It's the "Valley Tough" Life for us: The biogeochemistry and occupational hazard of a pathogenic fungus, *Coccidioides*, in California's San Joaquin Valley

by

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A Senior Essay

Submitted to the Department of Earth and Planetary Sciences

Yale University

In Partial Fulfillment of the Requirements

for the Degree of Bachelor of Science

May 2024

I. INTRODUCTION

Coccidioidomycosis, more commonly known as “Valley fever,” is a respiratory infection which, despite initially presenting with flu-like symptoms, can worsen to pneumonia, bronchitis, meningitis, and, in severe cases, death (Mayo Clinic, 2023). Onset of symptoms usually occur 1-3 weeks after inhalation of soil particles containing the fungus *Coccidioides spp.* (*Coccidioides immitis* and *Coccidioides posadasii*). This parasitism of *Coccidioides* raises the most public health concerns, prompting further research into the virulence and geographic distribution of different *Coccidioides* strains.

All *Coccidioides* are infectious to mammals upon inhalation (Friedman et al, 1955). Different strains of the fungus show varying severities of virulence. One significant characteristic of more virulent strains are spherule outer wall glycoproteins (SOWgp). The concerted evolution of SOWgp with long proline/aspartate-rich motifs has been suggested as a mechanism by which *Coccidioides* can survive the natural immune response (Johanneson et al, 2005). Virulence, alone, does not explain the severity of disease that can develop. In fact, severity of disease depends largely upon the amount of pathogenic material inhaled and the individual organism’s natural immune response to thwart dissemination of coccidioidomycosis. Moreover, analysis shows that events of coccidioidomycosis outbreaks are less driven by genetic capabilities to invade living hosts, but, instead, largely the result of environmental events (Fisher et al., 2000). Endemic regions, thus, endure greater incidences of coccidioidomycosis resulting from environmental causes.

Valley fever is a relatively rare infection according to the Centers for Disease Control (CDC), reporting on average 200,000 cases per year in the United States (CDC, 2022). However, the majority of cases are highly concentrated in areas where *Coccidiodes spp*. is endemic; that is the Southwestern United States and parts of Mexico (Kirkland & Fierer, 1996). Over the span of just two decades, reports of coccidioidomycosis have spread rampant across the Central Valley of California, reaching distances as far as Nevada, Colorado, and New Mexico (Kirkland & Fierer, 1996 ; Partlow, Penney, & Houten, 2023 ; see Figure 1). Now, the CDC reports that regions as far east as the Rocky Mountains and much of the Great Plains may possess soils capable of fostering growth of *Coccidioides* (CDC, 2022; see Figure 2). In 2010, individual reports of coccidioidomycosis were reported in Washington, followed by outbreaks in the southeastern portion of the state (Marsden-Haug et al., 2013 ; Marsden-Haug et al., 2014). Despite initial interpretations of Valley fever being endemic to the southwestern region, a once state-wide issue is slowly becoming a public health concern for much of the western United States.

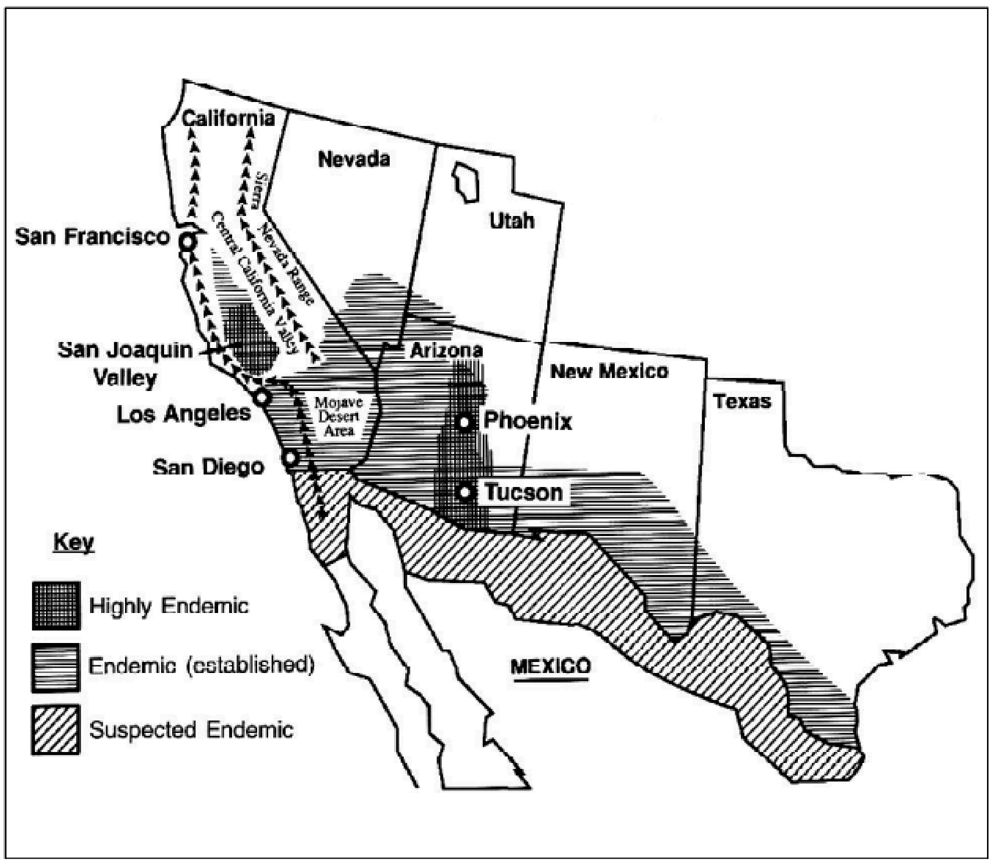


Figure 1. Kirkland & Fierer (1996) illustrating the regions in which coccidioidomycosis is endemic and other areas where *Coccidioides* is suspected to inhabit.

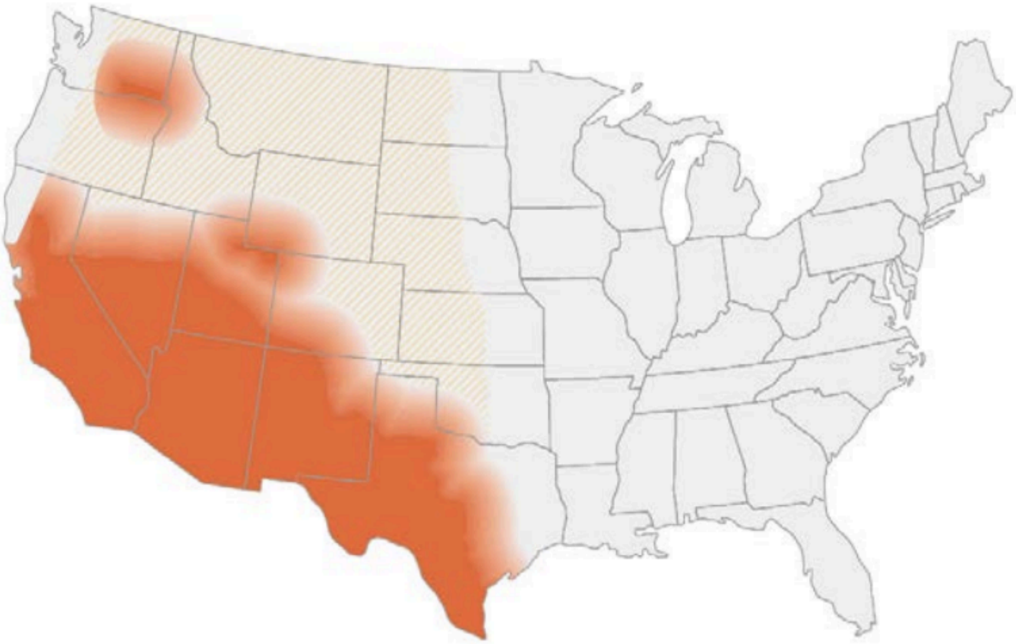


Figure 2. CDC (2022) highlighting, in orange, regions of documented Valley fever outbreaks. The regions shaded in light orange marks regions where *Coccidioides* is thought to possibly inhabit.

Current research has focused intensely on the pathogenesis of Valley fever, whereas far less is understood about the provenance, ecology, and metabolism of the fungus. *Coccidioides* is difficult to identify *in situ*, prompting further research into the geochemical demands and ecological niches of the fungus to discover more reliable methods of predicting the geospatial distribution of *Coccidioides* (Baptista-Rosas et al., 2007). Today, the biogeochemistry of *Coccidioides* is fairly understood by metabolic testing and element tracing. These findings have supported mechanisms by which the effects of environmental events on Valley fever outbreaks arise. In tandem, the biogeochemistry and public health case studies prompt questions concerning the impact of anthropogenic activities on *Coccidioides* growth and coccidioidomycosis hazards, particularly in agriculture—a field in which labor workers are routinely exposed to airborne soil particles. While current occupational standards do not recognize *Coccidioides* to require uniquely tailored safety standards, the lack of information regarding Valley fever emphasizes the necessity to shed light on this public health concern as is the aim of this research.

II. THE BIOGEOCHEMISTRY OF *Coccidioides spp.*

Life Cycle & Dimorphism

Coccidioides is opportunistic and adaptive due to its dimorphic life cycle. This life cycle is characterized by the saprobic and parasitic phases, which can transition into each other. Each phase is defined by their distinct morphologies of the fungus through development (see Figure 3).

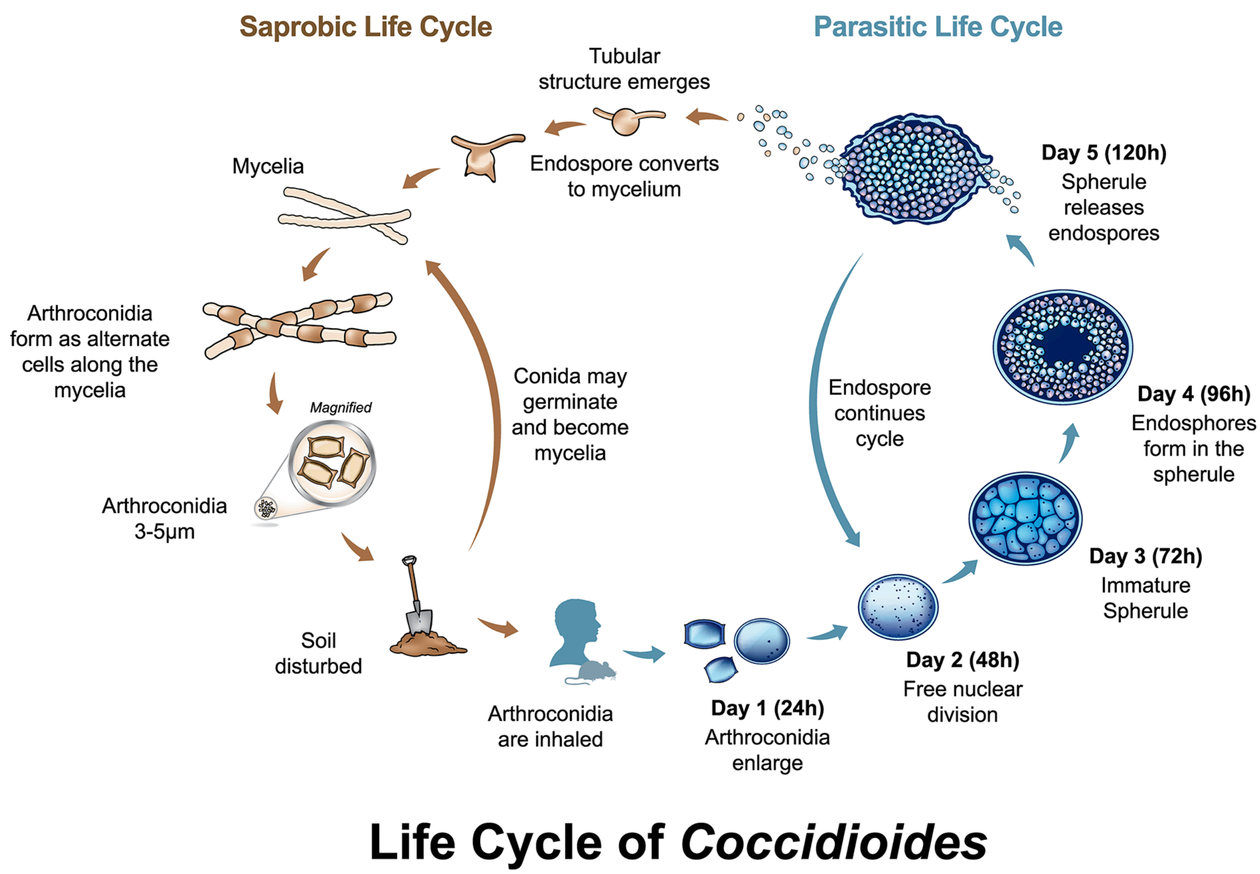


Figure 3. Lewis, Bowers, & Barker (2015), illustrating the life cycle of *Coccidioides* through dimorphic phases, saprobism and parasitism.

The saprobic phase is characterized by two stages—mycelial and arthroconidial—wherein the fungus undergoes growth and germination in topsoil environments. In the mycelial stage, tubular forms sprout from fungal endospores to promote the conversion of the endospore into mycelium. The mycelium functions as a transport pathway for the fungus to disseminate nutrients to all parts. Once the mycelia have grown too large to sustain adequate nutrient absorption, the arthroconidial stage initiates. Alternate cells begin to appear throughout the mycelium and further develop into arthroconidia. The desiccation and disarticulation of hyphae liberate individual arthroconidia, and when matured progress the *Coccidioides* life cycle through two pathways: (1) the arthronodia germinate to produce more mycelium, keeping the fungus in its saprobic phase or (2) the arthroconidia are inhaled by a live host, initiating its parasitic phase.

The parasitic phase of *Coccidioides* defines its behavior in the tissues of a living host organism. The parasitic phase is characterized by two stages, uninucleate endospores and multinucleate endospores. Within the initial 24 hours of arthroconidia inhalation, arthroconidia (2-5 µm in diameter) will shed their outer layer, revealing spores (Akram & Kairala, 2023). After 48 hours, these spores will undergo nuclear division. After 72 hours, the amount of nuclear division will have produced an immature spherule, concluding the uninucleate endospore stage. The multinucleate endospore stage is initiated after 96 hours; multiple endospores begin to fill up the spherule until sufficient endospores develop and burst out of the mature spherule (75 µm in diameter). Spherule release can occur as early as 120 hours after inhalation of arthroconidia, providing the mechanism by which infection becomes disseminated throughout the body and *Coccidioides* reproduce to spread across long distances (Akram & Koirala, 2023).

Reproduction

Coccidioides are a dimorphic fungus group which asexually reproduces in either the saprobic or parasitic forms, initiating juvenile mycelial growth (Lewis, Bower, & Barker, 2015). In the saprobic phase, the disarticulation of arthroconidia is fostered by soil disturbance, such as wind and agricultural practices, like tilling. In the parasitic phase, after endosporic development has taken place and spherule release is prompted via exhalation, respiration of the live host can expel spherules into the environment, returning the fungus to the soils to undergo germination. In this event, nutrient uptake will foster tubular growth from the spherules, promoting a transition from the parasitic to the saprobic phase by inducing mycelial growth. Alternatively, if arthroconidia are not inhaled by a live host, conidia will directly undergo germination, giving rise to mycelial growth.

Sex has not been documented in *Coccidioides spp.*, but the measurably large genetic diversity observed across the two species indicates frequent recombination between *C. immitis* and *C. posadasii* (Lewis, Bowers, & Barker, 2015). Although the asexual reproduction of *Coccidioides* is understood, investigations concerning the possible sexual reproduction among geographically proximal groups have not been explored.

Coccidioides spp. demonstrate genetic similarities to heterothallic fungi in known reproductively-significant loci. *MAT1-1* and *MAT1-2*, two loci found in sexually reproducing filamentous ascomycetes, are found in both *C. immitis* and *C. posadasii* (Mandel et al, 2007). Genetic sequencing at three different geographic sites showed ratios of these loci of nearly 1:1 which is expected of sexually reproducing groups. This observation helps substantiate the mass recombination occurring across *C. immitis* and *C. posadasii*. However, more research is necessary to understand and, one day, observe sexual reproduction in *Coccidioides spp.*

Ecology

Coccidioides are a group of soil-residing fungi, belonging to the family Onygenacaea in the division Ascomycota. Unlike typical ascomycetes, *Coccidioides* do not solely associate with plant tissues (Sharpton et al, 2009). In the United States, *C. immitis* is largely found in only central California sweeping into Nevada and Arizona in primarily desert, chaparral, and forested foothills environments while *C. posadasii* is found in southern California and Arizona (Hernandez, Erives, & Martinez, 2019). These regions provide the aridity and nutrients sufficient to foster the growth and development of *Coccidioides*.

Competing hypotheses have prevailed concerning factors, abiotic and biotic, which would help identify soils most commonly populated with *Coccidioides*. Mycelial *Coccidioides* was commonly accepted as a mold residing in soils, developing and aggregating hyphae for nutrient absorption. The original hypothesis suggests *Coccidioides* to be present randomly throughout the soil. But, after identifying *Coccidioides*-associated granulomas in the lungs of some small mammals, new lines of research began to identify a relationship between the fungus and animals (Emmons, 1942 ; Ashburn & Emmons, 1942 ; Taylor & Barker, 2019). This bore the small rodent hypothesis which claims encounters of *Coccidioides* should increase near rodent burrows and carcasses (Emmons, 1942). Emmons found a positive correlation between the fungus and rodent burrows in Arizona. However, 20 years later, a study in Kern County, California examining the presence of *Coccidioides* in the midden of known infected mammals found that the fungus, although present in the midden, could not be found in the surrounding soils (Swatek & Plunkett, 1967). While bioturbated soils show an increased presence of *Coccidioides*, the fungi's absence in midden signifies an inaccuracy of the small-rodent hypothesis purporting a largely biotic link to regions of habitation.

