians/Native Hawaiians-Pacific Islanders, Blacks, Hispanics/Latinos, and Whites is: 14.1, 2.0, 3.5, and 0.6 per 100,000 people respectively.

Foreign-born people represent well over half of all TB cases in 2020, and 89.2% of these cases arrived from Mexico, Laos, Cambodia, and India. Social and behavioral risk factors identified in 2020 TB cases include alcohol and drug abuse, contact with an active TB case, migrant/seasonal work, institutionalism (correctional and long-term care residencies), and homelessness. Medical risk factors identified in 2020 TB cases include diabetes, HIV, end stage renal disease, and a prior TB diagnosis.

As in 2019, the MDR-TB incidence in 2020 remained 0.0 per 100,000 people.

Tuberculosis Cases and Incidence in Fresno County

Tuberculosis (TB) is a common communicable disease caused by the bacterium *Mycobacterium tuberculosis*.[8] It most commonly infects the lungs, but can infect almost any organ system. In 2020, 36 new cases of active TB were diagnosed in Fresno County (3.5 per 100,000 population), a 5.3% decrease in the annual number of cases from 2019 (Figures 1-2). During 2020, out of the 61 health jurisdictions in California, the active TB incidence in Fresno County ranked 16, and Fresno County reported 2.16% of the total number of TB cases reported in California.[6]

Figure 1. Annual New Active TB Case Counts in Fresno County – 2006-2020

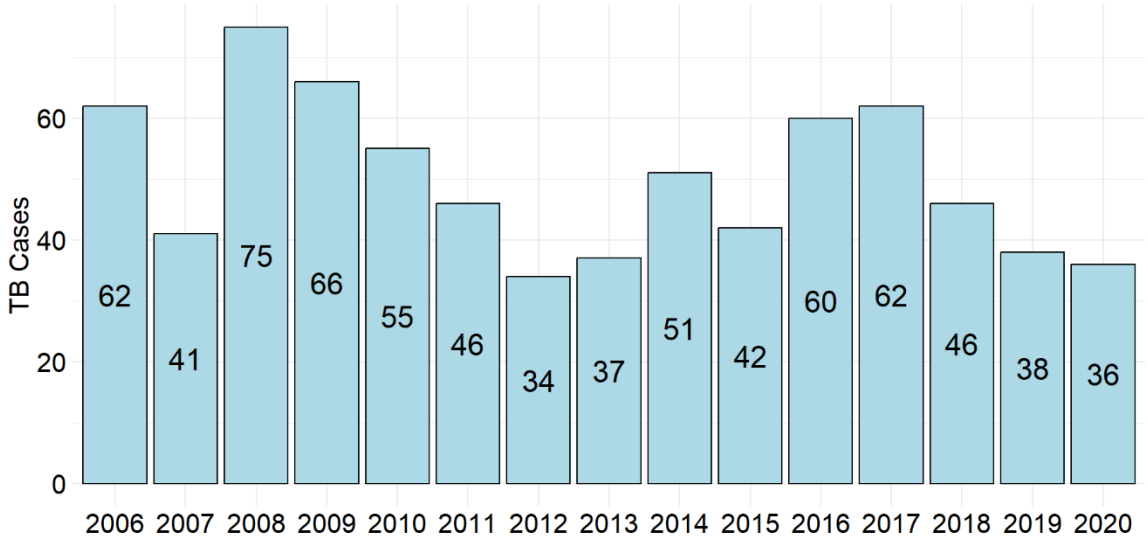
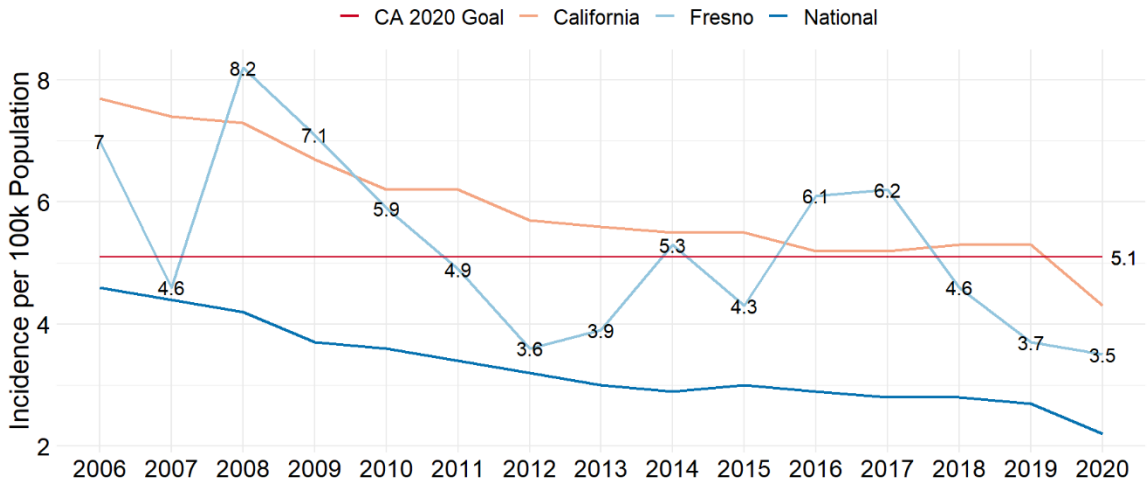


Figure 2. Annual National and State TB Incidence Compared to Fresno County – 2006- 2020*



*Data Sources:
Tuberculosis Control Branch, Provisional California Tuberculosis Data Tables. California Department of Public Health, Richmond, CA. January 2022.
Deutsch-Feldman M, Pratt RH, Price SF, Tsang CA, Self JL. Tuberculosis - United States, 2020. MMWR Morb Mortal Wkly Rep 2021;70:409-414.

Demographic Characteristics in Fresno County

Sex and Age

In 2020, 24 (66.7%) cases were male and 12 (33.3%) were female (Figure 3). Most TB cases in Fresno County occurred in older adults (Figure 4), and 20 (52.8%) cases during 2020 were over age fifty (data not shown). No TB patients were under the age of fifteen (Figure 4). The average age of TB patients in Fresno County during 2020 was 50.7 years with a range from 21 to 85 years (Figure 5).