New hypotheses concerning *Coccidioides* regions of habitation combine abiotic and biotic factors, suggesting the partial influence of ecologic and geologic on fungal spread. *Coccidioides* must consume carbon from organic material. The most obvious source comes in the form of dissolved organic material permeating through soils. Hence, rodent burrows and areas surrounding decaying rodents show a positive correlation with *Coccidioides* encounters (Kollath et al, 2019). But *Coccidioides* are not strictly saprotrophic like other ascomycetes. Recent genetic studies on *Coccidioides* have revealed the prevailing parasitic tendencies and the significance of the fungi's parasitic phase. Kollath et al (2019) examined the importance of living hosts in the maintenance of *Coccidioides* populations. The study found that *Coccidioides* is three times more likely to be detected in animal burrows than in soils unassociated with animal activity. Kollath et al (2019) also found that the biotic relationships of *Coccidioides* extended beyond rodents, also found in the fecal samples of coyotes, dogs, jackrabbits, cottontails, and squirrels. These biotic interactions, however, are not necessary for the fungus to survive.

The endozoan hypothesis, the currently prevailing hypothesis, attributes the prominence of *Coccidioides* populations to the combined abiotic and biotic factors which affect the opposing stages of the dimorphic fungi's life cycle. There are particular geologic conditions which promote the mycelial growth: pH, salt concentration, aridity of soil, humidity, and nutrient runoff. Moreover, plants do play a role in the growth rates of *Coccidioides*, although it is indirect and rather insignificant when compared to the role of respiring mammals (Taylor & Barker, 2019). However, *Coccidioides* have diversified themselves from other ascomycetes genetically, demonstrating a decrease in gene sequences known for the metabolism of plant material and increase in gene sequences known for the metabolism of animal material (Sharpton et al., 2009). Although the presence of animals is not necessary for the survival of the fungus, behaving as an endozoan in the lungs of mammals may play a significant role in the spread and asexual reproduction of *Coccidioides* (Reyes-Montez et al, 2016 ; Taylor and Barker, 2019). While residing in the host, the arthroconidia are either destroyed by the natural immune response or survive, developing into spherules and causing ailment in the host. Through exhalation, the host spreads the spherules across long distances above ground, where then the fungus can transition into its saprobic phase and produce hyphae in the soils. In severe cases of disseminated disease, coccidioidomycosis, where the host dies, the loss of body heat promotes hyphae production of the spherules, transitioning the fungus into its saprobic phase. The endozoan hypothesis considers the soil conditions necessary for mycelial growth but emphasizes the integral nature of the parasitism of *Coccidioides* in its reproduction and migration.

Biochemical Demands of *Coccidioides spp.*

In *Coccidioides*, mycelia foster the transportation of three necessary nutrients of interest; these are nitrogen, phosphorus—in the form of phosphate ion (PO_4^{3-})—and organic carbon. Soil conditions—primarily salinity and aridity—must also support and maintain *Coccidioides* survival. However, as the fungus metabolizes the nutrients in the soil, the biogenic waste produced alters the conditions of the surrounding environment. Tracing the element uptake by *Coccidioides* metabolism provides insight to the types of soils which are both nutrient-rich and geochemically resistant in order to sustain mycelial growth.

Coccidioides are osmotrophic chemoorganotrophs, taking up dissolved organic carbons, and other nutrients, from the surrounding soils. *Coccidioides* uptake nitrogen from organic and inorganic sources, preferring either source based upon its morphological stage within its saprobic phase (i.e. mycelia or arthroconidia). Nitrogen is necessary for the growth of mycelial

Coccidioides. In lab conditions, *Coccidioides* grows on simple agar plates, requiring only the smallest amounts of nitrogen (Bump, 1929). The absence of nitrogen, on the other hand, results in no growth. Interestingly, *Coccidioides* is unable to consume atmospheric nitrogen (N_2). This inability to perform nitrogen fixation indicates that all nitrogen consumed, therefore, must come from the surrounding soil environment in the form of mineral nitrogen (i.e. NO_2^-, NO_3^-, and NH_4^+) and organic nitrogen (Bump, 1929 ; Goldschmidt & Taylor, 1957). Organic nitrogen uptake, however, plays a more significant role in later saprobic stages.

Fragmentation, the production of arthrospores, also requires nitrogen. But, unlike in mycelial development, the optimal geochemical conditions to promote fragmentation differ from mycelial growth in nitrogen source, requiring more organic material (i.e. amino acids from detritus). Although nitrogen-containing salts provide greater growth potential with mycelial colonies, the production of arthrospores, instead, requires proline as the primary nitrogen source (Goldschmidt and Taylor, 1957). Ammonium acetate, often used in laboratory conditions for *Coccidioides* growth, can be replaced by ammonium lactate ($NH_4CH_3CHOHCOO$) or ammonium succinate ($(NH_4)_2COOC_2H_4COO$), both of which are biogenically produced salts. In natural environments, these nutrients are likely absorbed from the detritus of decaying organic matter. Then, as arthroconidia break off from the hyphae and are transported from their site of development, *Coccidioides* can continue through its dimorphic life cycle depending upon the air composition of its new environment.

Gaseous materials provide the necessary nutrients to *Coccidioides* for metabolism and morphological transitioning. Oxygen is integral to mycelial growth. The mycelia are obligate aerobes, requiring oxygen (O_2) for respiration (Bump, 1929). Once there is insufficient nutrients or O_2 to support mycelial growth, arthroconidia may form as segmented cell groups along the hyphae. The arthroconidia are then broken off by soil disruption (i.e. wind, bioturbation, etc.) whereafter these particulates can be inhaled and transition into the parasitic phase. This transition of arthroconidia to endosporulating spherules can only occur in the lungs of mammals as this process necessitates the presence of carbon dioxide (CO_2). Air compositions of 5-20% CO_2 (i.e. approximately 50 mmHg CO_2 within the alveolar space) are sufficient to induce parasitic transitioning (Klotz et al, 1984). Without the presence of CO_2 in the air, arthroconidia will germinate, leading to hyphae production. Although *Coccidioides* is unable to fix atmospheric nitrogen (N_2), the gaseous environment surrounding *Coccidioides* plays a pivotal role in its growth and development.

Phosphate plays a key role in the development of *Coccidioides* in all parts of its life cycle. Not too much is understood regarding the individual role of phosphate in each stage of *Coccidioides* life cycle. However, it has been emphasized that in all experiments conducted, phosphate has been observed in *Coccidioides* as a major buffer system (Bump, 1929 ; Goldschmidt and Taylor, 1957). Although studies surrounding the individual effects of phosphate on *Coccidioides* growth and morphological transitions have not been performed, examination of this buffer system through different phases of the dimorphic life cycle could provide insight to the adaptability and resilience of *Coccidioides* as an extremophile.

III. GEOLOGIC & ENVIRONMENTAL CONSIDERATIONS

Soil Conditions

As evidenced by the metabolic pathways driving elemental cycling, a multitude of chemical factors affect the growth and reproduction of the *Coccidioides*. In this vein, soil chemistry provides insight into the biologic processes that sustain *Coccidioides*. However, the physical soil conditions give rise to the mechanisms by which nutrient absorption, respiration, and mobility occur. Properties like texture, porosity, permeability, and infiltration capacity characterize a soil profile, determining the arid conditions which support microbial life in these environments (Selinus et al., 2005). *Coccidioides* provides an interesting consideration as its dimorphic phases are best supported by varying soil conditions. Fluctuations of aridity, pH, depth, bioturbation, and infiltration capacity help progress *Coccidioides* through its life cycle. Furthermore, because of its ability to sustain life in extreme conditions, *Coccidioides* has yet to be observed *in situ* with an antagonizing organism (Swatek, 1970). An examination of these extreme environmental conditions in which *Coccidioides* uniquely lives can help understand the geospatial distribution of *Coccidioides* in the western United States.

Soil texture greatly affects the growth and development of *Coccidioides*. Texture has five key impacts on soil: (1) infiltration capacity, (2) porosity, (3) rate of reactions, (4) control of plant root penetration, and (5) aeration (Selinus et al., 2005). These properties together produce the arid conditions in which *Coccidioides* thrive. Infiltration capacity refers to the ability of a soil to absorb water. *Coccidioides* best thrive in soils which do not readily absorb large quantities of water, but instead allow water to pass through them transiently (Fisher et al., 2007). Soils with moderate-low infiltration capacities and high porosity provide these optimal conditions. Porosity, the percent volume of soil space occupied by non-solid material, provides the availability of water and air throughout the subsurface layers. With higher porosity, there is increased surface area of the soil-reactant interface, allowing for increased reaction rates (Selinus et al., 2005). This would provide *Coccidioides* with increased nutrients required for growth. In the same vein, aeration of soils plays a significant role in fostering *Coccidioides* growth because the fungus is an obligate aerobe; observations of increased mycelial and arthroconidial growth were measured with increased rates of aeration (Goldschmidt & Taylor, 1957). Beyond its mycelial stage, with loose-textured soils, increased rates of parasitism (i.e., reports of coccidioidomycosis cases) would also be expected to increase as a result of an inability to hold on to vegetation roots and increased erodibility. Decreased vegetation is often met with increased rates of coccidioidomycosis, suggesting the increased mobility of arthroconidia in these environments (Morgan, 2009). In many ways, the physical properties of soil have large impacts on the growth and development of *Coccidioides*.

Another variable to consider in the soil conditions for *Coccidioides* growth is pH. pH does not significantly affect fungal growth rates. Yet, lower pH is associated with higher production of NH_4^+ by *Coccidioides* (Bump, 1929). These increased rates of NH_4^+ release are observed until soil conditions reach pH 6. Although maintaining higher pH shows no effects on mycelial growth rates, the necessity of biogenic NH_4^+ release allows for fragmentation to occur. Arthrospore formation occurs after mycelial growth cannot acquire sufficient nutrients (Lewis, Bowers, & Barker, 2015). Afterwards, arthroconid disarticulation grants *Coccidioides* the possibility to transition into parasitism. Disarticulation, unlike hyphae growth, demonstrates pH-dependent success. At low pH, disarticulation does not readily occur. Instead, as pH increases, disarticulation occurs more readily, exhibiting peak disarticulation at a pH of 5.5 (Goldschmidt & Taylor, 1957). This suggests *Coccidioides* may have adapted biogenic pathways in its metabolism to release NH_4^+ for optimal arthroconid disarticulation. Fluctuations in pH reveal capabilities of *Coccidioides* to optimize its own development by inducing optimal soil conditions for morphological transitions. This evidence illustrates *Coccidioides* as an adaptive organism which can thrive in ecologically extreme conditions.

Environmental Disturbances

Despite occupying an ecological niche of such harsh environments, *Coccidioides* still thrives in certain regions of the world. The southwestern United States bears witness to the annual affliction the fungus poses on desert (and desert-like) communities, enduring spikes in coccidioidomycosis outbreaks after environmental episodes. California, in particular, possesses a variety of climates and geographies, providing the state with such diverse flora and fauna. In addition, California also experiences a myriad of natural events from forest fires to tempestuous winds which all have their corresponding geochemical consequences and, by extension, effects on *Coccidioides* growth, subsequently increasing coccidioidomycosis reporting.

Wildfires are among the most notable natural disasters which annually afflict California, leading firefighters from around the state to leave home during the "fire season" (late April through early October). The amount of occupational hazards firefighters must face during a wildfire outbreak is innumerate and among these hazards is the risk of inhalation of *Coccidioides* arthroconidia. In October 2003, the Ventura County fires blazed across the southern central coast and southwestern San Joaquin Valley. By February 2004, Ventura County saw rates of coccidioidomycosis increase to nearly six times greater than annual spikes observed in July, when coccidioidomycosis cases were at their peak in the previous year (MacLean, 2014). The 2004 Ventura County event is the first incidence of coccidioidomycosis outbreaks following a wildfire event in California. A working theory suggests that removal of surface vegetation or disturbance of soils by firefighting activities could provide a mechanism for this outbreak. The loss of vegetation also contributes to degradation of soils (Morgan, 2009). The absence of plant roots in soil decreases its water-carrying capacity, consequently, increasing the soil's aridity and rate of erosion. This suggests that even beyond the immediate effects wildfires pose to local communities in regards to coccidioidomycosis reports, the loss of vegetation can perpetuate these effects beyond the time of burning. The 2004 Ventura County fires were just the first reported case of coccidioidomycosis outbreaks following wildfires. A similar outbreak was reported again, following the 2017 wildfires in southern California.

The California Department of Public Health was alerted on August 17, 2017 that a cluster of coccidioidomycosis cases had afflicted a group of inmate wildland firefighters; 10 patients were clinically confirmed positive for coccidioidomycosis with two becoming hospitalized (Laws, et al. 2021). A survey of the inmate firefighters revealed that most individuals who became ill used hand tools and worked in “dusty” conditions, corroborating suspicions after the 2003 wildfires. Despite the lack of wildfire-coccidioidomycosis correlation studies in the scientific literature, the two events do still raise public health concerns. Particularly, the 2004 Ventura County fires—although just one instance—is of great intrigue because the outbreak occurred when coccidioidomycosis cases are otherwise typically at their lowest, during the “rainy season”.

The effects of the “rainy season” (January through March) on coccidioidomycosis reports in California has been largely monitored since the 1950s. Characteristically, seasons of greater coccidioidomycosis reporting occur during drier periods (i.e. low precipitation); in the same vein, periods of increased precipitation are negatively correlated with reported incidences of coccidioidomycosis (Tamerius & Comrie, 2011 ; Taylor & Barker, 2019). As a result, there is an observable peak in cases during the June/July months during a season of low precipitation and decreased soil moisture (Kolivras & Comrie, 2003 ; Tamerius & Comrie, 2011 ; Gorris et al., 2018). As soils endure drying, soil tops containing pathogenic material become more arid and, therefore, prone to becoming airborne, explaining reported increases in disease incidences.

However, the relationship between precipitation and *Coccidioides* is not so black-and-whihte. Longitudinal studies have presented an additional link between precipitation and rates of coccidioidomycosis cases after a lag period. Reports of increased coccidioidomycosis rates have been correlated with increased levels of precipitation 1-1.5 years prior to the outbreak (Kolivras & Comrie, 2003 ; Comrie, 2005). Increased precipitation followed by drying events may provide conditions optimal for initial microbial growth during the antecedent wet season and pathogenic spread during the subsequent dry season. Due to the porosity and infiltration capacity of soils known to foster *Coccidioides* growth, increased levels of precipitation may promote *Coccidioides* growth deeper into the soil column. Then, as a result, during greater drier periods, a greater portion of the soil column becomes arid and susceptible to soil disturbance, providing a mechanism for greater pathogenic material to become airborne.

Soil disruption is the most understandable and direct exposure to *Coccidioides*, raising concern for disease outbreaks following three natural phenomena: earthquakes, landslides, and wind storms. In 1994, the January 17th Northridge earthquake (magnitude 6.7) devastated the Los Angeles area (Schneider et al, 1997). Causing severe damage to buildings and roadways, the earthquake also induced subsequent landslides around the Santa Susana mountains (see Figure 4). In the weeks following the earthquake, a spike in coccidioidomycosis reports was observed. In Ventura County, 203 cases—not including patients under 13 years old—were recorded with 55% of patients becoming hospitalized (Schneider et al., 1997). The majority of cases (56%) occurred in Simi Valley, a city just south of the Santa Susana mountains. As a result of the earthquake and subsequent landslides, a prominent dust cloud enshrouded Simi Valley and other nearby valley cities, causing a spike in coccidioidomycosis cases just two weeks after the earthquake. Soil disruption by earthquakes and landslides can wreak havoc on local communities—especially those in arid climates——which must endure the ephemeral dust clouds. However, the consequences of these events become exacerbated when airborne particulates are then carried long distances by the wind.

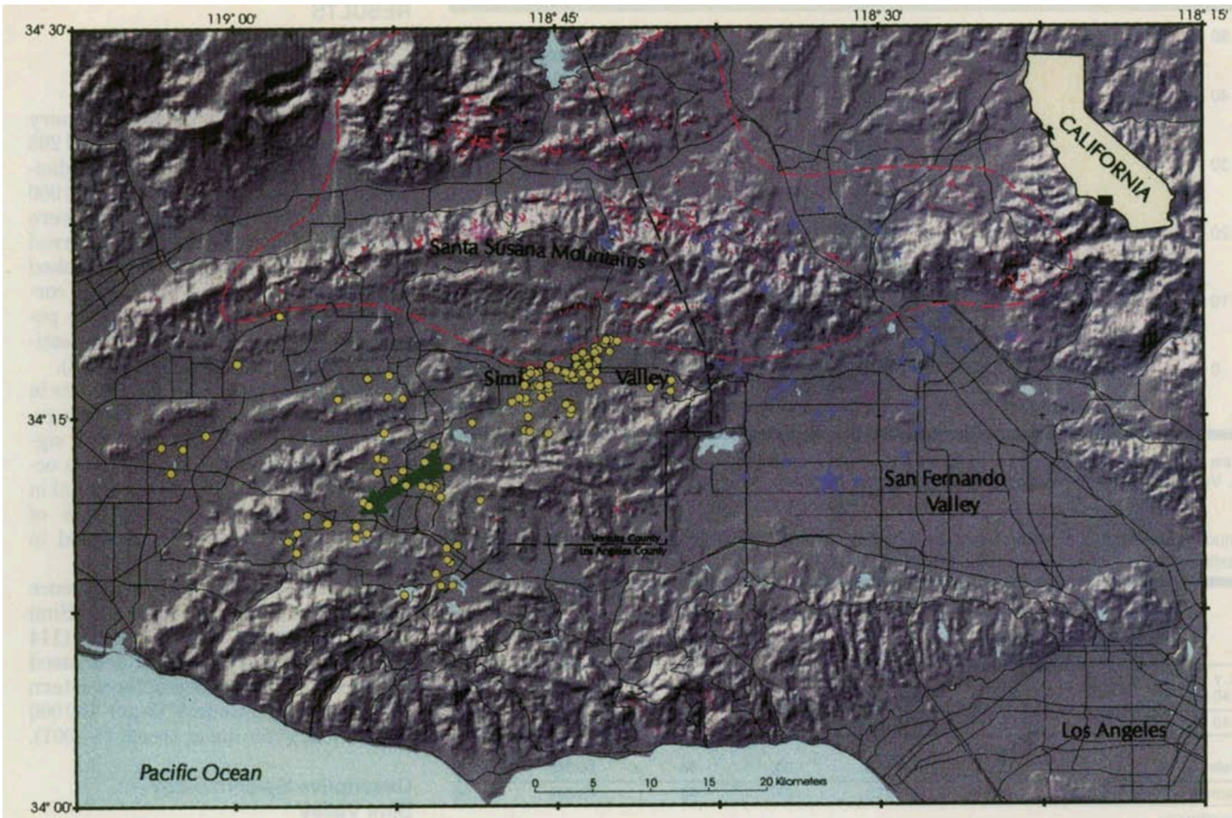


Figure 4. Schneider et al (1997) mapping outbreaks of coccidioidomycosis (yellow) after the 1994 Northridge earthquake. The map also marks individual landslides (red dots), concentration of landslides (red lines), wind direction (green arrow), earthquake epicenter (blue star), and aftershock centers (blue dots).

Wind funnels through southern California valleys with regularity, thereby raising concern as a vector carrying an airborne pathogen across the state. After the 1994 Northridge earthquake, Simi Valley withstood the dust cloud and, consequently, the spike in coccidioidomycosis cases which resulted. However, the effects did not remain local. Winds funneled through the Santa Susana mountains carried soil particles beyond the sites of landsliding (where Simi Valley is located) and into neighboring valleys (Schneider et al., 1997). Windstorms present an even more detrimental factor in the transport of *Coccidioides* arthroconidia across much longer distances. In December 1978, a dust storm blew through Kern county, with winds blowing north west through the San Joaquin Valley. Dust particulates reach elevations on the order of thousands feet, resulting in massive deposits along the coast as far north as Marin and Sacramento counties (Pappagianis and Einstein, 1978 ; see Figure 5). In the following weeks, the University of California, Davis was reporting new cases of coccidioidomycosis in counties previously regarded as "non-endemic" and, by the end of January, had reported 216 cases in this northern California region (Pappagianis and Einstein, 1978). Therein evidences wind as a mode of transport for *Coccidioides* via dust particles. But soil may not be the only vehicle on which *Coccidioides* spreads.

The spread of *Coccidioides* following wildfires is seldom understood. Phillips et al. (2023) attempted to find the correlation between wildfire incidence and coccidioidomycosis case reports within target populations. The primary population of interest were firefighters, having the most direct exposures to *Coccidioides* infested soils through their work, compared to the general public. The case study focused on 13 wildfires from 2003 through 2015, noting the amount of coccidioidomycosis reports within a hexagonal region surrounding the wildfire. The results found that there was no link between wildfires as an inducing mechanism towards coccidioidomycosis outbreaks among the general population (Phillips et al, 2023). However, when looking at regions already afflicted with high rates of coccidioidomycosis contraction, the study found that outbreaks did, in fact, follow wildfire episodes. Moreover, a separate study published in the same year examined the role of wildfire smoke to carry microbial material long distances. Mulliken et al. (2023) expanded the regions of interest to communities which received large quantities of wildfire smoke from wildfires between 2014 and 2018. These results showed

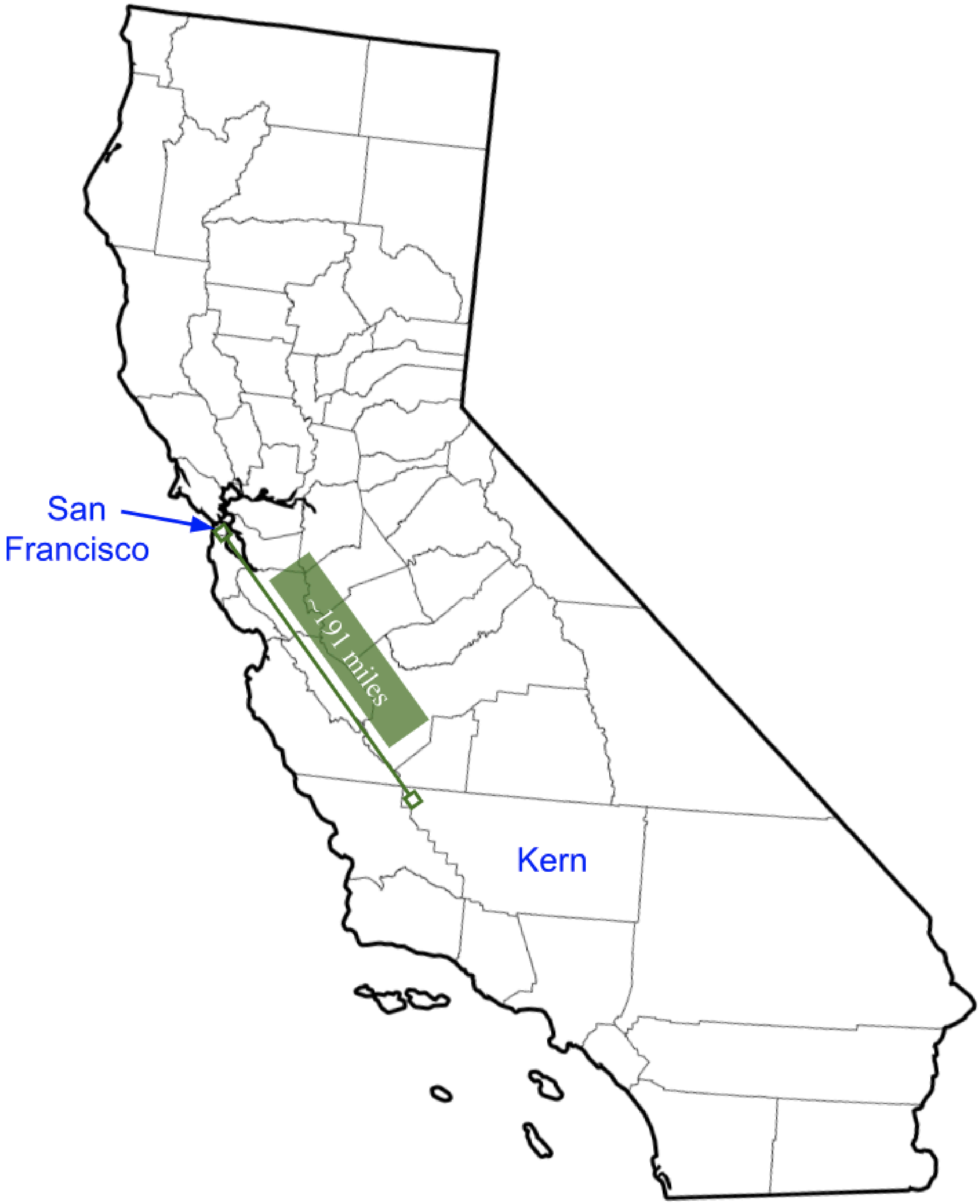


Figure 5. Map of counties in California, marking Kern and San Francisco counties. The two counties are approximately 191 miles apart.

that increases in coccidioidomycosis rates correlated with smoke exposure (Mulliken et al, 2023).While these results do not prove a causal relationship between wildfire/smoke exposure and contraction of coccidioidomycosis, further examination should be explored.

As soil containing *Coccidioides* arthroconidia becomes airborne, the threat of disease contraction by local communities, in turn, is only thwarted by minimizing the amount of unfiltered outside air breathed. However, knowing that increased rates of *Coccidioides* growth and transport are largely driven by environmental mechanisms (Fisher et al., 2000), this raises concerns about the effects anthropogenic activity may have on fungal growth and the subsequent public health consequences. The San Joaquin Valley, a prominent agricultural center, also provides an interesting perspective providing insight into the impacts—beyond nutritional—agriculture may have on a community's public health. What role, if any, does agriculture play in the disease reporting of coccidioidomycosis? And does this correlation align with the geochemical and geophysical effects of agriculture on regional soils?

IV. QUANTIFYING AGRICULTURAL PRACTICES and EFFECTS

Methods

Data used to conduct statistical analyses were all collected online from publicly available statistics for the State of California. County statistics on reported coccidioidomycosis incidences from 2015 through 2021 were retrieved online from the "EPIDEMIOLOGIC SUMMARY OF VALLEY FEVER (COCCIDIOIDOMYCOSIS) IN CALIFORNIA, 2020-2021" (California Department of Public Health, 2022). Data on agricultural production by county were gathered online from the "County Agricultural Commissioner's Reports" for the crop years 2015-2016 through 2020-2021 (California Department of Food and Agriculture, 2023). Statistical tests included counties within the San Joaquin Valley: Fresno, Kern, Kings, Madera, Merced, San Joaquin, Stanislaus, Tulare. The San Joaquin Valley was chosen for analysis due to the region's agricultural productivity (see Figure 6) and high rates of coccidioidomycosis (see Figure 7). Further statistical analyses were performed using counties which (1) are classified by the California Department of Food and Agriculture as Central Coast and Southern California and (2) border the San Joaquin Valley: Monterey, San Luis Obispo, Ventura, Santa Barbara, Los Angeles, and San Bernardino. Contra Costa, Alameda, Santa Clara and San Benito counties were not included in the statistical testing as data concerning coccidioidomycosis rates for these years were deemed potentially unreliable by the Department of Public Health. The same concern also excluded bordering counties from the Sacramento Valley (i.e. Sacramento and Solano) and the Sierra Nevada (i.e. Amador, Calavera, Inyo, Mariposa, Mono, and Tuolumne). All data were downloaded as a csv file and filtered through base R.

County	Rank Without Timber				
	2020		2021		Percent Change
	$1,000	*Rank*	*$1,000*	*Rank*	
Kern	7,568,984	2	8,342,178	1	10.2
Fresno	7,966,308	1	8,109,917	2	1.8
Tulare	7,229,365	3	8,089,377	3	11.9
Monterey	3,908,317	4	4,100,240	4	4.9
Merced	3,473,093	5	3,697,992	5	6.5
Stanislaus	3,437,722	6	3,471,196	6	1.0
San Joaquin	3,048,128	7	3,211,550	7	5.4
Kings	2,179,476	8	2,338,144	8	7.3
Imperial	2,026,427	9	2,287,312	9	12.9
Ventura	1,983,478	10	2,052,020	10	3.5
Madera	1,941,618	11	2,045,553	11	5.4
Santa Barbara	1,847,075	12	1,918,186	12	3.8

Figure 6. California Department of Food and Agriculture (2022) ranking the top 12 most agriculturally productive counties in the state and noting the percent change from 2020 to 2021. The highlighted counties are those located in the San Joaquin Valley.

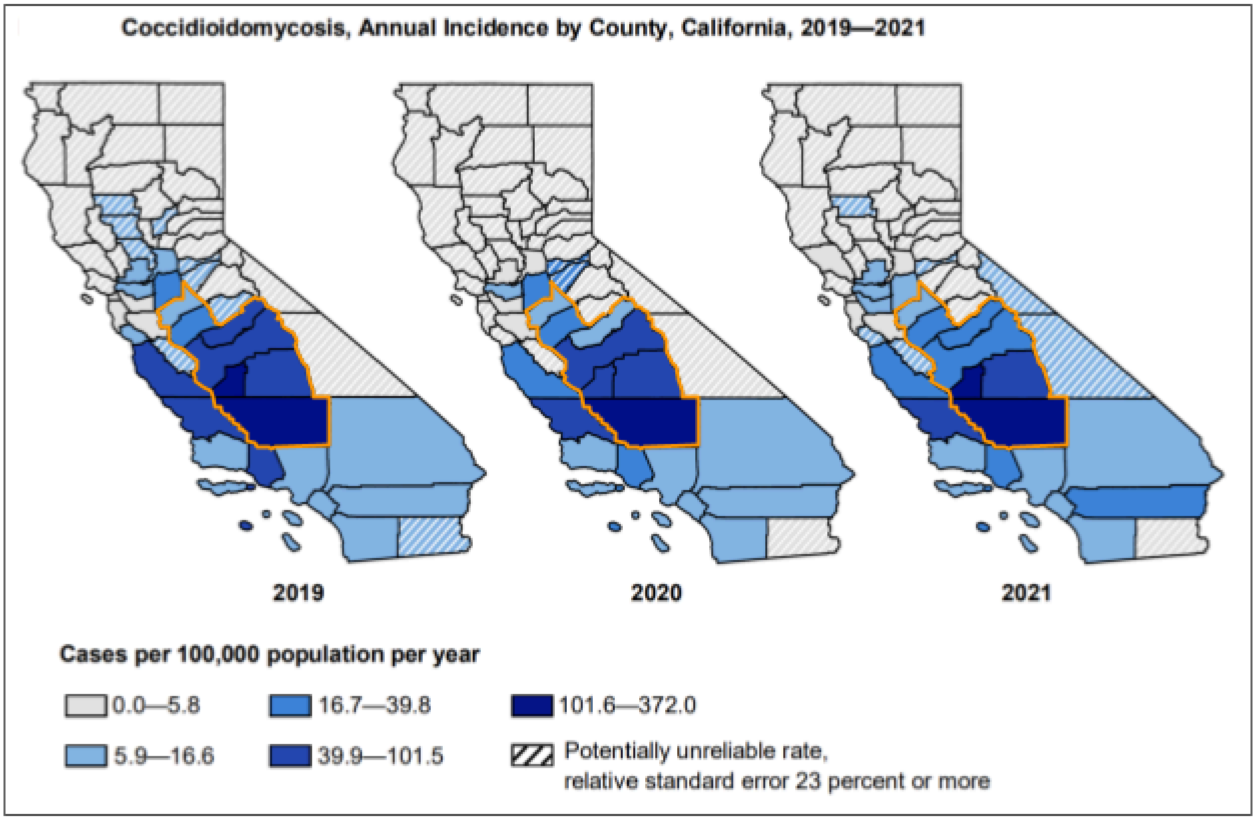


Figure 7. California Department of Public Health (2022) showing the rate of coccidioidomycosis in each county of California. The region outlined in orange marks the San Joaquin Valley.

All statistical analysis testing was performed using base R (Rstudio Team, 2021). ANOVA statistical analysis testing was used to measure significance between Gross Production Value (GPV) of agricultural yields and reported coccidioidomycosis cases within each county. Spearman's Rank Correlation analysis was used to determine correlative relationships between the two variables. Aggregate data were also compiled to measure the large-scale correlation between GPV and coccidioidomycosis cases across all counties as one large region. Statistical significance was determined by two thresholds: (1) a p-value below 0.01 ($p < 0.01$) indicating statistical significance although more data would be desired and (2) a p-value below 0.001 ($p < 0.001$) indicating significance.

Results

Data from the California Department of Public Health regarding reports of coccidioidomycosis cases were collected and graphed using baseR (Rstudio, 2021). Two counties outnumber the rest in coccidioidomycosis rate reports through the time period: Kern and Kings counties (see Figure 8). Kern County showed a peak in coccidioidomycosis rates in 2019 with 372.0 (per 100,000). Kings County showed a peak in coccidioidomycosis rates in 2017 with 181.6 (per 100,000). These two years, 2017 and 2019, present trends of interest for all counties. The graph illustrates two noticeable increases in disease rate, observed at 2017 and 2019 with respect to years prior; Kern County reported rate changes of +57.5 and +42.8 (per 100,000), respectively; Kings County reported rate changes of +23.6 and +30.0 (per 100,000), respectively. Other counties, too, demonstrated increases in disease rate at these times, although not as drastic as in Kern and Kings counties. Similar trends were observed throughout Coastal California and Southern California counties; San Luis Obispo and Ventura counties also exhibited high rates of disease in 2017 and 2019 (see Supplementary Figure A). These data were then compared and correlated to data concerning Gross Production Value of the different crop categories in each county.