Figure 3. Percent Male vs Female TB Cases in Fresno County – 2015-2020

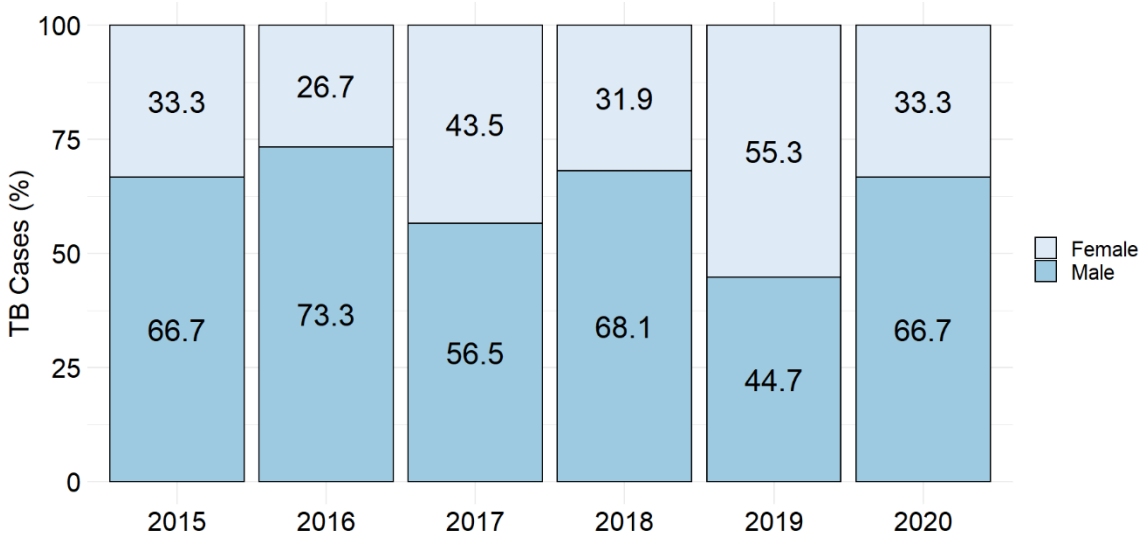


Figure 4. Age Distribution of TB Cases in Fresno County – 2020

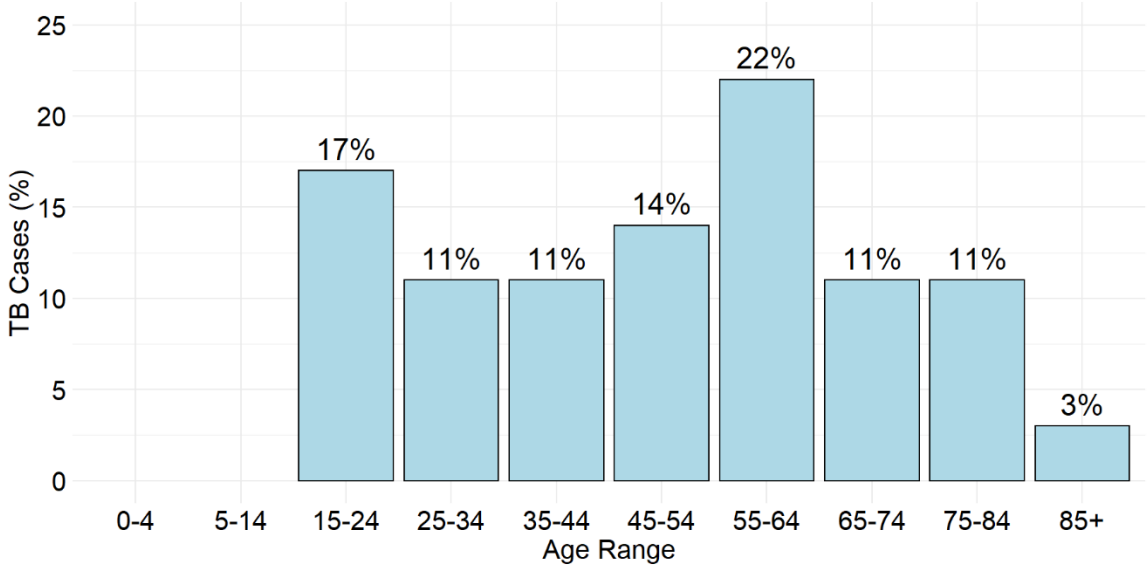
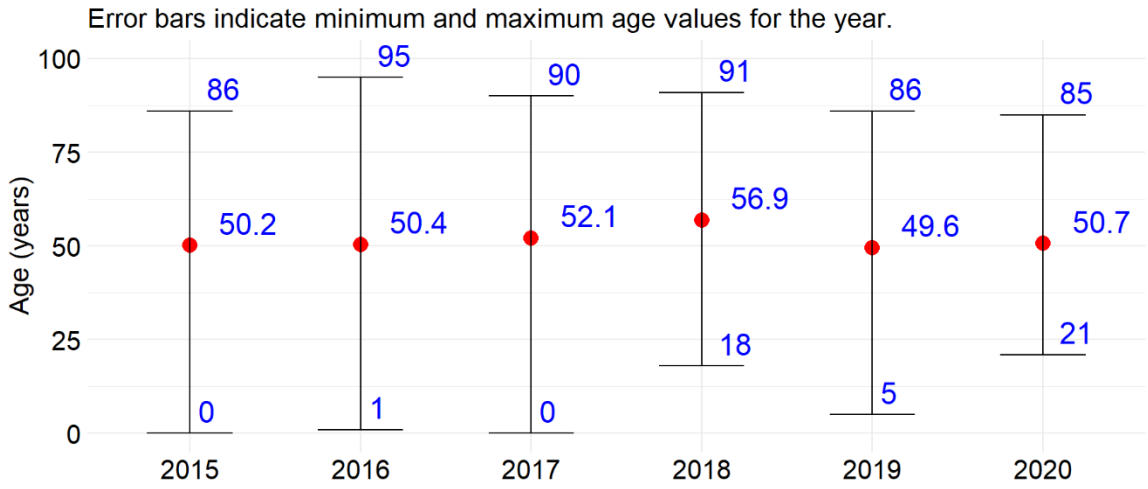


Figure 5. Average Minimum and Maximum Age at TB Diagnosis in Fresno County – 2015-2020



Nativity

Similar to prior years, during 2020 a smaller percentage of TB cases were among US-born residents compared to foreign-born people (Figure 6). The top four countries represented by foreign-born TB cases, accounting for 89.2% of all foreign-born cases, are Mexico, Laos, Cambodia, and India. Other countries represented by 2020 TB cases include the Philippines and Ethiopia (Figure 7). One foreign-born case in 2020 had an unknown country of origin. During 2020, foreign-born TB patients spent an average of 16.5 years in the US prior to their TB diagnosis (Figure 8).

Figure 6. Nativity of TB cases in Fresno County – 2015-2020

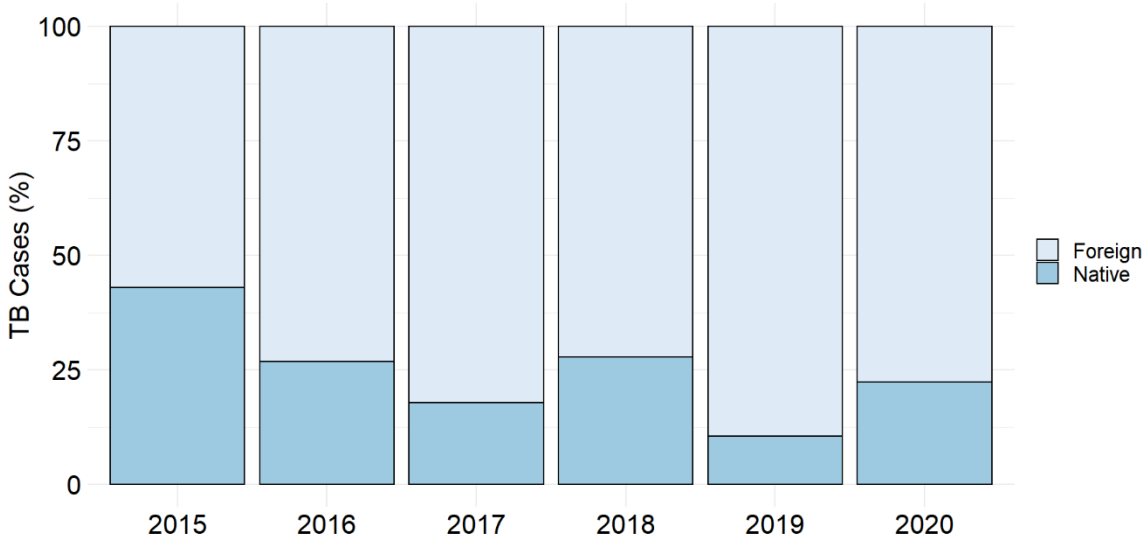


Figure 7. Birth Country for Foreign-Born TB Cases in Fresno County – 2020

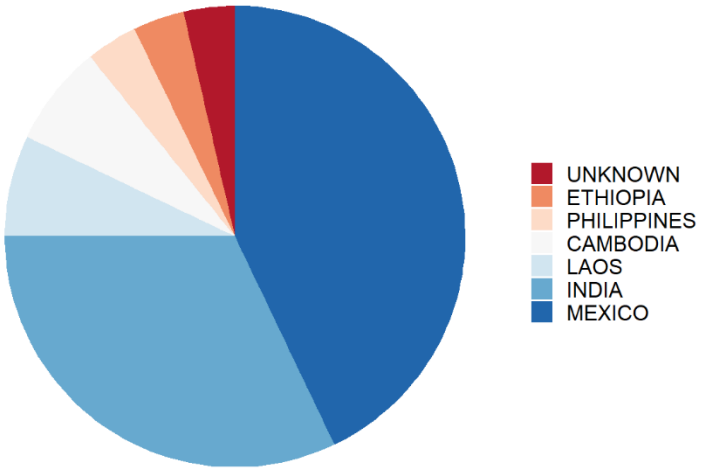
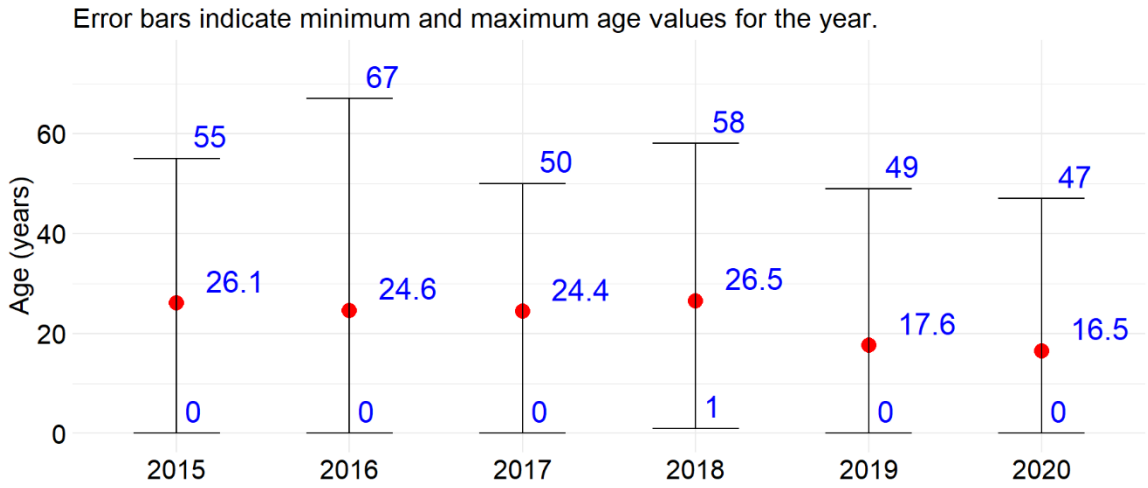