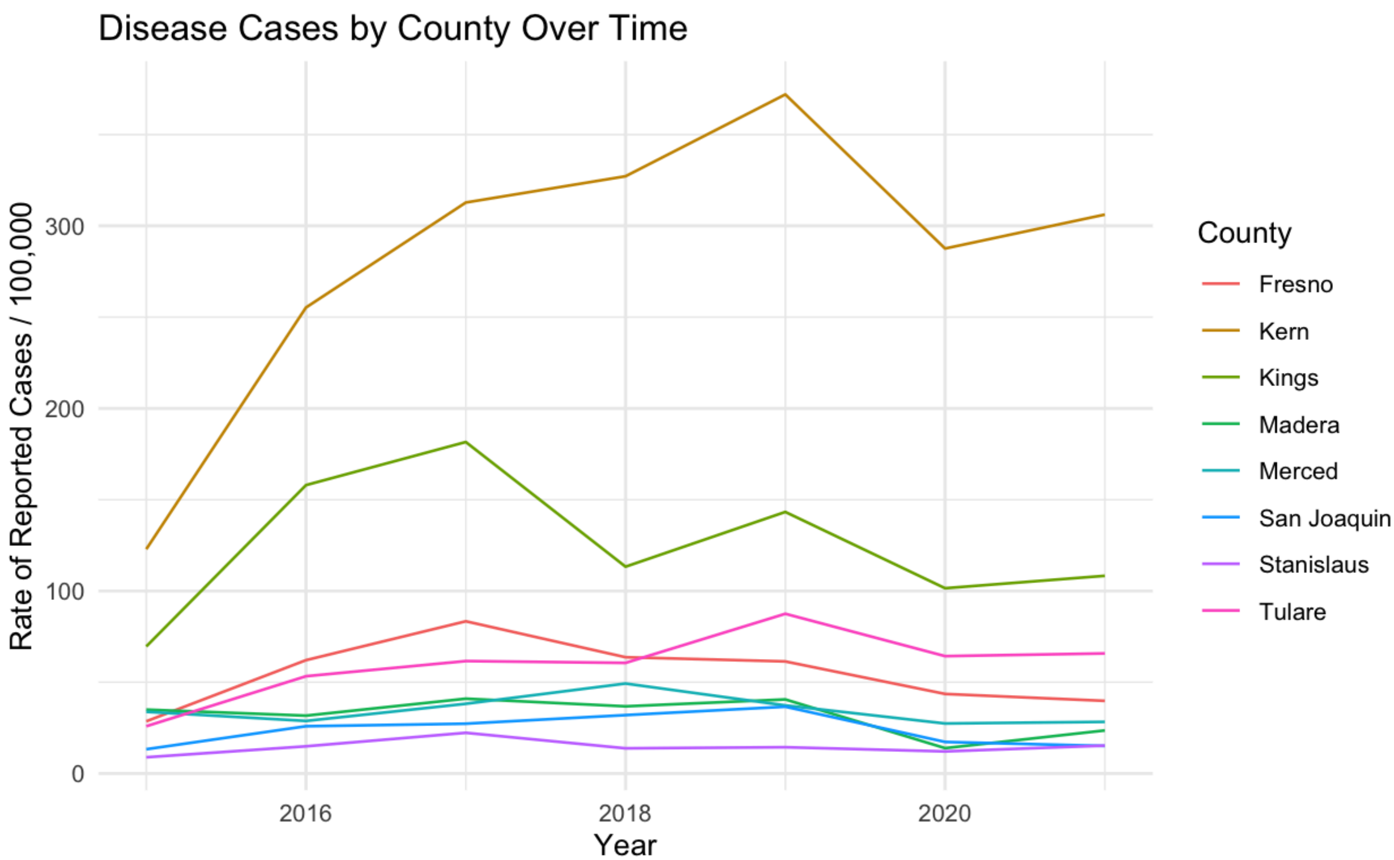
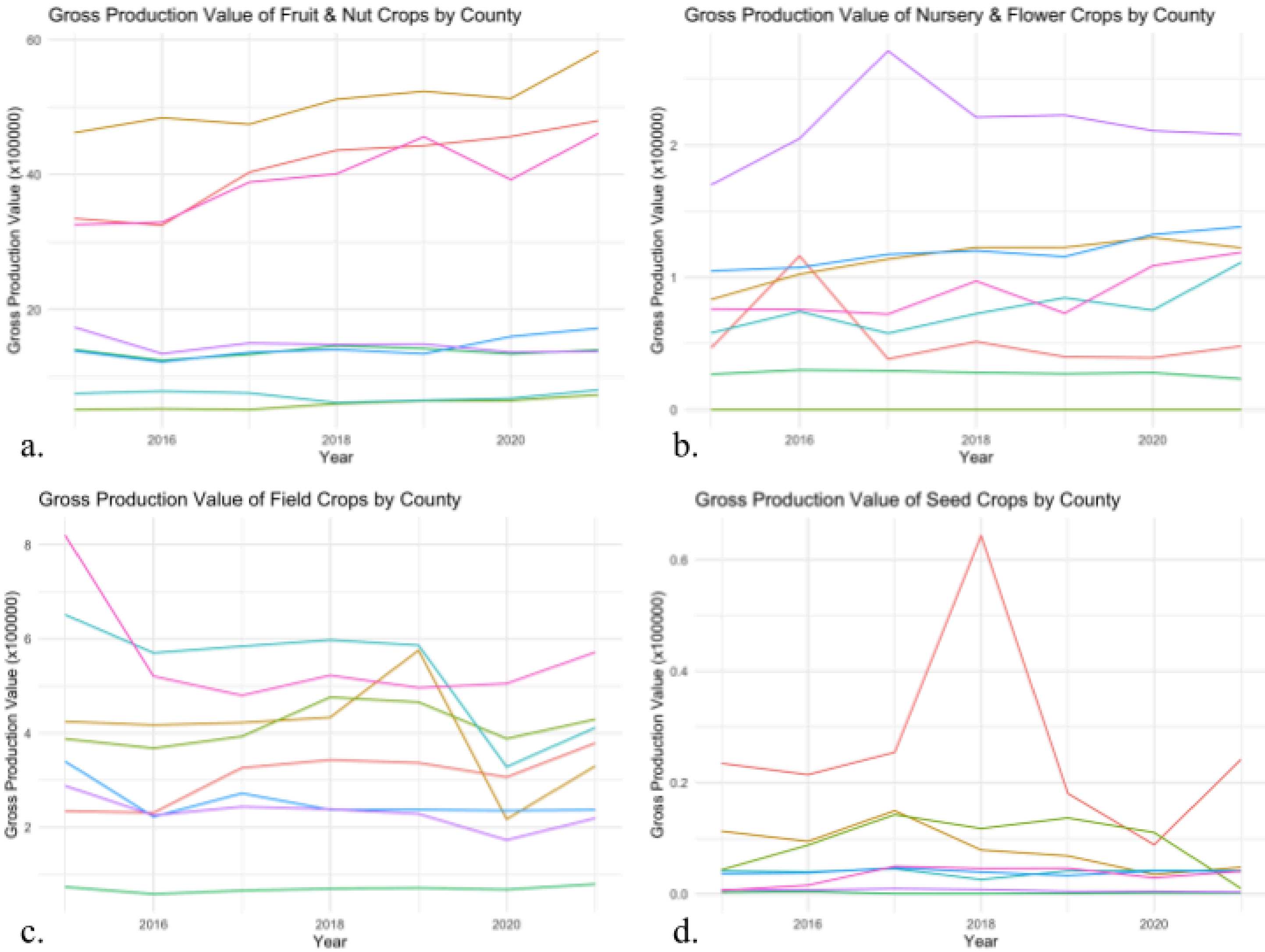


Figure 8. Rates of coccidioidomycosis (per 100,000 people) in San Joaquin Valley counties from 2015 to 2021.

The California Department of Food and Agriculture separates crops into five categories—Fruits & Nuts (FruN), Nursery & Flowers (NuF), Field Crops (FC), Seed Crops (SC), and Vegetable Crops (Veg)—which were used in subsequent analyses. Data retrieved from the "COUNTY AGRICULTURAL COMMISSIONERS' REPORTS" provided information regarding the Gross Production Value (GPV) of each crop group in all counties for each crop year. These data were collected for all crop years from 2015 through 2021 and graphed to illustrate crop yield trends in each county (see Figure 9). Certain counties demonstrate distinctive production in some crop categories: Kern, Tulare and Fresno outperform all other counties in FruN production (see Figure 9a ; see Supplementary Figure B) ; Fresno outperforms all other counties in SC production (see Figure 9d ; see Supplementary Figure E) ; and Monterey



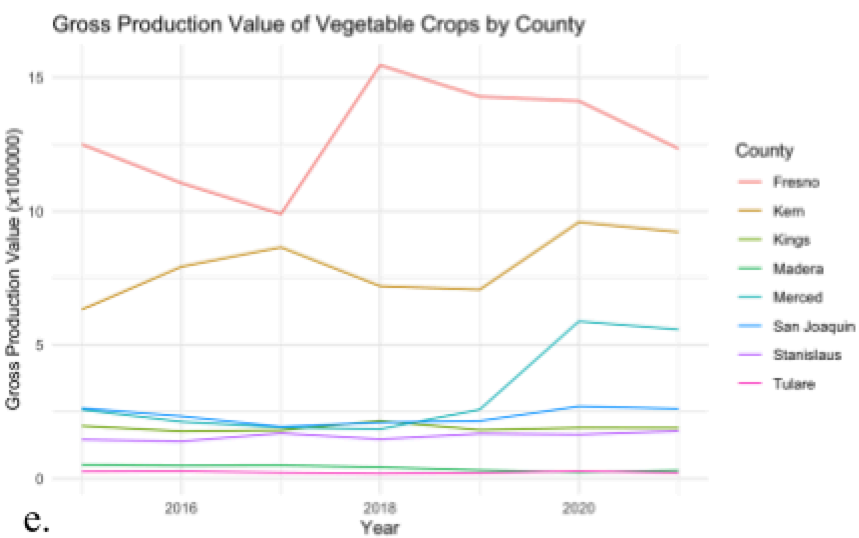
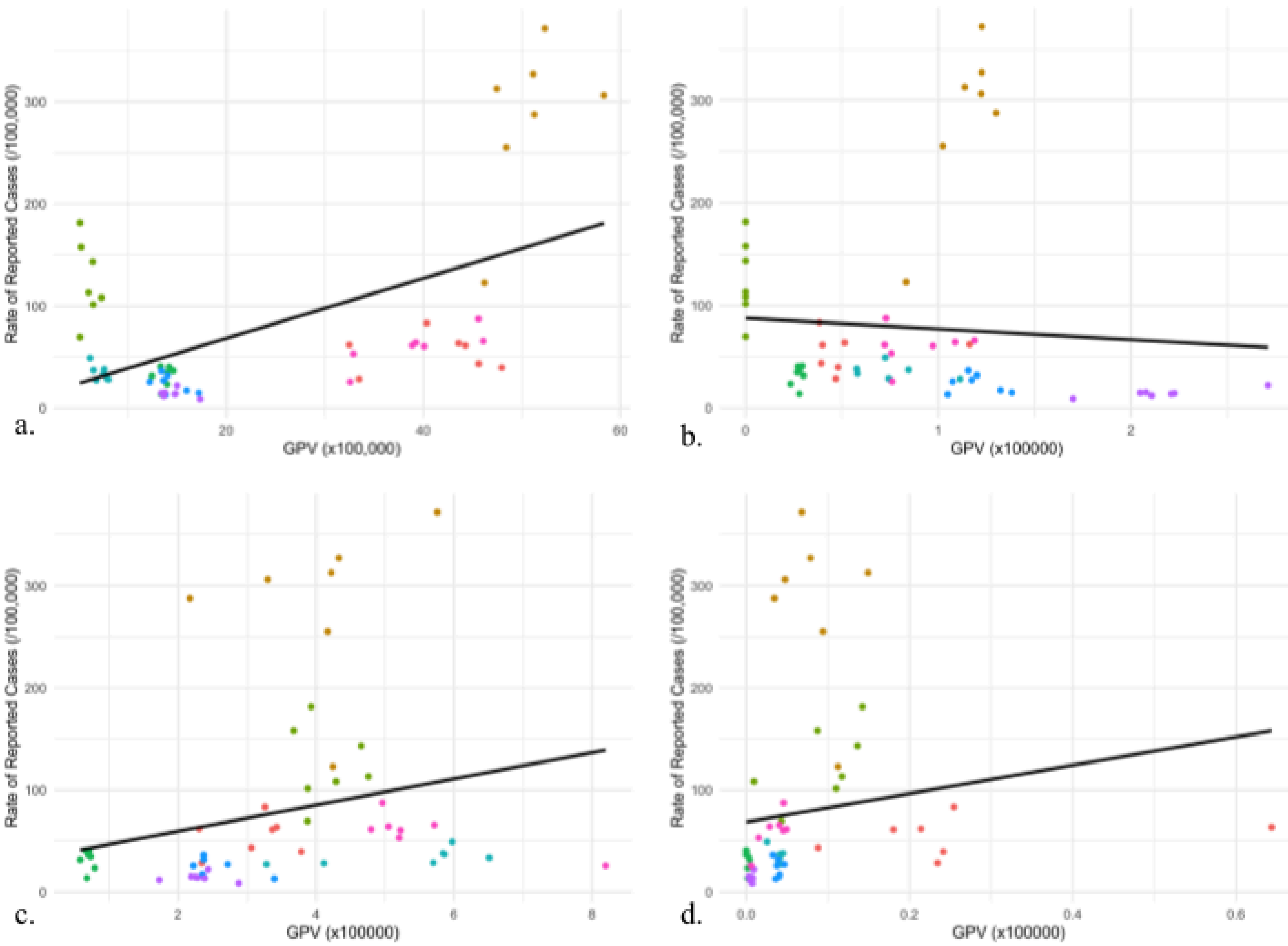


Figure 9. Gross Production Value for each county from 2015-2021.
9a. Fruits and Nut Crops
9b. Nursery and Flower Crops
9c. Field Crops
9d. Seed Crops
9e. Vegetable Crops

outperform all other counties in Veg production, although Fresno and Kern demonstrate notably greater productions of Veg crops than other San Joaquin counties (see Figure 9e ; see Supplementary Figure F).

Investigating the relationship between agricultural production and coccidioidomycosis reports, analyses were first conducted to measure the correlation between the two variables across the San Joaquin Valley, Coastal California, and Southern California (see Supplementary Figures G-K). For the region at large, positive correlations with significance, linking agricultural production and disease rate, were observed in four crop categories: FruN ($r = 0.5450919$; $p < 0.001$), FC ($r = 0.5615282$; $p < 0.001$), SC ($r = 0.37445$; $p < 0.001$), and Veg ($r = 0.3103193$; $p < 0.001$). A negative correlation with significance was observed in NuF ($r = –0.2486171$; $p < 0.01$).

Focusing specifically on the San Joaquin Valley, Spearman's correlation tests and ANOVA statistical analyses were conducted to see if a region booming with agricultural production would demonstrate links between production of certain crops and a county's rate of coccidioidomycosis (see Figure 10). Positive correlations and significance were observed in two crop categories: FruN ($r = 0.5468764$; $p < 0.001$) and Veg ($r = 0.3461491$; $p < 0.01$) (see Figures 10a and 10e, respectively). No statistical significance was observed in the other crop categories.



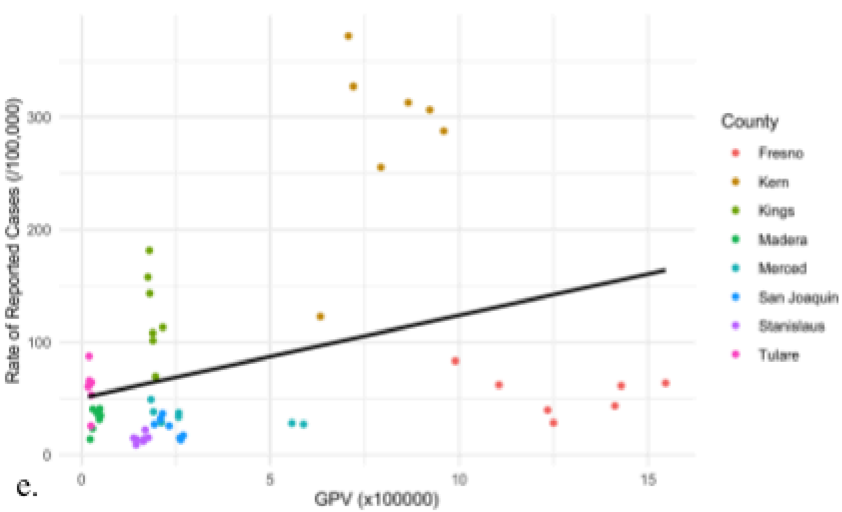


Figure 10. Rate of Reported Cases of coccidioidomycosis by Gross Production Value (GPV). 10a. Fruits and Nut Crops (r= 0.5468764; p= 1.295×10^{-5}) 10b. Nursery and Flower Crops (r= –0.07553668; p= 0.5801). 10c. Field Crops (r= 0.2431539; p= 0.07096). 10d. Seed Crops (r= 0.1567238; p= 0.2487). 10e. Vegetable Crops (r= 0.3461491; p= 0.008969)

Statistical testing was then conducted against rain data, in order to ensure coupled crop yield and disease rate increases were not simply the result of increased precipitation during the wet months. Data concerning precipitation in each county during the wet months were collected from NOAA National Centers for Environmental information. All counties experienced increased precipitation in 2017 and 2019 (see Figure 11; see Supplementary Figures L-W). For the greater region of interest including the San Joaquin Valley, Coastal California, and Southern California, a positive correlation and statistical significance were observed ($r = 0.2972157$; $p < 0.01$; see Supplementary Figure X). Contrastingly, for the San Joaquin Valley only, no statistically significant correlation was observed between precipitation events and rates of coccidioidomycosis ($p = 0.2881$; see Figure 12).

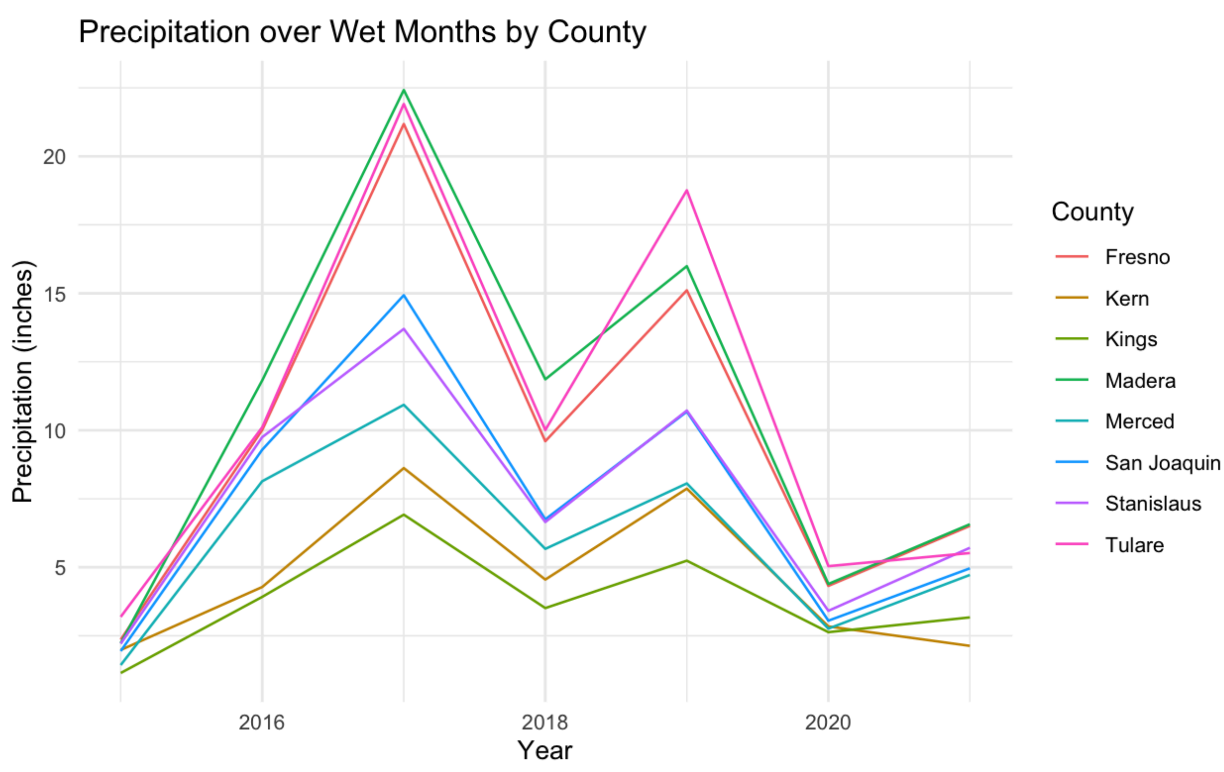


Figure 11. Precipitation (in inches) for each San Joaquin valley county during the "wet months" (i.e., January-March).

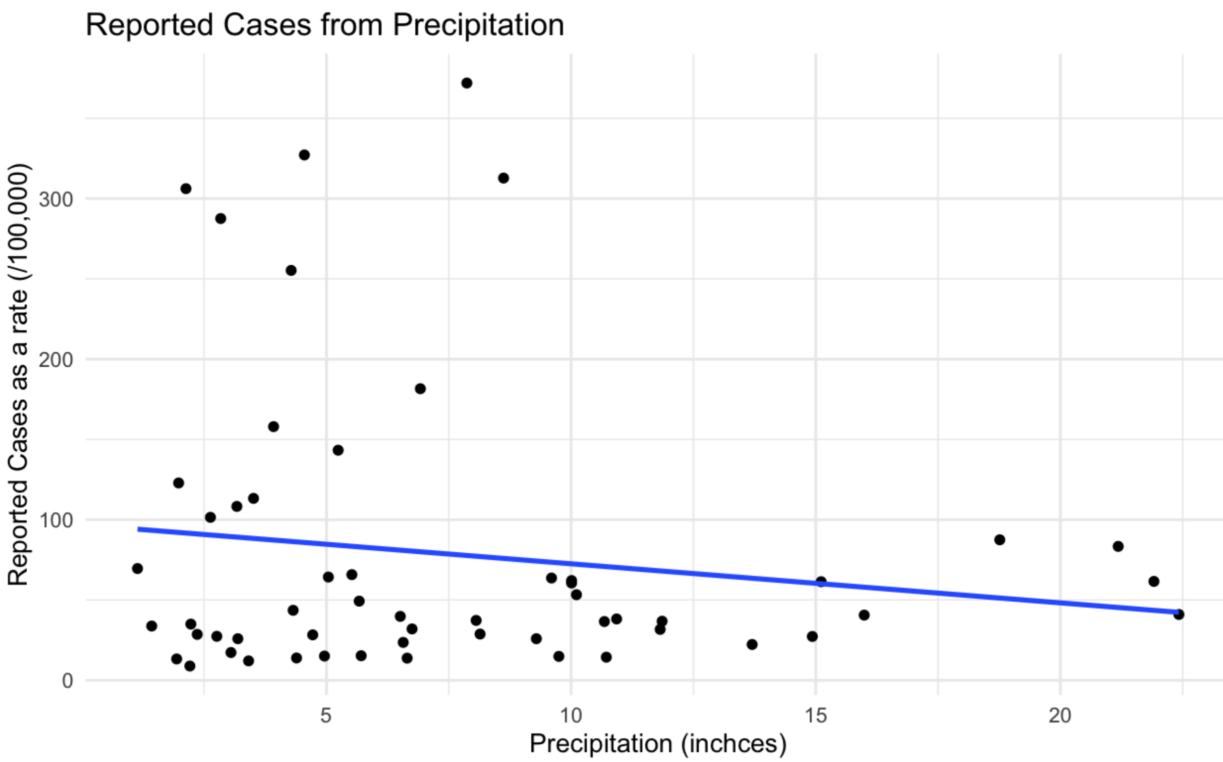


Figure 12. Scatter plot of reported cases (as a rate per 100,000 people) by precipitation in inches. (r = -0.1444705 ; p-value = 0.2881)

DISCUSSION

Results substantiate claims linking agricultural practices to coccidioidomycosis rates. Initial testing across the San Joaquin Valley, Coastal California, and Southern California was performed to consider a region which is not wholly composed of prominent agricultural centers. ANOVA analysis confirmed that across this large region, all crop categories (except NuF) demonstrated a positive correlation between GPV and rate of coccidioidomycosis reporting. This correlation could be the cause of having greater percentages of farmland. Kern and Fresno counties—the areas with the first and fourth highest rates of coccidioidomycosis incidence, respectively— possess the greatest amount of land dedicated for crop farming (Kern: ~964108 acres; Fresno: 1136112.60 acres ; see Table 1). Regular tilling and harvesting on these soil tops would provide sufficient soil aeration for *Coccidioides* growth and soil disturbance for

Coccidioides arthroconidia release. Given the land requirements needed for greater agricultural productivity, it is possible that this link is explained by the mass amount of exposed soil tops. Kings County, however, is a very small county and, yet, possesses the second highest rate of coccidioidomycosis in the state. This is possibly the result of having a large cropland per capita ratio. Kings County has an acre of cropland per capita ratio of 3.181 which is nearly three times greater than Kern (1.052 acres/capita) and Fresno (1.119 acres/capita). Moreover, all San Joaquin Valley counties have high cropland acres per capita ratios which are much greater than Southern California counties (see Table 1). By having a landmass which largely concentrates a population within these farmlands, this increases exposure potential to a wider group of people.

Region	County	Farmland (acres)	% Cropland	Total Acreage	% Land	Poulation	acre/capita
San Joaquin	Fresno	1646540	0.69	3840000	0.296	1015000	1.119
	Kern	2295497	0.42	5224000	0.185	916108	1.052
	King	615958	0.79	1363200	0.357	152981	3.181
	Madera	645358	0.54	1377920	0.253	160256	2.175
	Merced	946385	0.58	1267000	0.433	290014	1.893
	Stanislaus	722546	0.56	969600	0.417	551275	0.734
	Tulare	1250121	0.58	3097000	0.234	477544	1.518
Coastal California	Monterey	1340142	0.27	2413440	0.150	432858	0.836
	San Luis Obispo	931291	0.26	2314240	0.105	282013	0.859
Southern California	Los Angeles	57809	0.51	3041920	0.010	9721000	0.003
	Orange	32401	0.30	606720	0.016	3151000	0.003
	Riverside	263796	0.68	4673920	0.038	2474000	0.073
	San Bernardino	68228	0.43	12867200	0.002	2194000	0.013
	Santa Barbara	715067	0.20	2424960	0.059	443837	0.322
	Ventura	260102	0.47	1413120	0.087	832605	0.147

Table 1. Proportions of land allocated to farming in each county. This lists farmland (in acres), percentage of farmland allocated to crops, the total size of the county (in acres), the percentage of land in each county allocated for crop farming (cropland / total acreage), the population of each county from the 2022 census, and the estimated cropland per capita ratio. Land-use data were collected from the US Department of Agriculture, 2017 CA State and County Census of Agriculture, and population data from the US Census Bureau.

Despite these data, and the observable differences in land-use compositions across counties, linking agricultural practices to rates of coccidioidomycosis is complicated by a factor with known effects on the growth of both crops and *Coccidioides*: rain. ANOVA analysis showed that within the San Joaquin Valley, precipitation during the wet months, prior to peaks in coccidioidomycosis reporting, there is no statistically significant correlation between precipitation and rates of disease. However, ANOVA analysis comparing precipitation during the wet season across all counties of study (i.e. in the San Joaquin Valley, Coastal California, and Southern California) demonstrated a statistically significant positive correlation between the two variables. Results across all counties coincide with previous studies which have identified this link between increased precipitation and coccidioidomycosis rates (Taylor & Barker, 2019). However, these large scale trends may not be applicable to all regions. The loss of significant data observed in the San Joaquin Valley could indicate that precipitation is not a key factor in this region. These results, in tandem with the statistically significant data linking agricultural practices to rates of disease, suggest that the effects of precipitation on coccidioidomycosis rates in the San Joaquin Valley are outweighed by the effects of agricultural practices. But, more research regarding precipitation in the San Joaquin Valley should be conducted to further substantiate these findings.

In the same vein, analyses of these significant agricultural practices in the San Joaquin Valley were performed in order to observe correlations between certain crop production and rates of coccidioidomycosis. Of the five crop categories, two demonstrated significant correlations to rates of coccidioidomycosis: FruN and Veg. These crop categories demonstrating a link to coccidioidomycosis incidences suggest mechanisms of disease propagation through soil disturbance and fungal growth. Veg crops have previously been identified as an occupational hazard, particularly among Hispanic field workers in Kern County (McCurdy et al., 2020). Most Veg crops require plant uprooting for the harvest of bulbs or roots. As a result, many field workers are in close proximity and exposed to great amounts of upturned soils. This repeated exposure directly links Veg crops to incidences of coccidioidomycosis. FruN crops, however, pose more considerable connections. Most FruN crops grow on trees, with the product of interest growing from the branches. Some orchards do hire labor workers for hand harvesting. This poses little risk of soil disturbance and subsequent exposure to coccidioidomycosis. However, many large orchards will use machine harvesting to collect their produce. Machine harvesting for nuts comes in two stages: first, a “shaker” will approach each tree, grasp the trunk, and vigorously shake the nuts onto the floor; then, after 7-10 days of resting on the floor, a “sweeper” will pass through the rows of trees, collecting the sun-baked nuts off the floor (Almond Living Magazine). Other machines, like the Tenías Almond Harvester™, will shake the trees and collect the nuts on the same pass through the orchard (Tenías Digital Catalog). Through either process, mechanical shaking produces large dust clouds as a result of vibrations traveling down to the roots, dislodging soil from the ground. Machine harvesting, although performed by a single machine operator, promotes the greatest risk for large-scale *Coccidioides* arthroconidia exposure, producing dust clouds with the potential for longer transport of pathogenic material. There is no doubt that Veg and FruN crop harvests promote soil disturbance with substantial exposure risk for contraction of coccidioidomycosis. The crops themselves, however, prompt further interest in their role as a biotic factor with their respective geochemical effects.

As much nutrients as they require, certain species of trees can provide nutrients back to the soils in return, especially on the roots of arid-soil adapted trees. Fertilizers can provide already fertile soils even more plant nutrients, like nitrogen sources. But tree-soil interactions, too, have long been studied, noting the variations in nutrient content beneath the roots of different species, and how these geochemical effects subsequently can foster the revitalization of faunal soil communities by increasing concentrations of available nitrogen, phosphorus, and organic carbon (Zou, 1993 ; Binkley & Giardina, 1998 ; Warren & Zou, 2002). These effects have been utilized in agriculture to harbor peak productivity while resisting soil degradation (Melnyk & Meyerowitz, 2015). *Prunus dulcis* (almond trees) are best adapted to Mediterranean, arid, and desert climates, making them very well suited for growth in California—primarily in the San Joaquin Valley (Micke & Kester, 1998). Soils surrounding the rootstocks of *P. dulcis* show increased levels of organic carbon and nitrogen, promoting microbial development (Macci et al., 2012 ; Macci et al., 2013). Unlike almond trees, however, most fruit trees are not innately best fit for the San Joaquin Valley soils and climate. As a result, many farmers have adapted their crops to the soils by grafting their trunks to the rootstock of native species—namely the blue oak (*Quercus douglasii*) and valley oak (*Quercus lobata* Nee)—in order to survive the harsh soil conditions (Tietje, Foott, & Labor, 1990). *Quercus* trees also provide similar nutrient return to soils, increasing concentrations of organic carbon, nitrogen, and phosphorus (Dahlgren, Singer, and Huang, 1997 ; Berman & Bledsoe, 2014). The advantages of planting *Prunus* and *Quercus* trees prompt farmers to routinely utilize their rootstocks to maintain soil fertility across years. Consequently, farmers may also be fostering the growth and development of *Coccidioides* through these practices. The geochemical impact of these crop roots provide another possible mechanism through which coccidioidomycosis runs rampant throughout the San Joaquin Valley, increasing the amount of pathogenic material which may later become airborne during a hazardous harvesting season.

The link between agricultural practices and rates of coccidioidomycosis is substantial and significant. Results comparing the San Joaquin Valley, a region prominent for its agricultural production, illustrated the impact farming and harvesting has on *Coccidioides* growth and increased exposure to arthroconidia and subsequent disease contraction. Hand harvesting of Veg crops has previously been noted (McCurdy et al., 2020), and large-scale harvesting practices, using heavy machinery, also presents causes of airborne pathogens. This not only confirms coccidioidomycosis as an occupational hazard for field workers, but also as a greater public health concern for those living near croplands, which in the San Joaquin Valley is nearly everybody as evidenced by the distribution of land for crop farming (see Table 1). Moreover, the particular crops themselves may be fostering growth of *Coccidioides*, potentially concentrating more pathogenic material within a region already expected to endure great exposure to disease. The San Joaquin Valley poses a great region of study for the effects of anthropogenic activity on the geospatial distribution and ecology of *Coccidioides*. Further research should be performed, especially in a changing climate where this particular public health concern is reaching new territories.

V. CONCLUSION

Coccidioidomycosis presents intriguing insights into the intersection between earth systems, microbial communities, and public health at large. The growth and development of *Coccidioides* provide the genus its adaptive and opportunistic characteristics, transitioning between morphologies to exploit its environment. This has allowed *Coccidioides* to inhabit harsh conditions like arid soils, hot climates, high salinity, and a range of pH levels (Lewis, Bowers, & Barker, 2015). In the United States, these conditions have long been recognized in the southwestern region, primarily California and Arizona. However, as climate warming exacerbates consequences of drought, *Coccidioides* can now be considered endemic to a much larger region—including Nevada, Utah, New Mexico, Texas, Colorado, and Washington—and is continuing to spread (Fisher et al., 2000, CDC, 2022).

The prevalence of *Coccidiodes* in the western United States raises public health concerns, highlighting the increasing threat to disease exposure after environmental events. Regions afflicted with coccidioidomycosis show annual trends, with peaks or outbreaks typically occurring in June/July and October/November (Comrie, 2005). Nevertheless, events like wildfires and precipitation can alter soil conditions to those favorable by *Coccidioides* (Kolivras & Comrie, 2003; MacLean, 2014). Case studies observing coccidioidomycosis cases after these events support hypotheses of environmental mechanisms of *Coccidioides* growth. Moreover, environmental events can also provide mechanisms for pathogenic material, arthroconidia, to become airborne, as is observed following landslides and wind storms (Pappagianis & Einstein, 1978 ; Schneider et al., 1997). This, then, presents the possibility of coccidioidomycosis incidences to occur at sites further away from the fungal source. Yet, natural phenomena are not the only factor affecting regional rates of coccidioidomycosis.

Anthropogenic activity, too, can foster and expose *Coccidioides* to local communities; the San Joaquin Valley is particularly vulnerable to coccidioidomycosis due to agricultural practices. The San Joaquin Valley provides the hot and arid climates perfect for *Coccidioides* growth. But, rates of coccidioidomycosis are especially high due to great agricultural production. By land mass, the San Joaquin Valley is 27% cropland and 20% non-crop producing land, meaning farmland constitutes 47% of the region's total landmass (US Department of Agriculture, 2019). Not only does this signify larger quantities of exposed arid-soil tops, but statistically significant correlations are observed between agricultural production and rates of coccidioidomycosis throughout the San Joaquin Valley. Particularly with FruN and Veg production, biogeochemical reactions and harvesting techniques may aid the development of *Coccidioides* and spread of Valley fever.

There is currently no state standard, requiring employers to provide protections against exposure to coccidioidomycosis. In fact, the California Occupational Safety and Health Administration (Cal/OSHA) requires no standard of protection against soil-pathogens like *Coccidioides*. Today, the General Duty Clause, Section 5(a)(1) of the Occupational Health and Safety Act of 1970, remains the only requirement in regards to coccidioidomycosis with which employers must comply (Cal/OSHA). All other means for employers to provide protections and training for their employees are mere recommendations. These recommendations include: disease training (personal prevention and risk assessment), using water to stabilize soils, adding landscaping/paving frequently traveled grounds, washing equipment, and providing employees with rest areas/locker rooms free of dust (Cal/OSHA ; CA Department of Public Health, 2013). Unfortunately, these recommendations are hardly implemented with regularity. For the construction industry, Valley fever training and hazard minimization are required (Cal/OSHA ; CA Department of Public Health, 2013), but this is not true in agriculture. Composed largely of spanish-speaking immigrants and indigenous peoples, farm laborers are often an exploited population, pushing many San Joaquin Valley farm laborers to become outspoken about the discrimination and environmental concerns faced at work (Mines, Nichols, & Runsten, 2010 ; Chandrasekaran, 2021). The lack of readily accessible reseaerch about Valley fever adds an additional layer of difficulty in addressing these issues, especially that which identifies coccidioidomycosis as an occupational hazard in agriculture. Through the dissemination of information regarding Valley fever and implementation of Valley fever standards of protection, agricultural practices can be carried out while also minimizing employees' exposure to disease in the near future.

In this vein, three measures should be put in place to better address and prevent the public health concern and its source:

(1) More geologic and biochemical research is necessary to better understand the fungus and its environment. Through this, we can hopefully find better ways of detecting *Coccidioides* in situ, and accurately predicting regional soils where it may be inhabiting.

(2) More reporting is needed from a public health standpoint. Many counties are considered data insufficient in regards to Valley fever incidences by the California Department of Public Health. Increasing reporting in these areas would increase the resolution of data results.

(3) There needs to be a push to educate and advocate for field workers in the San Joaquin Valley. Communication regarding Valley fever needs to be available to workers, potentially standardizing how they can best protect themselves from disease and how their employers *should* be providing protections for them as well.