Figure 8. Average Minimum and Maximum Time from United States Arrival to Diagnosis for Foreign-Born TB Cases in Fresno County – 2015-2020



Race/Ethnicity

Racial and ethnic disparities exist among populations with TB disease in Fresno County (Figure 9 & Figure 10). The crude TB incidence in Fresno County for 2020 is 3.5 per 100,000 people (Figure 2). The race/ethnicity specific incidence for Asians/NHPI, Blacks/African Americans, Hispanics/Latinos, and Whites is 14.1, 2.0, 3.5, and 0.6 per 100,000 people respectively (Figure 9).

Figure 9. TB Incidence* by Race/Ethnicity in Fresno County – 2010-2020

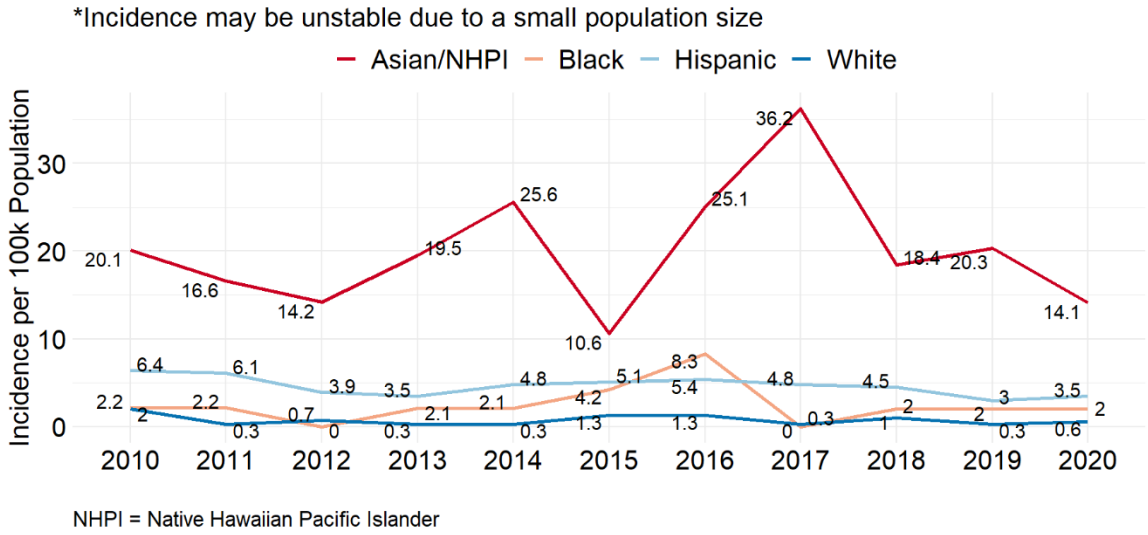
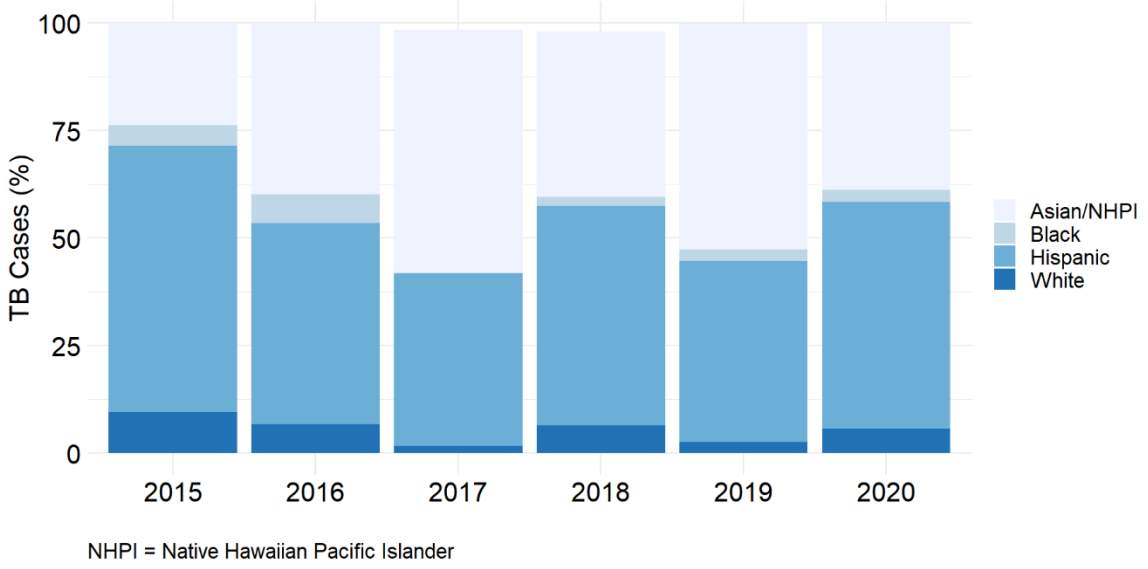


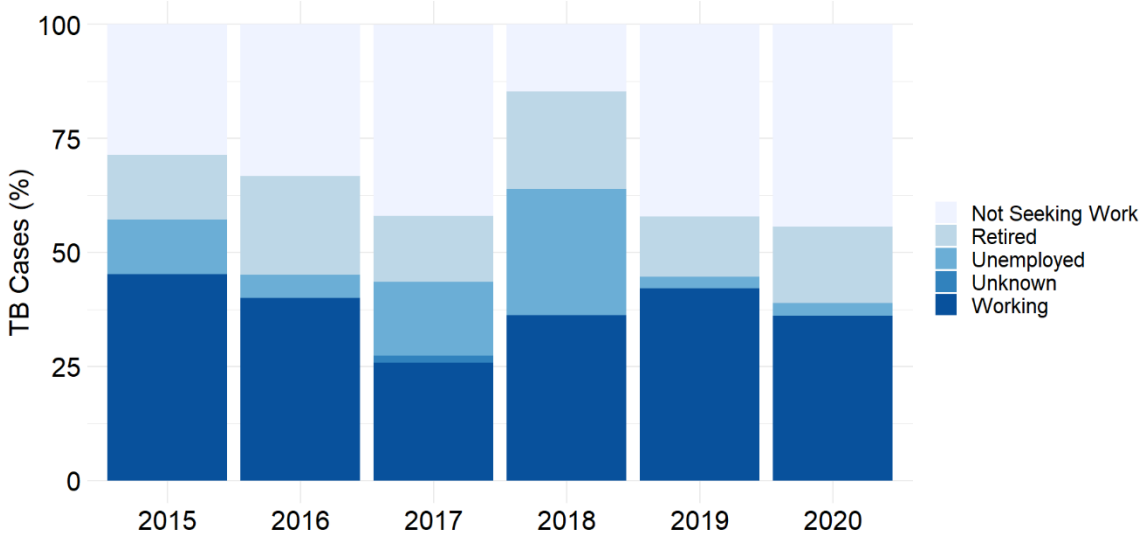
Figure 10. Percent of TB Cases by Race/Ethnicity in Fresno County – 2015-2020



Occupational Status in Fresno County

Figure 11 shows the occupational status of those with TB disease in Fresno County during 2020. Most cases, 23 (63.9%), were not employed because they were not seeking work, retired, or unemployed. Those with a TB diagnosis who were employed (13) represent 36.1% of cases.