From microbes to farm workers, agriculture plays a pivotal role in the life and culture of the San Joaquin Valley. Actions must be taken to protect the health and wellbeing of its community or, for that matter, to any other community which may soon endure the consequences of this spreading endemic soil-borne disease.

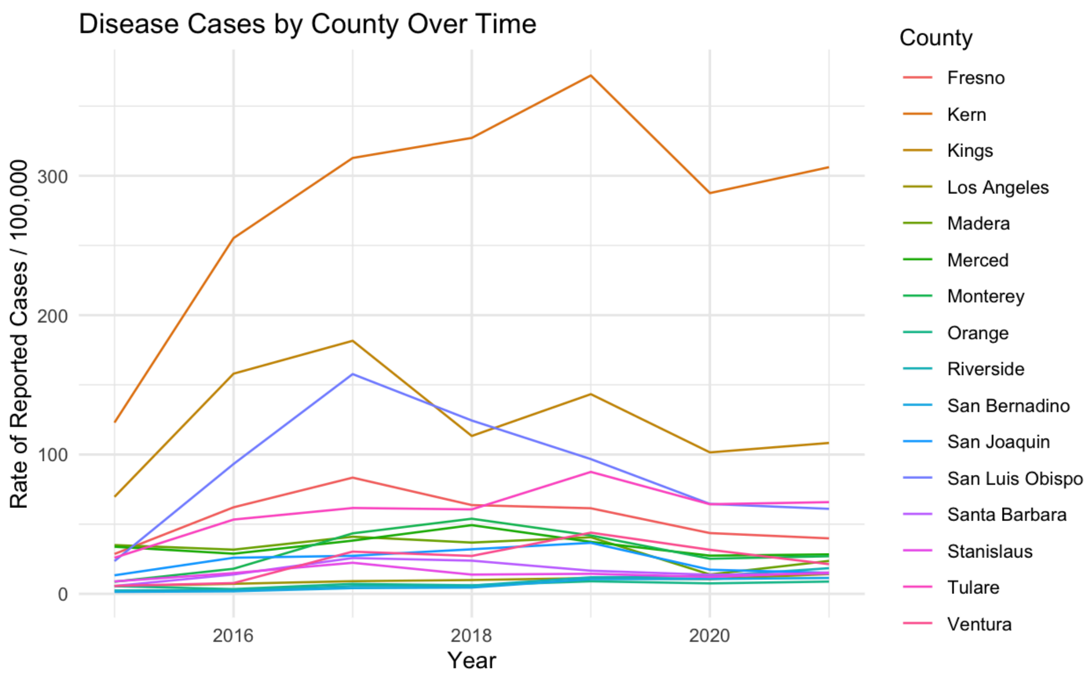


Figure A. Reported cases of coccidioidomycosis (as a rate per 100,000 people) for the San Joaquin Valley and nearby counties with sufficient data reporting from 2015 to 2021.

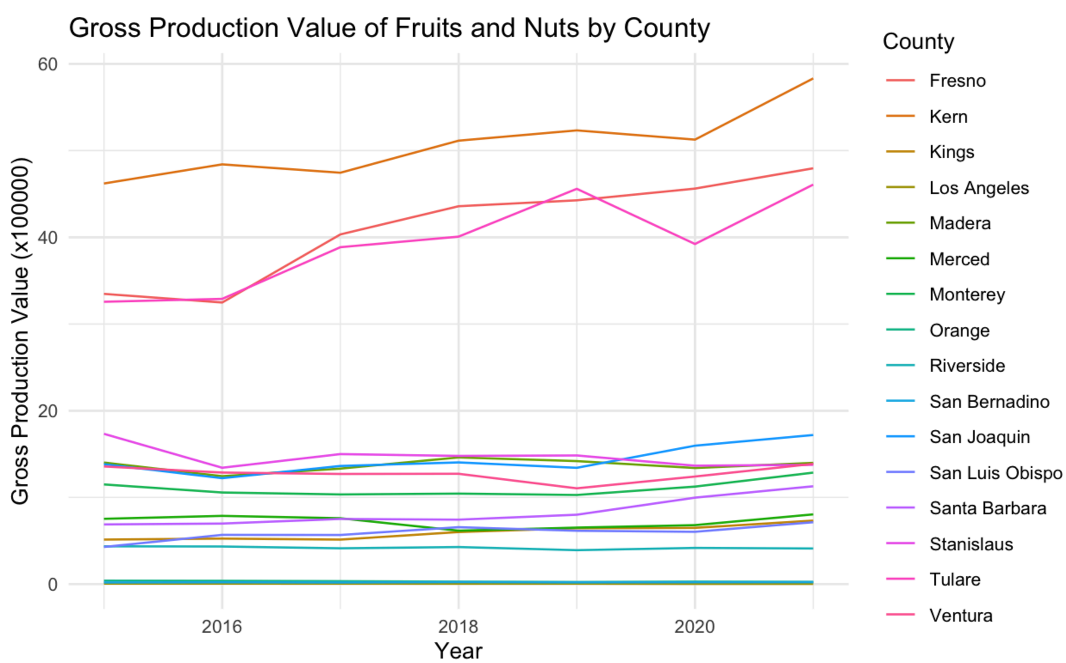


Figure B. GPV of fruits and nut crops for the San Joaquin Valley, Coastal California, and Southern California from 2015 to 2021.

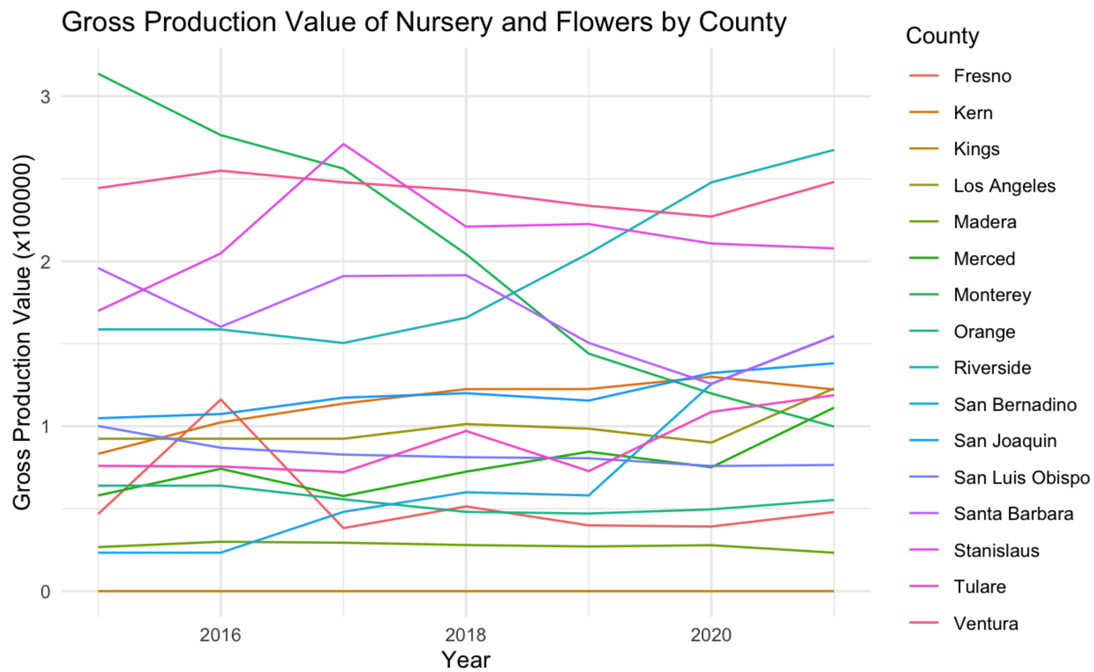


Figure C. GPV of nursery and flower crops for the San Joaquin Valley, Coastal California, and Southern California from 2015 to 2021.

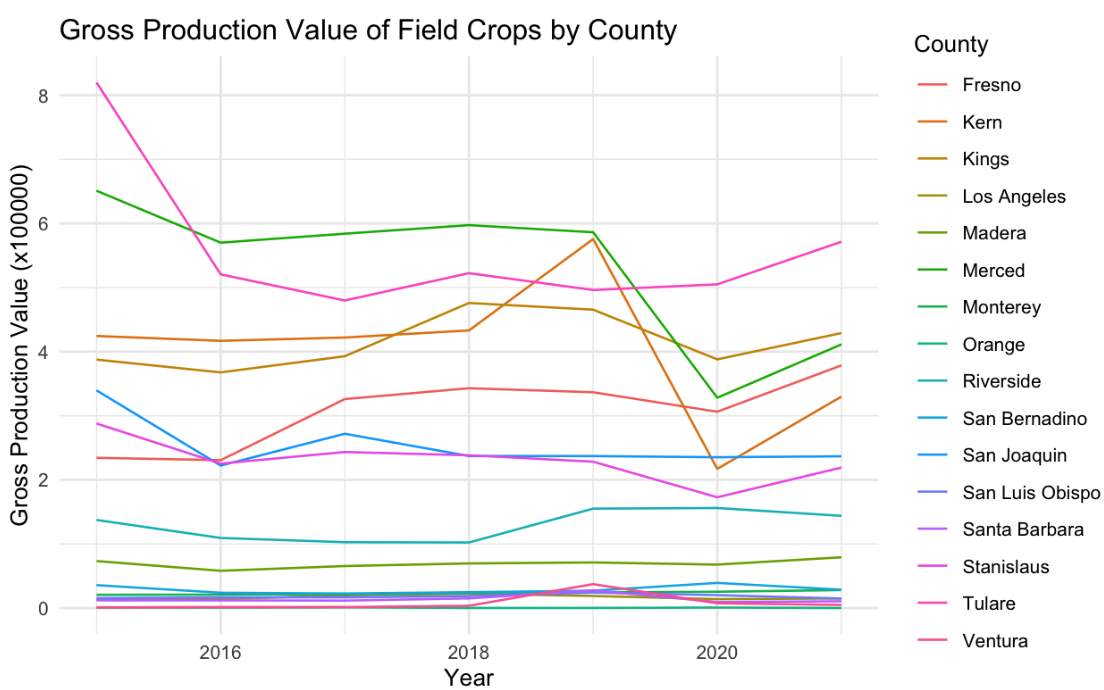


Figure D. GPV of field crops for the San Joaquin valley, Coastal California, and Southern California from 2015 to 2021.

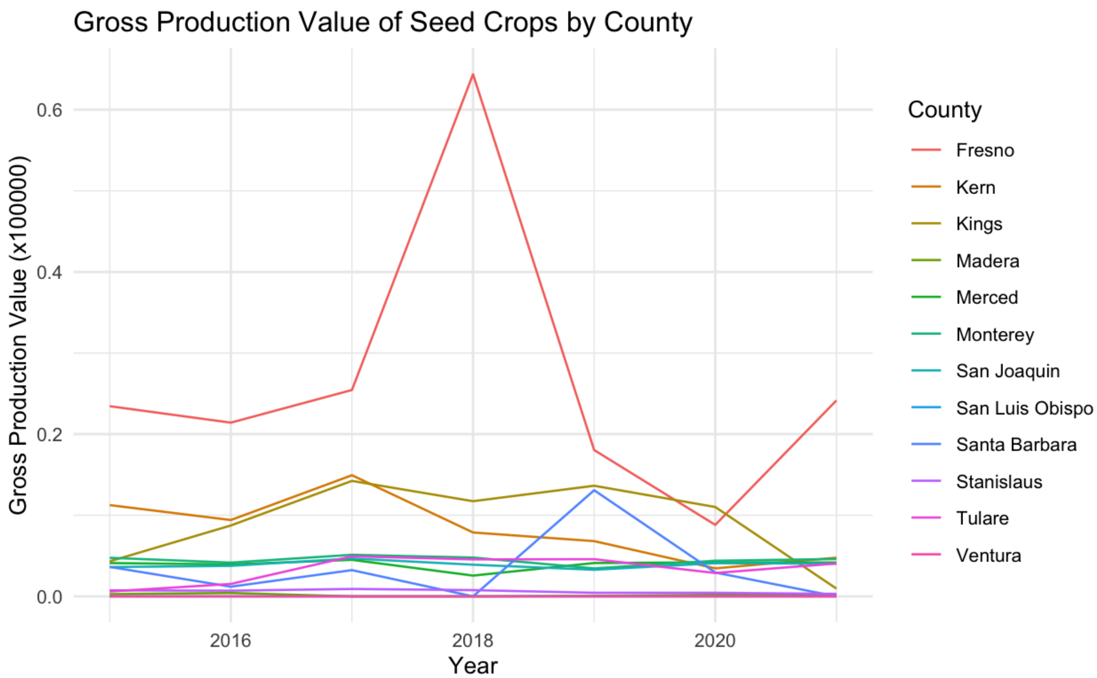


Figure E. GPV of seed crops for the San Joaquin Valley, Coastal California, and Southern California from 2015 to 2021.

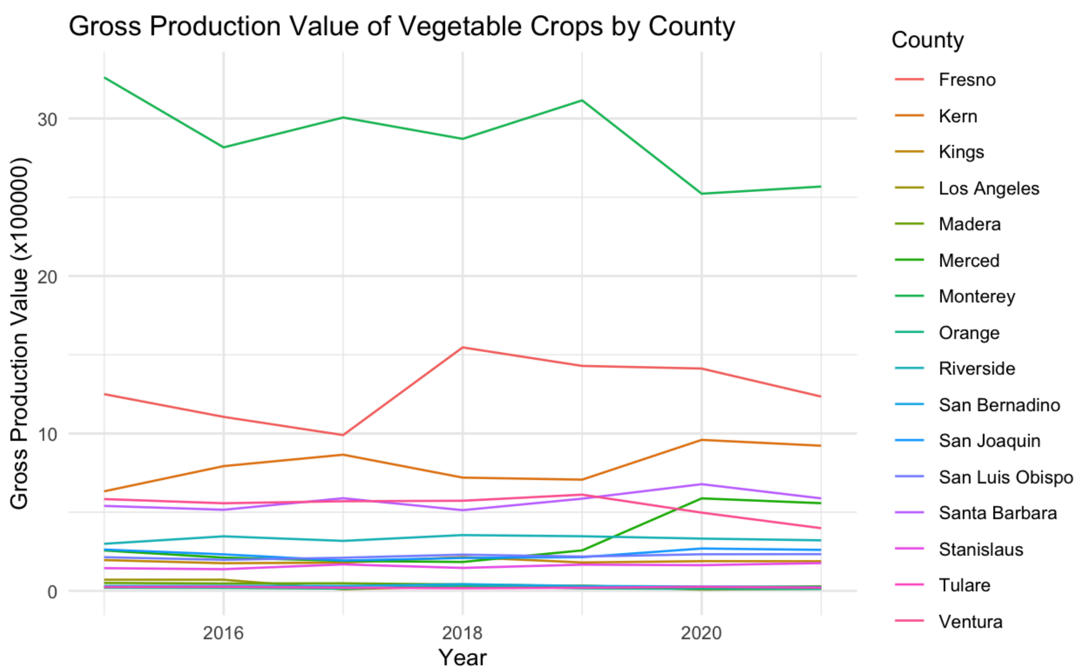


Figure F. GPV of vegetable crops for the San Joaquin Valley, Coastal California, and Southern California from 2015 to 2021.

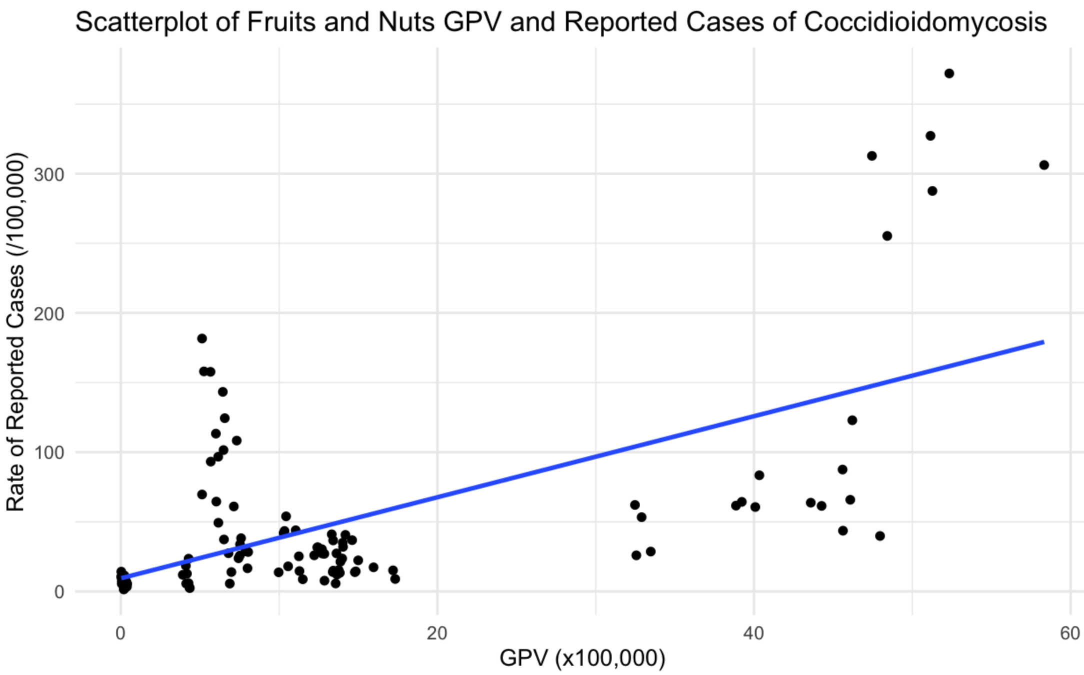


Figure G. Scatterplot of Gross Production Value (GPV) of fruits and nut crops and reported cases of coccidioidomycosis as a rate per 100,000 people (r = 0.5450919 ; p = 5.168 $x10^{-10}$)