Figure 11. Occupational Status of TB Cases in Fresno County – 2015-2020

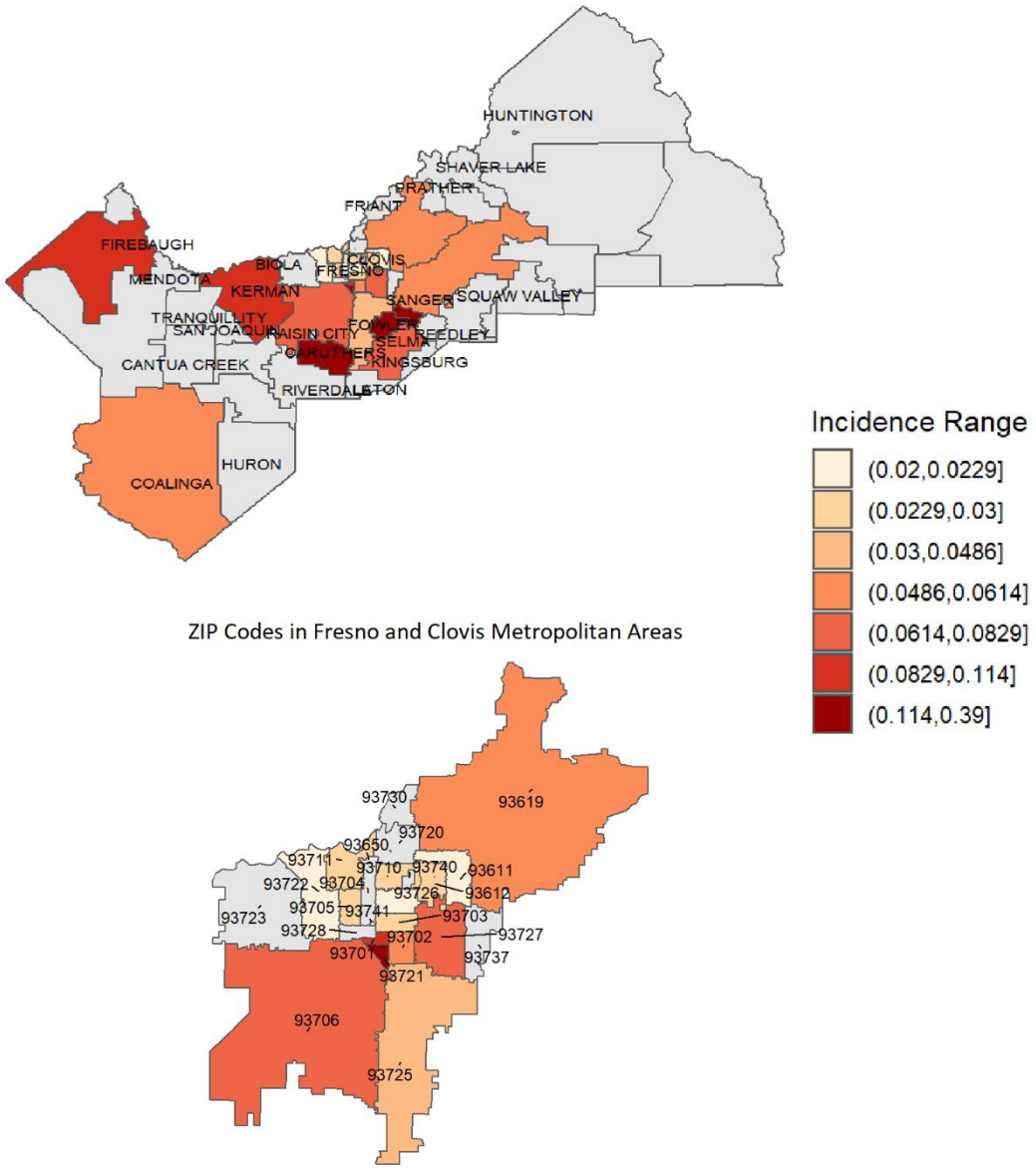


Geographic Distribution in Fresno County

Figure 12 shows the geographic distribution of TB cases within Fresno County by zip code. During 2020, the highest incidence of TB was located in zip codes: 93616, 93609, 93721, 93625, and 93622 (Figure 12).

Figure 12. TB Incidence by Zip Code per 1000 Population in Fresno County-2020*

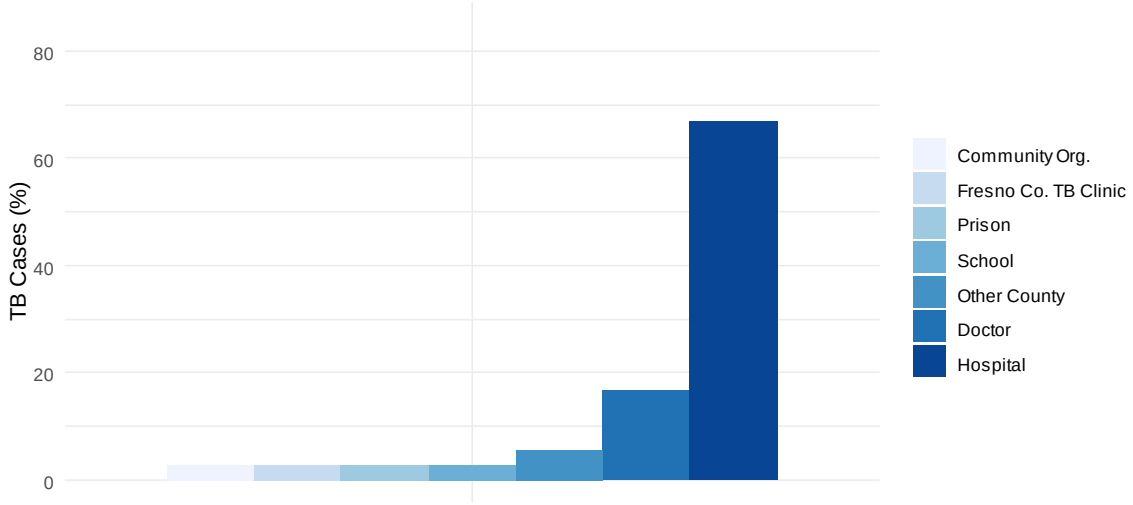
*Incidence per 100K residents may be unstable due to a small sample size.



Case Referral by Source in Fresno County

Cases of TB were identified and referred to the Fresno County Department of Public Health for treatment from different sources. During 2020, the top 3 referral sources accounting for 89% of the TB cases were: hospitals, doctors, and other counties. (Figure 13).