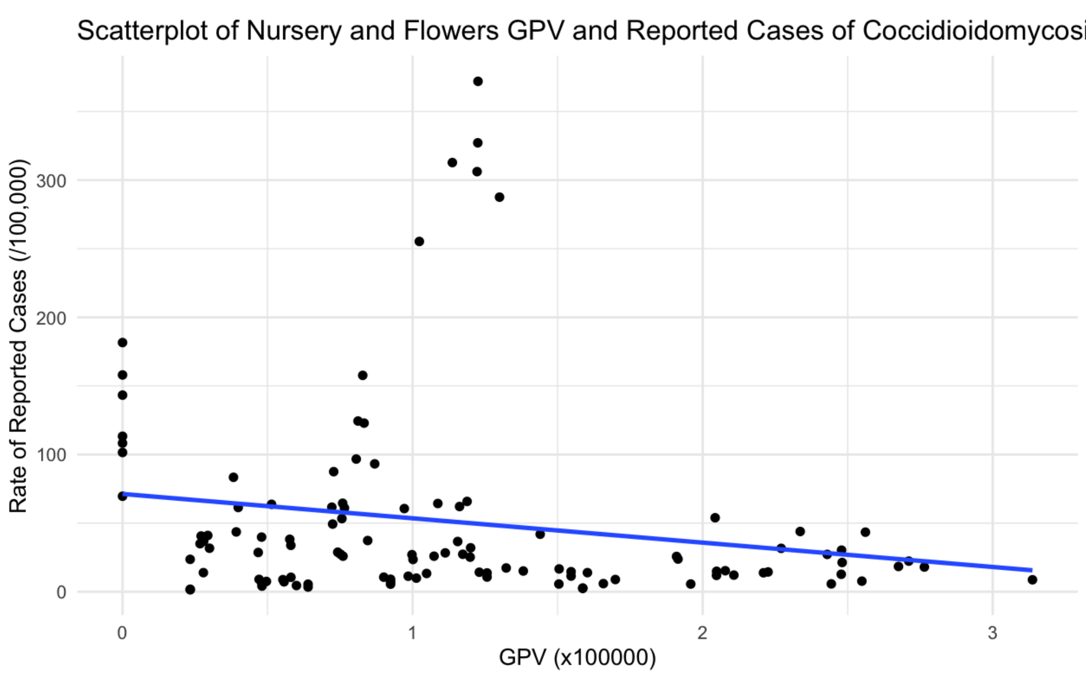


Figure H. Scatterplot of Gross Production Value (GPV) of nursery and flower crops and reported cases of coccidioidomycosis as a rate per 100,000 people (r = -0.2486171 ; p = 0.008212)

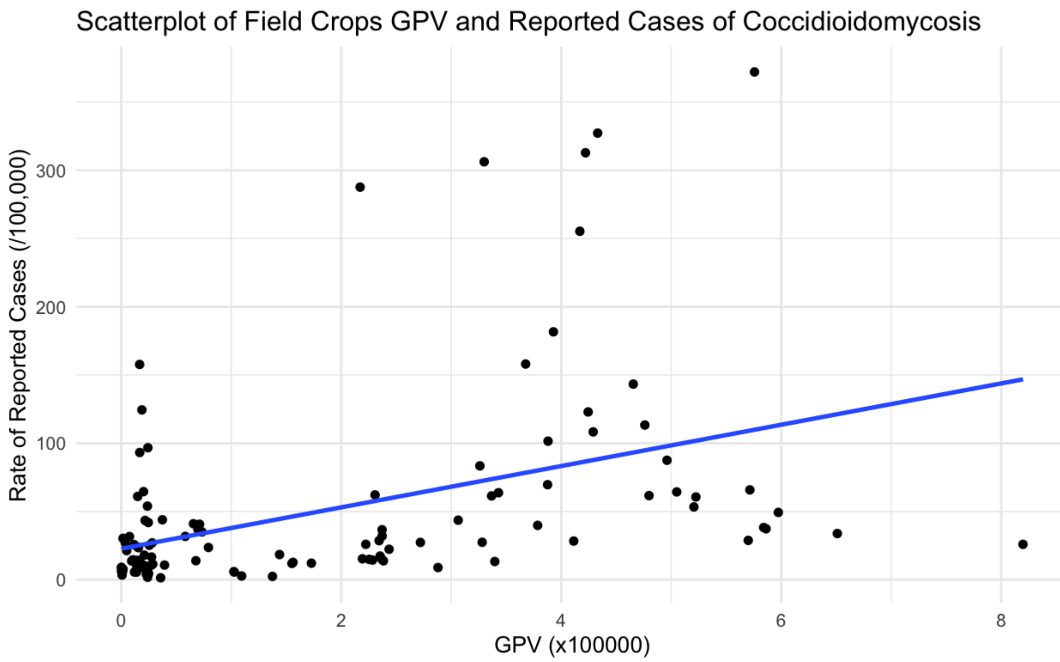


Figure I. Scatterplot of Gross Production Value (GPV) of field crops and reported cases of coccidioidomycosis as a rate per 100,000 people (r = 0.5615282 ; p = 1.188 x10^{-10})

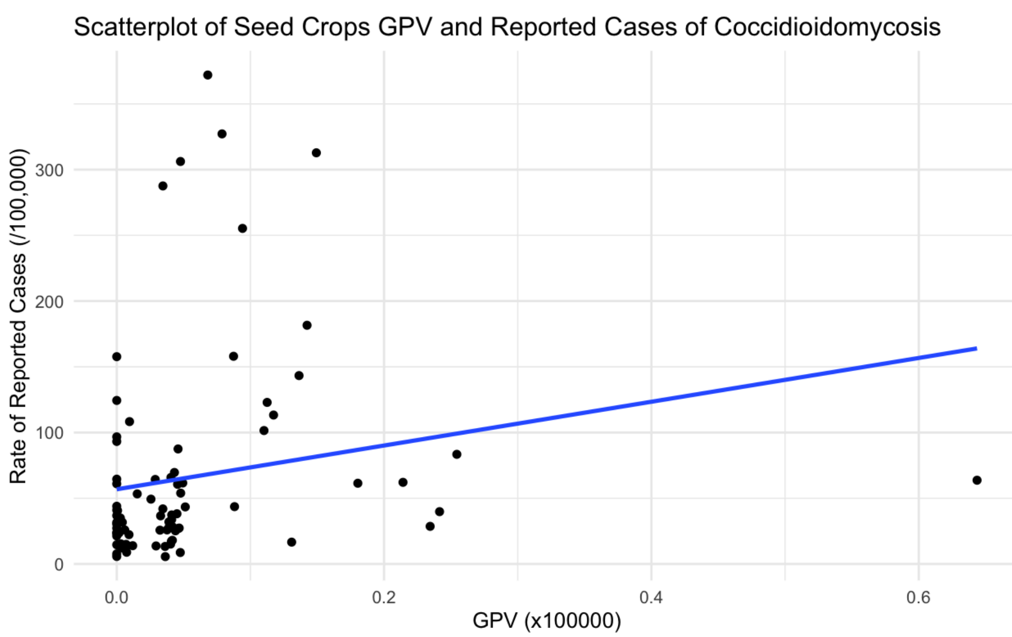


Figure J. Scatterplot of Gross Production Value (GPV) of seed crops and reported cases of coccidioidomycosis as a rate per 100,000 people (r = 0.37445 ; p = 0.0004497)

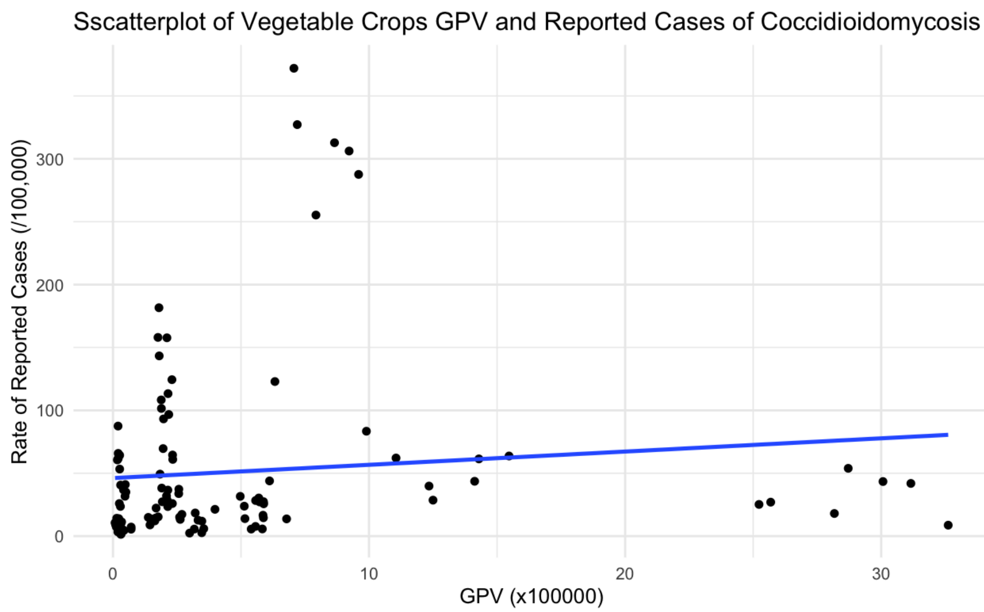


Figure K. Scatterplot of Gross Production Value (GPV) of vegetable crops and reported cases of coccidioidomycosis as a rate per 100,000 people ($r = 0.3103193$; $p = 0.0008689$)

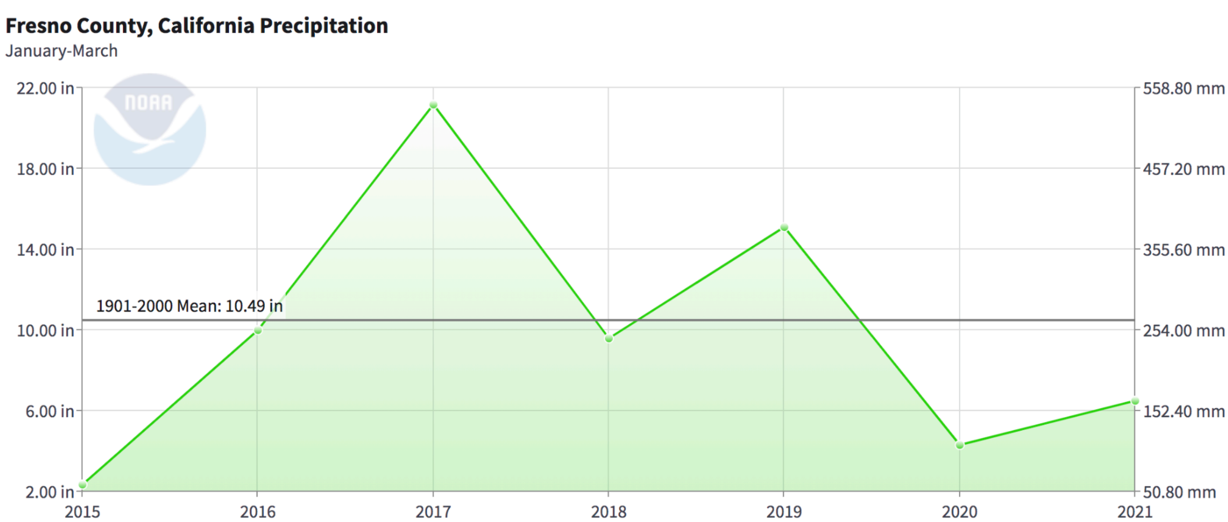


Figure L. Average rainfall (inches) in Fresno County during the rainy season (January-March) from 2015 to 2021. Data and graph collected from NOAA National Centers for Environmental information

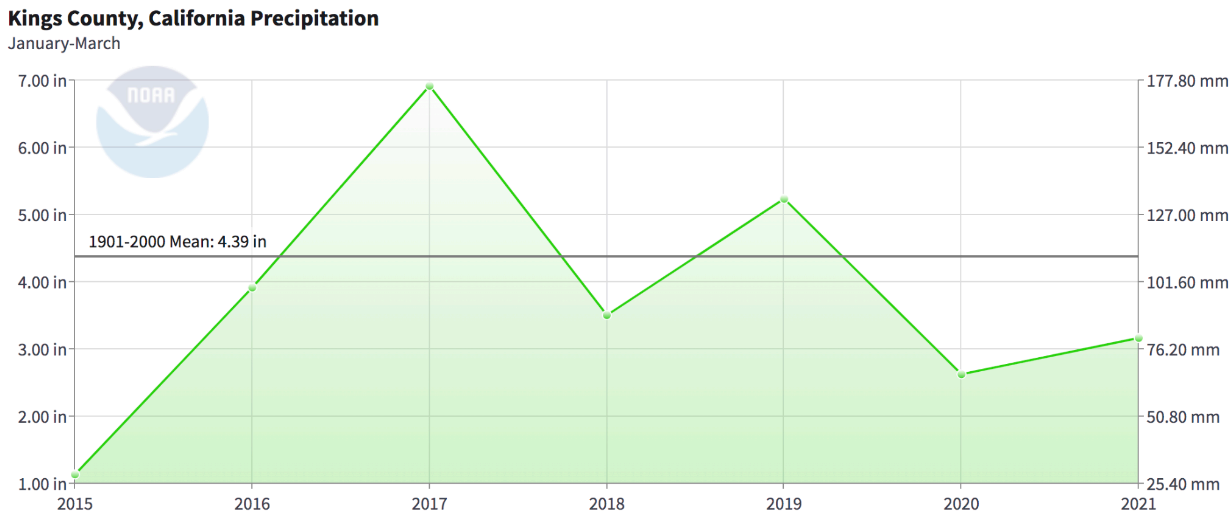


Figure M. Average rainfall (inches) in Kings County during the rainy season (January-March) from 2015 to 2021. Data and graph collected from NOAA National Centers for Environmental information

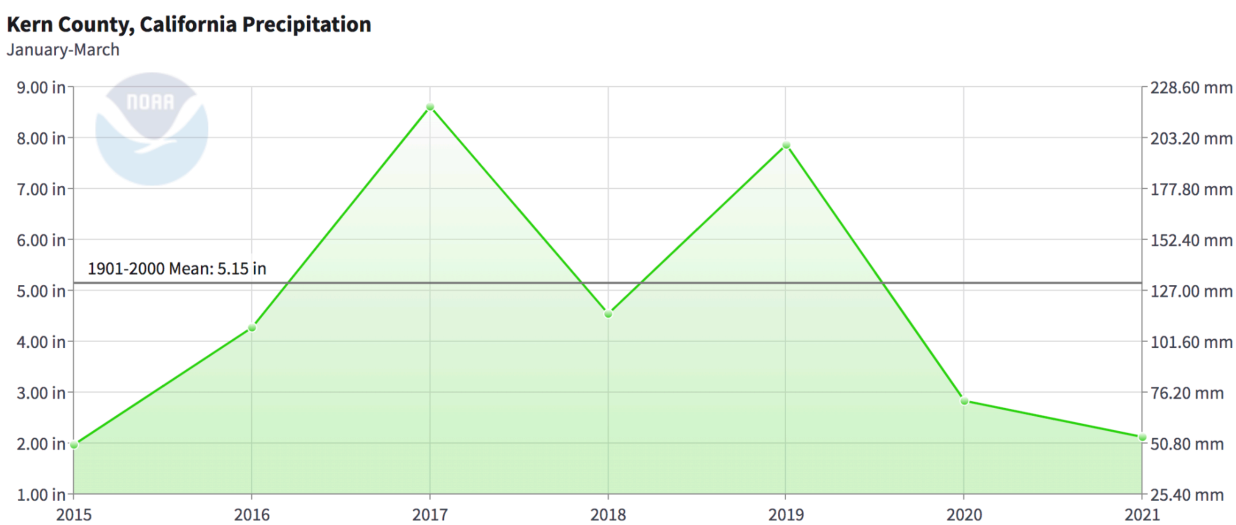


Figure N. Average rainfall (inches) in Kings County during the rainy season (January-March) from 2015 to 2021. Data and graph collected from NOAA National Centers for Environmental information

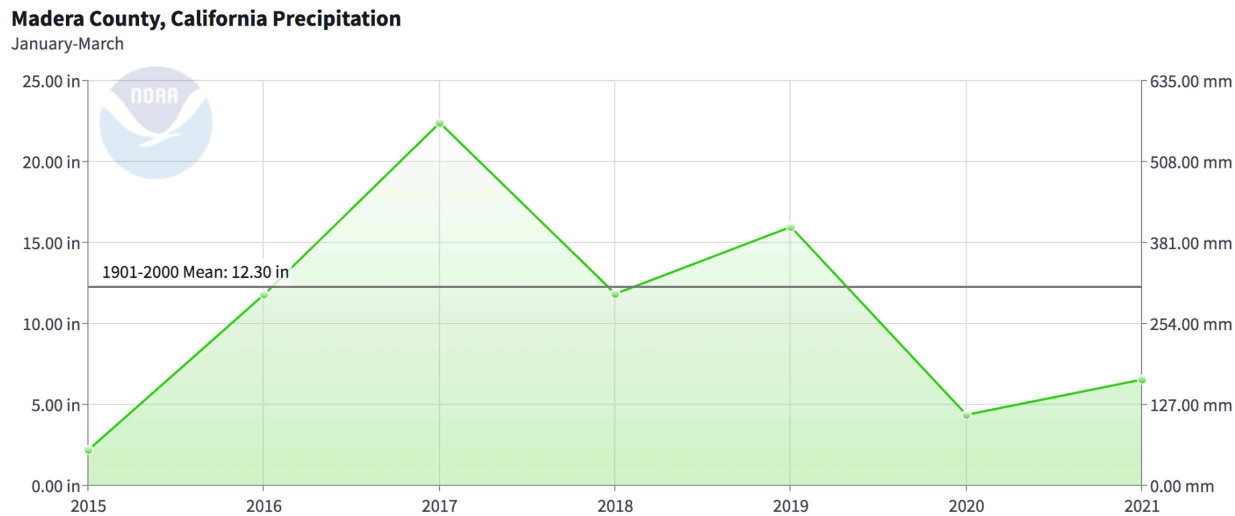


Figure O. Average rainfall (inches) in Madera County during the rainy season (January-March) from 2015 to 2021. Data and graph collected from NOAA National Centers for Environmental information