Figure 13. Referral Sources for TB Patients in Fresno County – 2020

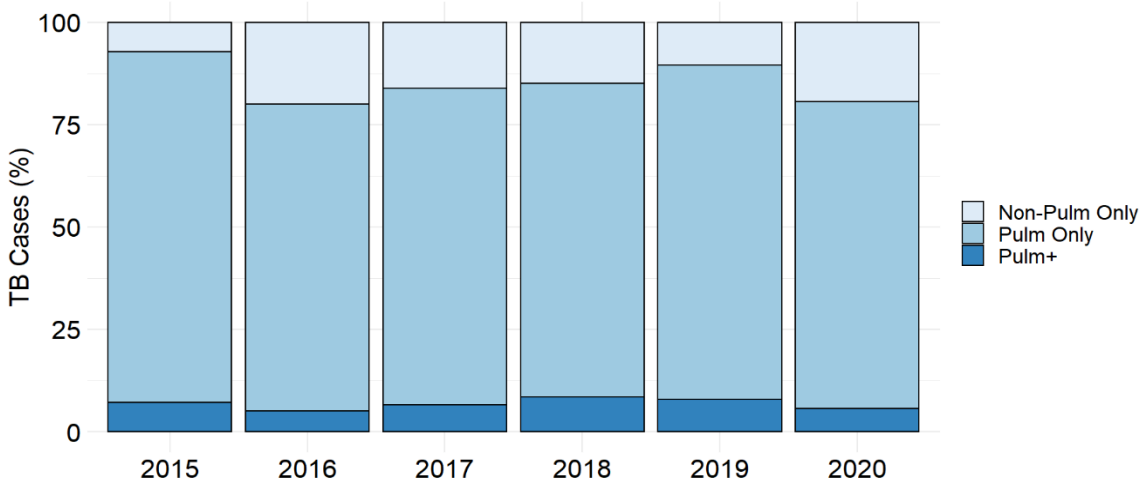


Pathology and Organism Characteristics in Fresno County

Infection Location

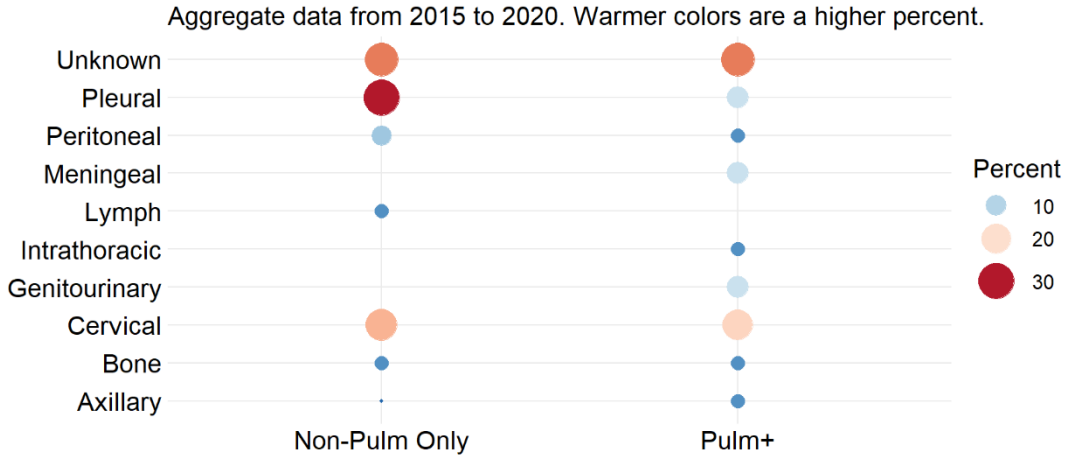
During 2020, 29 (80.6%) patients had lung involvement, of which 27 (75.0%) had lung involvement only (Figure 14). Pulmonary infection combined with infection in axillary and unknown tissues occurred in less than 15 patients (Data not shown). Extrapulmonary infections also occurred in less than 15 patients and were found in cervical, peritoneal, pleural and unknown tissues (Data not shown). Figure 15 shows the distribution of extrapulmonary TB infections using aggregate data from 2015 to 2020.

Figure 14. Pulmonary versus Extrapulmonary TB in Fresno County – 2015-2020*



*Pulm+ infections occur in both the lung and other tissues, while Non-Pulm Only infections occur outside the lung.

Figure 15. Infection Location for Extrapulmonary TB in Fresno County – 2015-2020*

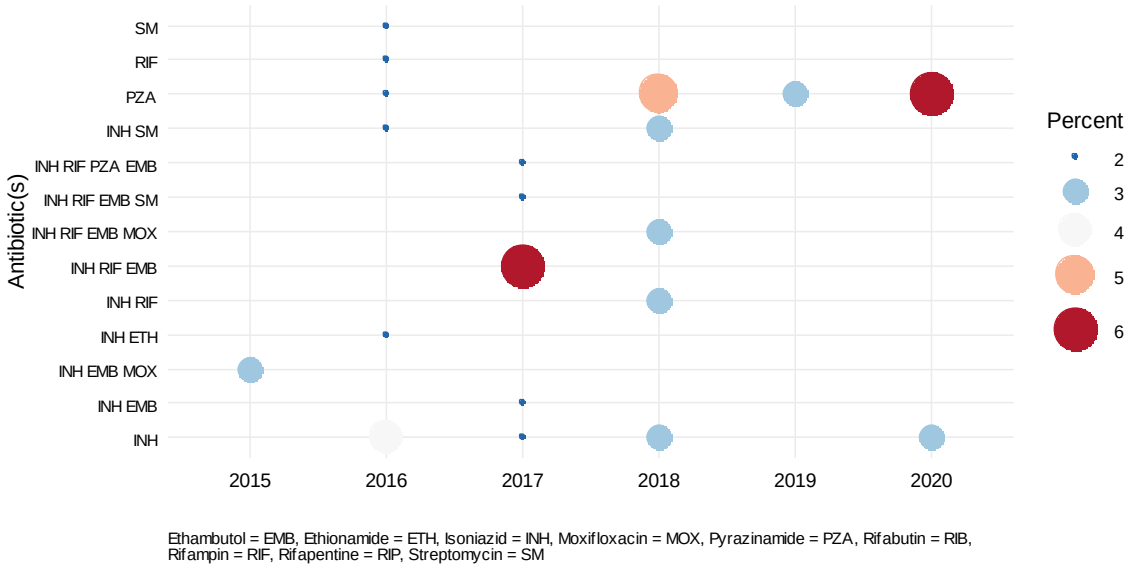


*Pulm+ infections occur in both the lung and other tissues, while Non-Pulm Only infections occur outside the lung.

Drug Resistance

Culture positive results were obtained from 22 (61.1%) of the 36 TB patients. No drug resistance was observed among culture positive cases with initial drug susceptibility results. Drug resistance to isoniazid and pyrazinamide was observed in cases that were not culture positive. The initial drug resistance profile of TB cases from 2015-2020 is shown in Figure 16.

Figure 16. Initial Drug Resistance as a Percentage of TB Cases Tested for Initial Drug Resistance by Year in Fresno County – 2015-2020

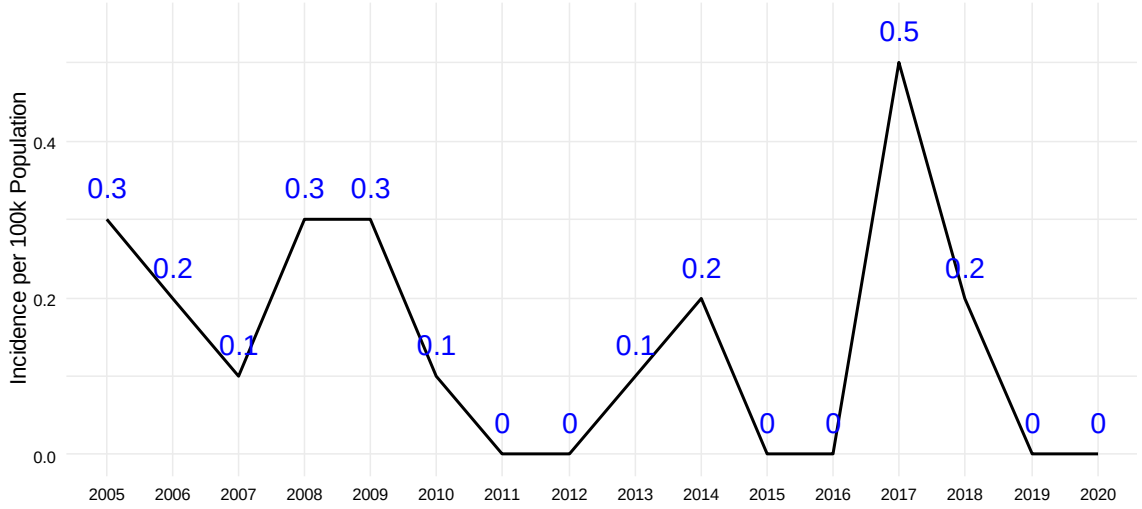


Ethambutol = EMB, Ethionamide = ETH, Isoniazid = INH, Moxifloxacin = MOX, Pyrazinamide = PZA, Rifabutin = RIB, Rifampin = RIF, Rifapentine = RIP, Streptomycin = SM

Multidrug-Resistant Tuberculosis (MDR-TB)

Multidrug-resistant TB (MDR-TB) is resistant to the strongest two primary anti-tuberculosis medications (Isoniazid and Rifampin), and extensively drug resistant TB (XDR-TB) organisms are resistant to these medications plus at least two of the principal secondary medications. Patients with XDR-TB have few treatment options because the drugs most effective against TB are ineffective against their disease. In 2020, the incidence of MDR-TB per 100,000 population was 0 and there were no XDR-TB cases in Fresno County (Figure 17).

Figure 17. Incidence of MDR-TB* in Fresno County – 2005-2020

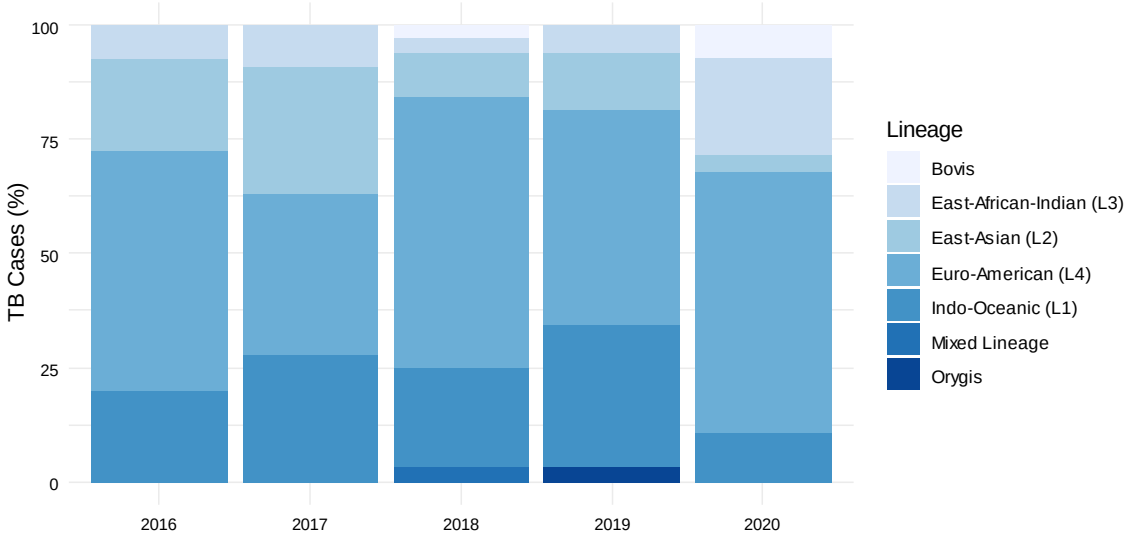


*Multidrug-resistant TB (MDR-TB) is resistant to the strongest two primary anti-tuberculosis medications (Isoniazid and Rifampin).

Genotype

The TB program can use genetic links between TB cases to investigate and stop common sources of transmission. Figure 18 shows the proportion of each lineage in TB cases sent for genotyping from 2016-2020. During 2020, 30 (83.3%) cases were genotyped and composed of five lineages: Bovis, East-African-Indian, East-Asian, Euro-American, and Indo-Oceanic.

Figure 18. TB Lineage by Year in Fresno County – 2016-2020



Contributing Risk Factors and Comorbidities in Fresno County

Risk Factors

During 2020, 35 (97.2%) of the 36 TB cases had at least one or more underlying factor that increased risk for TB infection or progression of infection to disease whether it be occupational, social, or medical. The proportion of TB cases by risk factor and nativity from 2016 to 2020 is in Table 1.

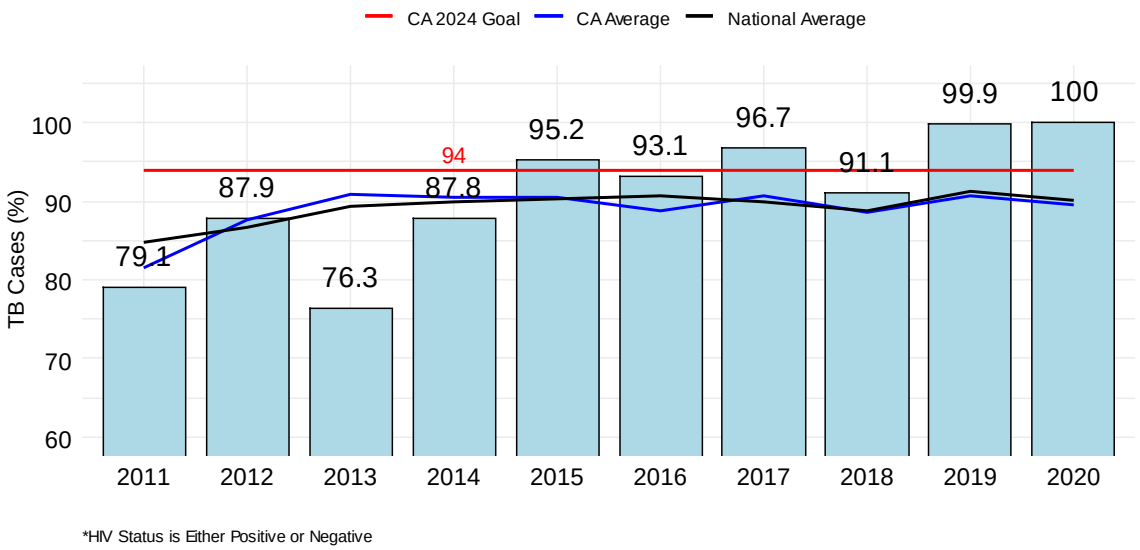
Table 1. Percent of TB Cases by Risk Factor and Nativity in Fresno County – 2016-2020

Risk Factor	Foreign Born %	US Born %
Alcohol Abuse	12.1	7.7
Correctional Facility Employee	0	0
Correctional Facility Resident	0	1.9
Diabetes	28.4	7.7
End Stage Renal Disease	2.6	3.8
Health Care Worker	0	0
HIV Positive	2.1	3.8
Homeless	3.7	11.5
Immunosuppression	2.1	7.7
Infectious Contact	1.6	19.2
Injection Drugs	0.5	3.8
Long Term Care Facility Resident	0.5	11.5
LTBI Incomplete Rx	1.6	1.9
MDR Contact	0	1.9
Migrant/Seasonal Worker	14.7	3.8
Missed Contact	0	0
Non-Injection Drugs	3.2	5.8
Post Organ Transplant	0	0
Previous TB Dx	2.6	3.8
TNF Antagonist Rx	0	0

HIV Testing

Of the 36 TB patients in 2020, 34 were eligible for HIV testing and of the eligible patients 34 (100%) completed testing (Figure 19).[9] Cases of TB are excluded from testing when they are very young or very old and do not have risk factors for HIV.

Figure 19. Patients with Known *HIV Status in Fresno County – 2011-2020



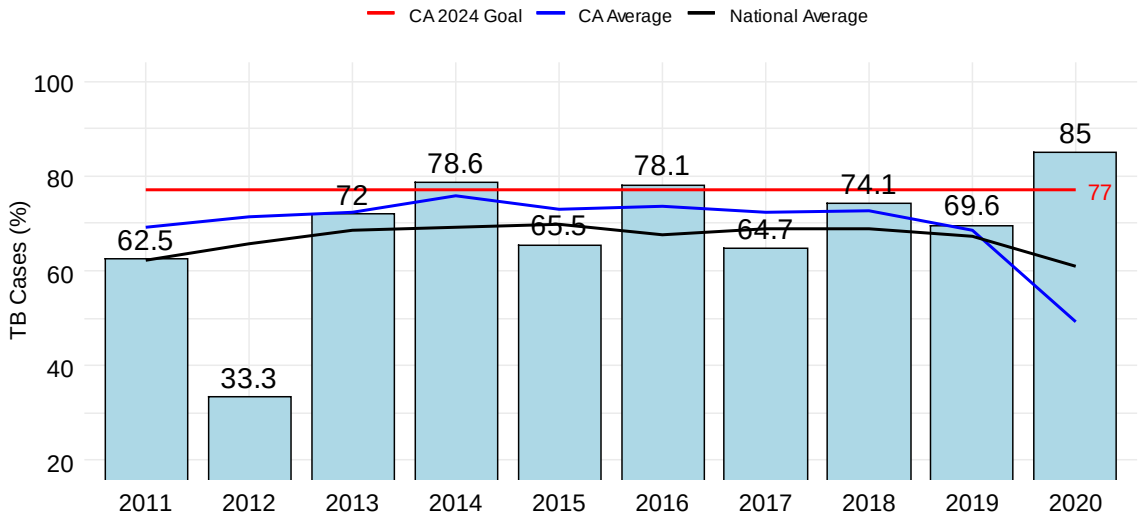
*HIV Status is Either Positive or Negative

Treatment Outcomes in Fresno County

Sputum Culture Conversion

Of the 36 cases of TB in Fresno County during 2020, 20 had positive sputum culture results at the time of treament initation. After 60 days of treament, 17 (85%) patients had sputum-culture negative results indicating they were no longer contagious for TB (Figure 20).[9]

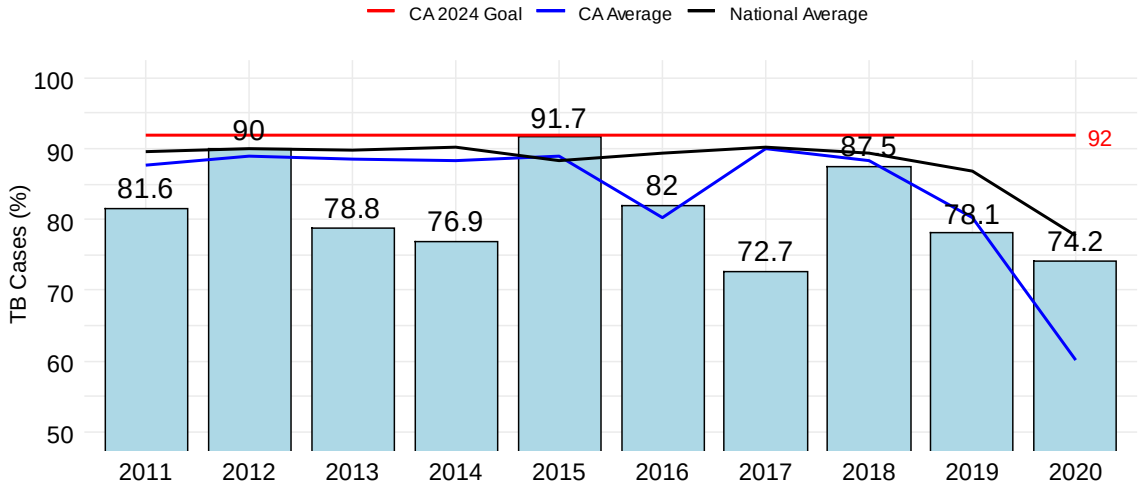
Figure 20. Sputum Culture Conversion Within 60 Days in Fresno County – 2011-2020



Active Tuberculosis Treatment Completion

Out of the 36 TB patients, 28 (77.8%) were eligible to complete treatment. Patients became ineligible to complete therapy if they died before treatment completion, had to stop treatment due to medication side effects, or moved outside Fresno County. As of the publication of this report, 26 (92.9%) of the eligible patients have finished treatment and 2 (7.1%) have not. Of those patients that did not finish their TB treatment, one was uncooperative and the other had a reactivation of their infection. During 2020, 31 (86.1%) of the 36 TB patients were eligible to complete their treatment within a 12 month period as defined by CDC criteria from the National Tuberculosis Indicators Project (NTIP).[9] Examples of ineligible patients include those with rifampin-resistant TB, meningeal TB, TB in the skeletal system, TB in the central nervous system, and children less than 15 years old with disseminated TB. Patients who moved out of the U.S within 366 days of initiating treatment are also ineligible to complete treatment within 12 months. Of those 31 patients, 23 (74.2%) completed their treatment within the 12 month period (Figure 21).[9] Delays or intermittent interruptions in treatment can result from factors such as: MDR-TB, patient non-compliance, underlying health conditions, and adverse effects of medication.

Figure 21. TB Patients Completing Treatment within 12 Months* in Fresno County – 2011-2020



*For patients with TB in which 12 months or less of treatment was indicated per NTIP criteria.

Latent* Tuberculosis *(LTBI) Treatment

Someone with latent tuberculosis (LTBI) has a TB infection, but their immune system suppresses the TB bacteria so they are asymptomatic. Without treatment, those with LTBI are at risk for developing active TB in the future. In California, about 80% of active TB cases result from patients with untreated LTBI.[7] Once-weekly isoniazid-rifapentine for 12 weeks (3HP) is a common therapy for LTBI used by the Fresno County TB Program. The number of patients identified and treated for LTBI by FCDPH declined in 2020 due to the effects of the COVID19 pandemic. To ensure quality patient care while simultaneously directing TB resources to assist with the COVID19 pandemic, LTBI treatment was shifted to primary care physicians. Patients were less likely to visit the TB clinic during the pandemic likely due to concerns over the virus and/or public-health measures designed to reduce viral transmission. As hospitals and clinics contended with patient care during the pandemic, referrals to the TB clinic for LTBI dropped when compared to prior years. Furthermore, with only 36 active TB patients in 2020 to investigate for contacts with LTBI, fewer people were identified with LTBI. Finally, the masking mandates might have reduced the transmissibility of tuberculosis resulting in less community infection. Consequently, in 2020, 14 patients began 3HP treatment, and only 10 were eligible to finish treatment. Patients became ineligible to continue 3HP treatment if they were switched to an alternative TB therapy or completed therapy through another medical provider. Of those eligible LTBI cases, (80%) completed 3HP therapy and (60%) completed therapy within 12 weeks (Figure 22). Patients receive other LTBI therapy when 3HP is not recommended or they do not tolerate 3HP treatment well.

Figure 22. LTBI Patients with 3HP* Treatment Completion in Fresno County – 2015-2020

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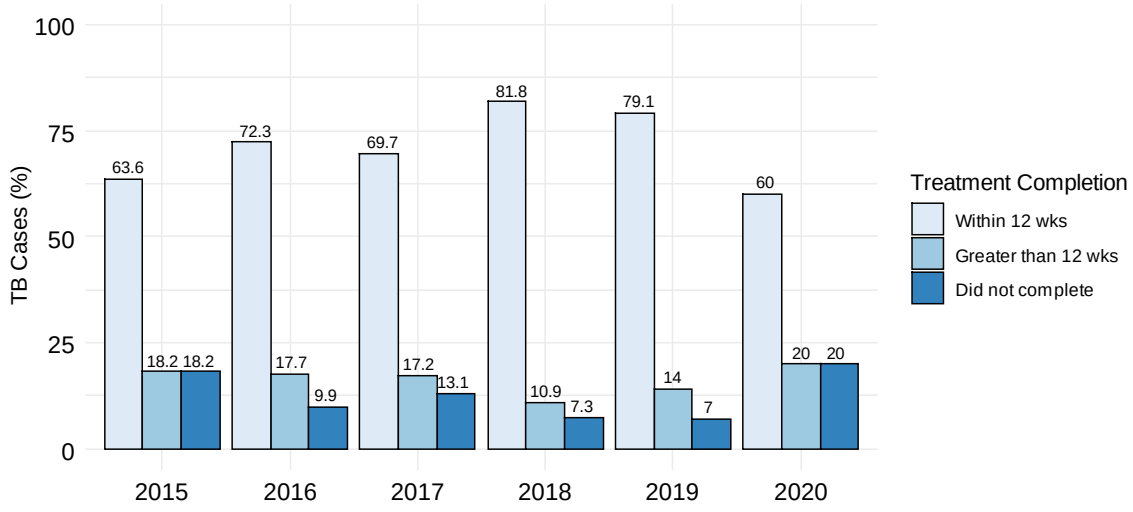


*3HP treatment consists of a once weekly dose of Isoniazid and Rifapentine for 12 weeks.

Contact Investigation in Fresno County

During 2020, 16 (44.4%) of the 36 TB cases were AFB smear-positive and all of these cases had contacts elicited for investigation. Out of the 157 AFB smear-positive contacts elicited, 115 (73.2%) of these contacts were examined for TB infection (Figure 23).[9] Out of those examined in 2020, 21 (18.2%) were discovered to have LTBI infection and 17 (81%) of these patients began treatment (Figure 24).[9] Treatment completion for the AFB Smear+ contacts with LTBI is available for years prior to 2020 (Figure 25).[9]

Figure 23. Contacts to AFB Smear+ Cases Examined for TB in Fresno County – 2011-2020

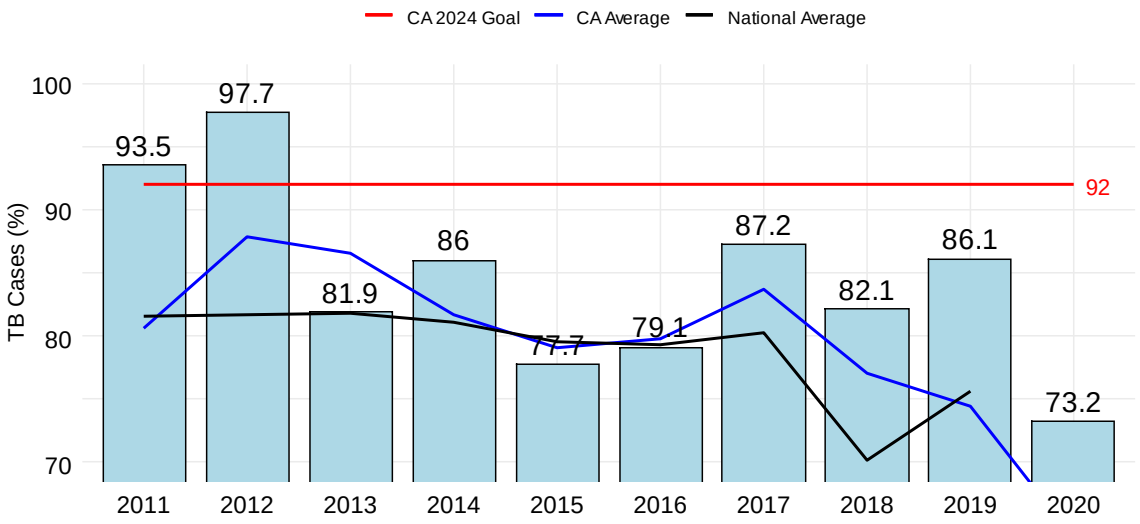


Figure 24. AFB Smear+ Contacts Who Started LTBI Treatment in Fresno County – 2011-2020

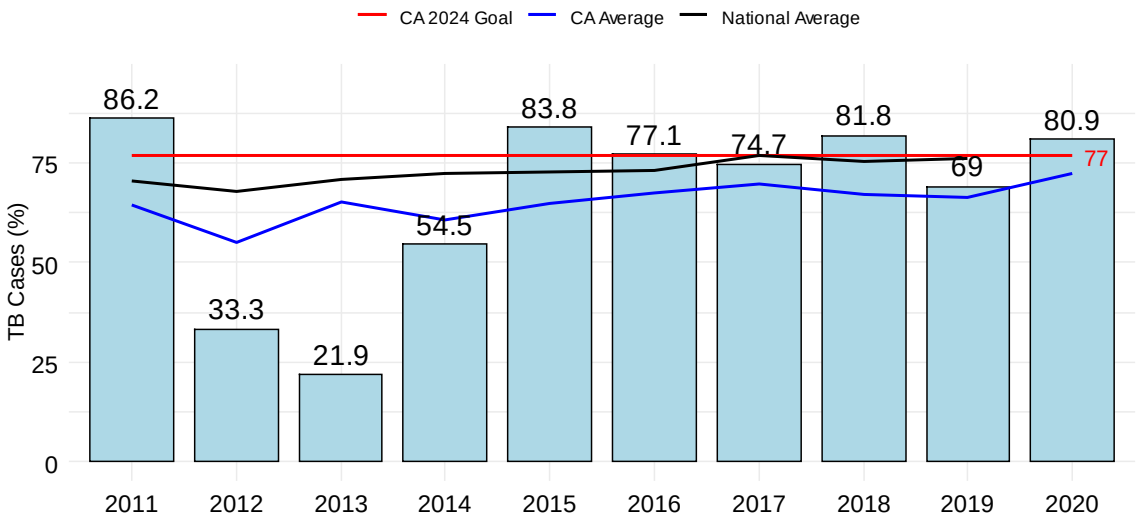
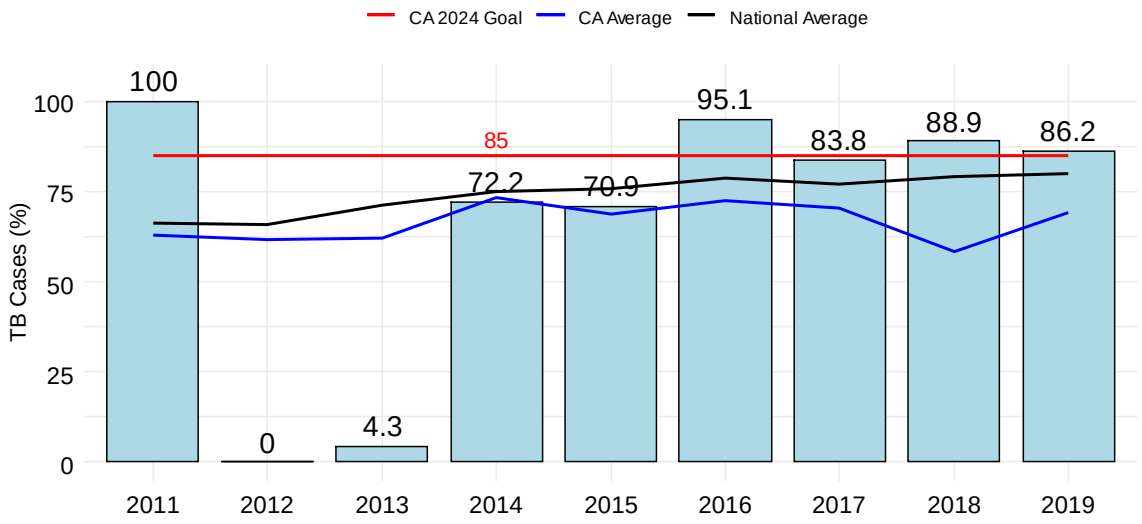


Figure 25. AFB Smear+ Contacts Who Completed LTBI Treatment in Fresno County – 2011-2019



Public Health Strategies to Control, Prevent, and Eliminate Tuberculosis

In 2020, the Fresno County Department of Public Health (FCDPH) TB Control Program provided treatment, contact investigation, and follow-up for all the 36 newly diagnosed active TB cases. The TB program staff continued to simultaneously provide care for patients diagnosed prior to 2020 who had not yet completed treatment (standard treatment regimens are 6-12 months; drug resistant TB patients may be treated for two years, and all treated patients require at least monthly visits). To ensure TB medication is taken correctly, department staff visit pulmonary TB patients daily to observe them take their medications; this is also known as Direct Observed Therapy (DOT).

Strategies to Control, Prevent, and Eliminate Tuberculosis Include:

1- Finding and adequately treating people that have active disease.
2- Identifying individuals who have been exposed to someone with TB disease, evaluating them for LTBI or active TB disease, and treating them if they have either of these.
3- Screening individuals for TB infection that are known to be at higher risk for infection with TB or at higher risk for developing TB disease if infected.
4- Applying control measures in high-risk settings.

The FCDPH TB Control Program identifies and treats TB disease, identifies and evaluates exposures to TB, and offers treatment if needed. FCDPH also screens certain high risk populations, and assists the public with the application of control measures in high risk environments.
Title 17 of California Code of Regulations requires that notification be given to the county health department of all diagnosed or suspected cases of TB by telephone or fax within one working day of identification. California Health and Safety Code 121362 also require that providers treating people with active TB report to the local health officer any pertinent information the health officer requests.

Additional Information Available

If you have any questions regarding TB infection, the disease, or the control of TB in Fresno County please contact our FCDPH Community Liaison Nurse at 559-600-3413.

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3. Deutsch-Feldman M, Pratt RH, Price SF, Tsang CA, Self JL. Tuberculosis — United States, 2020. MMWR Morb Mortal Wkly Rep 2021;70:409–414. CDC.

4. CDC. Drug – Resistant TB. https://www.cdc.gov/tb/statistics/reports/2020/drug_resistant.htm. Published 10/18/2021. Accessed 3/3/2022.

5. CDC. TB Risk Factors. https://www.cdc.gov/tb/topic/basics/risk.htm. Published 3/18/2016. Accessed 3/3/2022.

6. Tuberculosis Control Branch, Provisional TB Data Tables, 2020. California Department of Public Health, Richmond, CA.

7. Tuberculosis Control Branch, 2020 TB Snapshot. California Department of Public Health, Richmond, CA.

8. CDC. Basic TB Facts. https://www.cdc.gov/tb/topic/basics/default.htm. Published 3/20/2016. Accessed 3/3/2022.

9. National Tuberculosis Indicators Project (NTIP) Division of Tuberculosis Elimination National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention Centers for Disease Control and Prevention, Atlanta, Georgia, USA 30329

Technical Notes

Population Data

Population data used to calculate incidence comes from the following sources:

- California Department of Finance. Demographic Research Unit. Report P-2D: Population Projections by Total Hispanic and Non-Hispanic Race, California Counties, 2010-2060 (Baseline 2019 Population Projections; Vintage 2020 Release). Sacramento: California. March 2021.
- State of California, Department of Finance, E-6. Population Estimates and Components of Change by County — July 1, 2010–2020, December 2020.
- State of California, Department of Finance, Revised County Population Estimates and Components of Change by County, July 1, 2000-2010. Sacramento, California, December 2011.
- U.S. Census Bureau. (2020). 2015-2019 American Community Survey 5-Year Estimates by ZCTA for Fresno County.

Equations

$$Incidence = \frac{New\ Cases\ in\ Population\ at\ Specified\ Time}{Population\ at\ Risk} \times 100{,}000$$