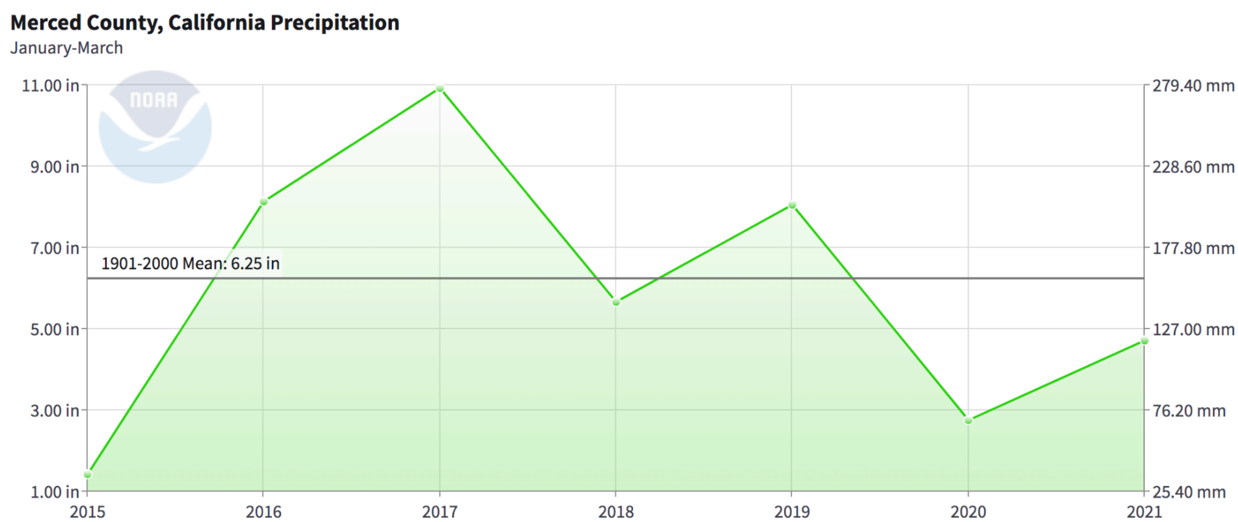


Figure P. Average rainfall (inches) in Merced County during the rainy season (January-March) from 2015 to 2021. Data and graph collected from NOAA National Centers for Environmental information

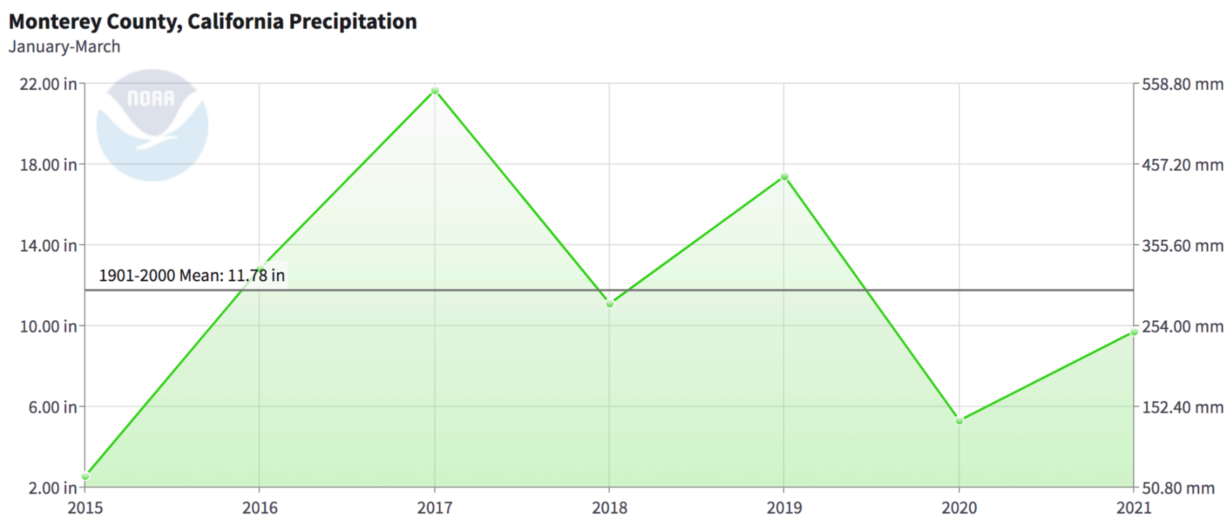


Figure Q. Average rainfall (inches) in Monterey County during the rainy season (January-March) from 2015 to 2021. Data and graph collected from NOAA National Centers for Environmental information

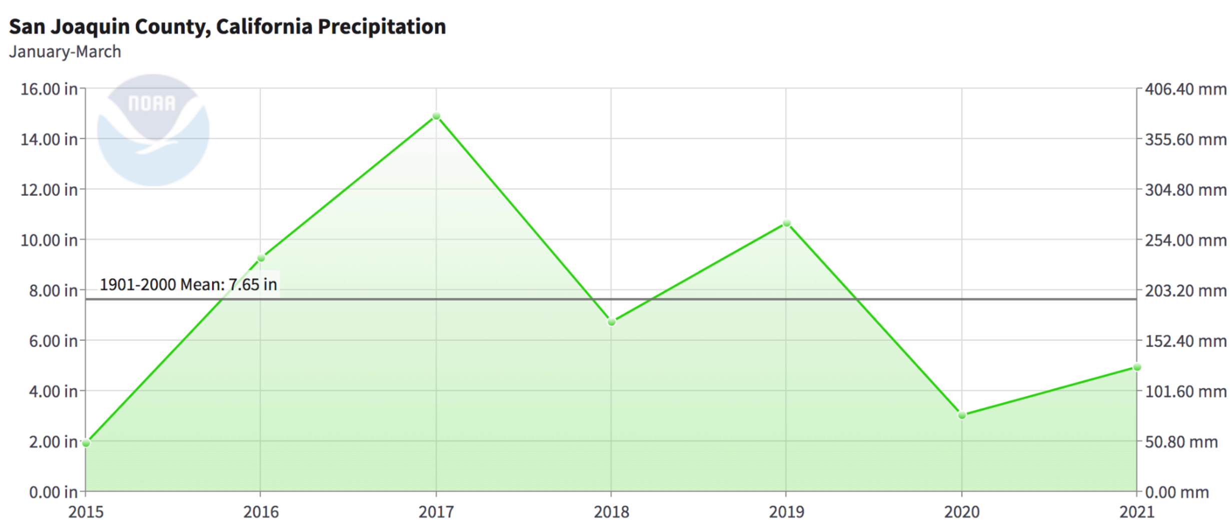


Figure R. Average rainfall (inches) in San Joaquin County during the rainy season (January-March) from 2015 to 2021. Data and graph collected from NOAA National Centers for Environmental information

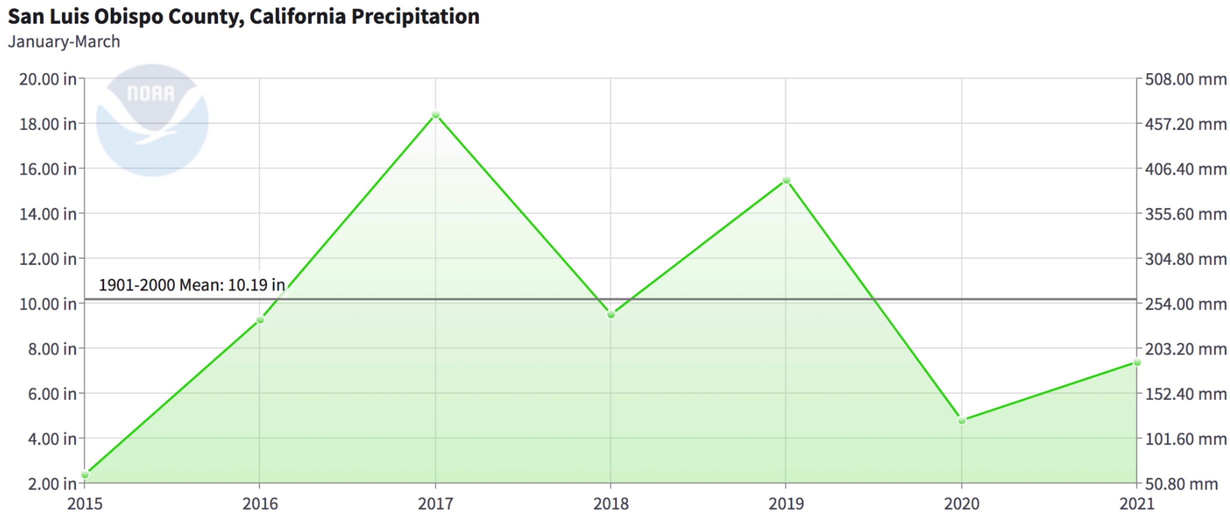


Figure S. Average rainfall (inches) in San Luis Obispo County during the rainy season (January-March) from 2015 to 2021. Data and graph collected from NOAA National Centers for Environmental information

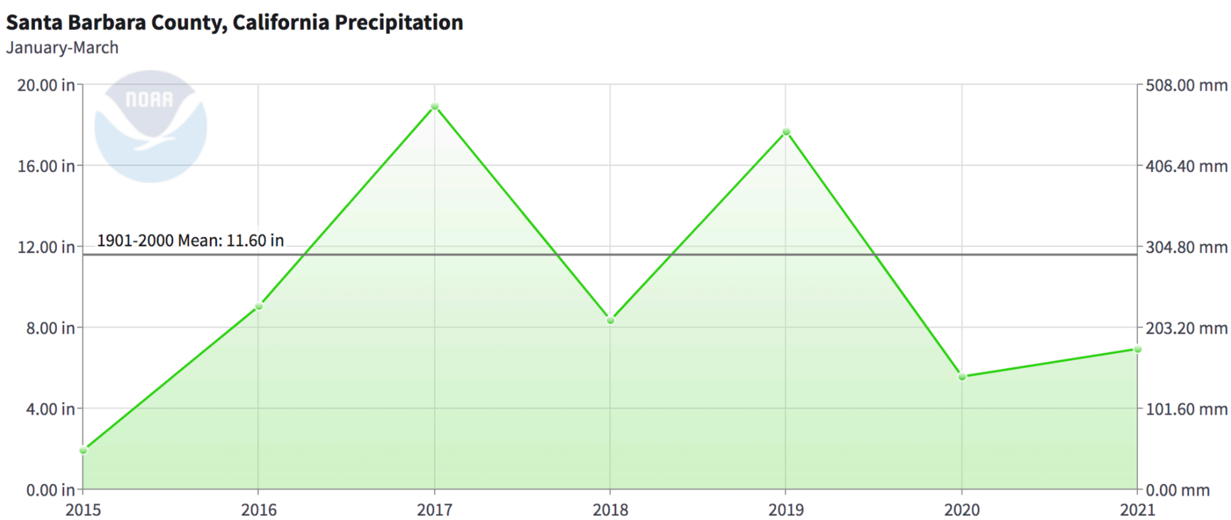


Figure T. Average rainfall (inches) in Santa Barbara County during the rainy season (January-March) from 2015 to 2021. Data and graph collected from NOAA National Centers for Environmental information

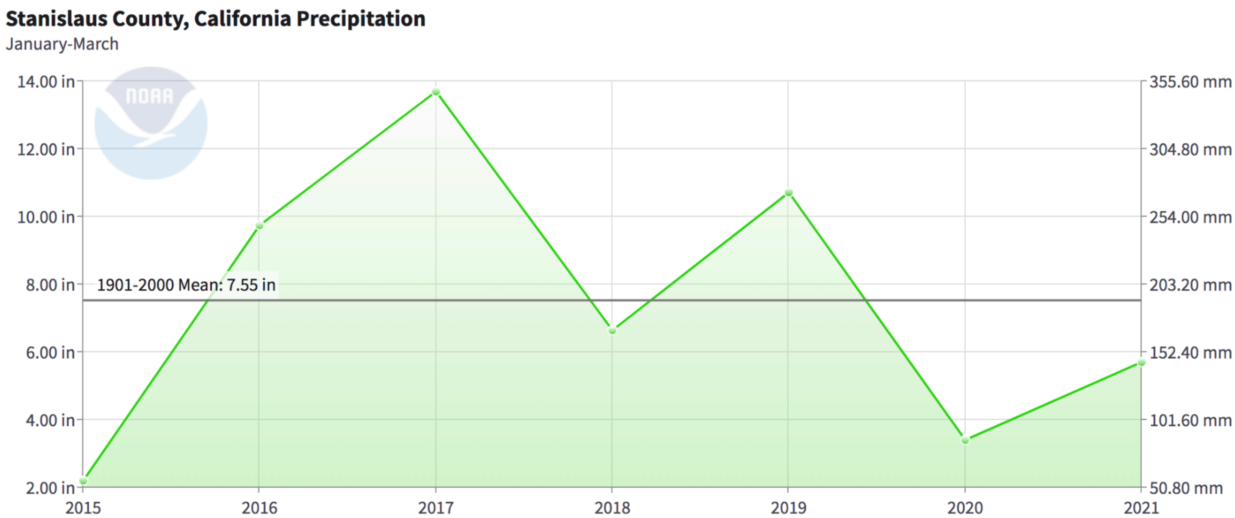


Figure U. Average rainfall (inches) in Stanislaus County during the rainy season (January-March) from 2015 to 2021. Data and graph collected from NOAA National Centers for Environmental information

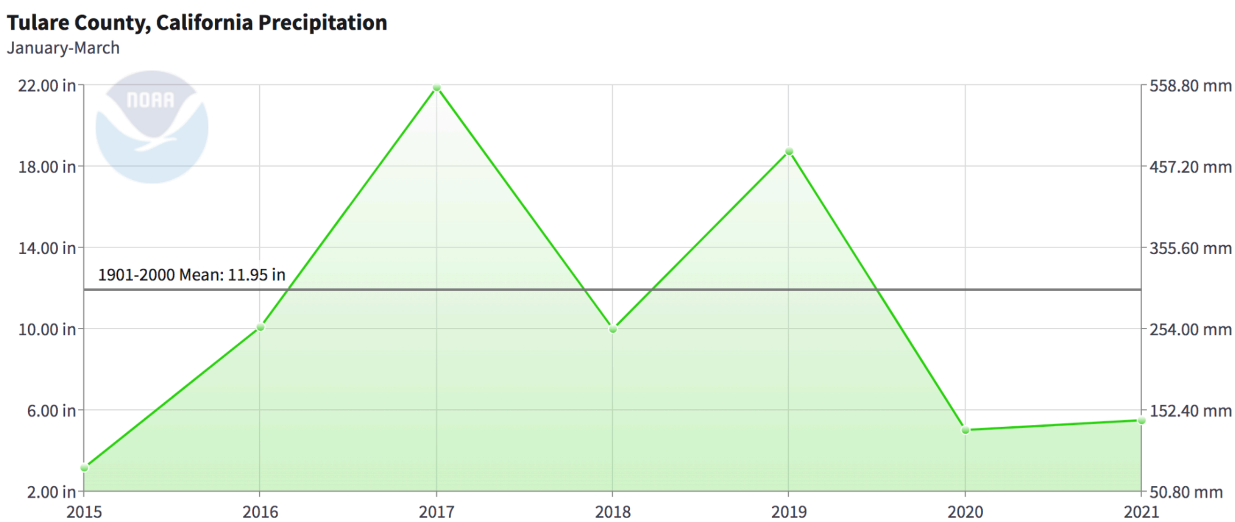


Figure V. Average rainfall (inches) in Tulare County during the rainy season (January-March) from 2015 to 2021. Data and graph collected from NOAA National Centers for Environmental information

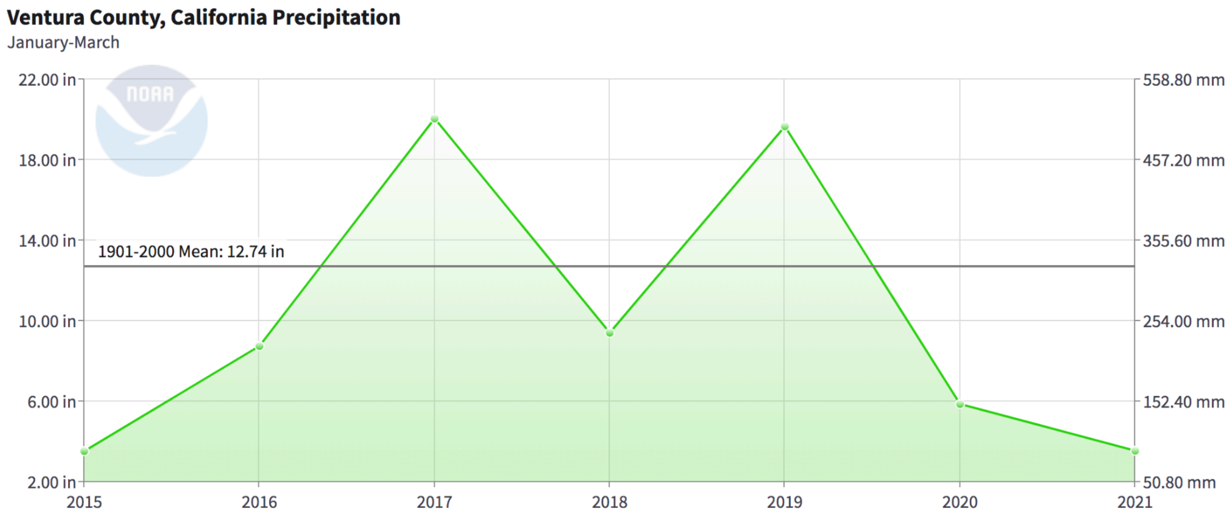


Figure W. Average rainfall (inches) in Ventura County during the rainy season (January-March) from 2015 to 2021. Data and graph collected from NOAA National Centers for Environmental information

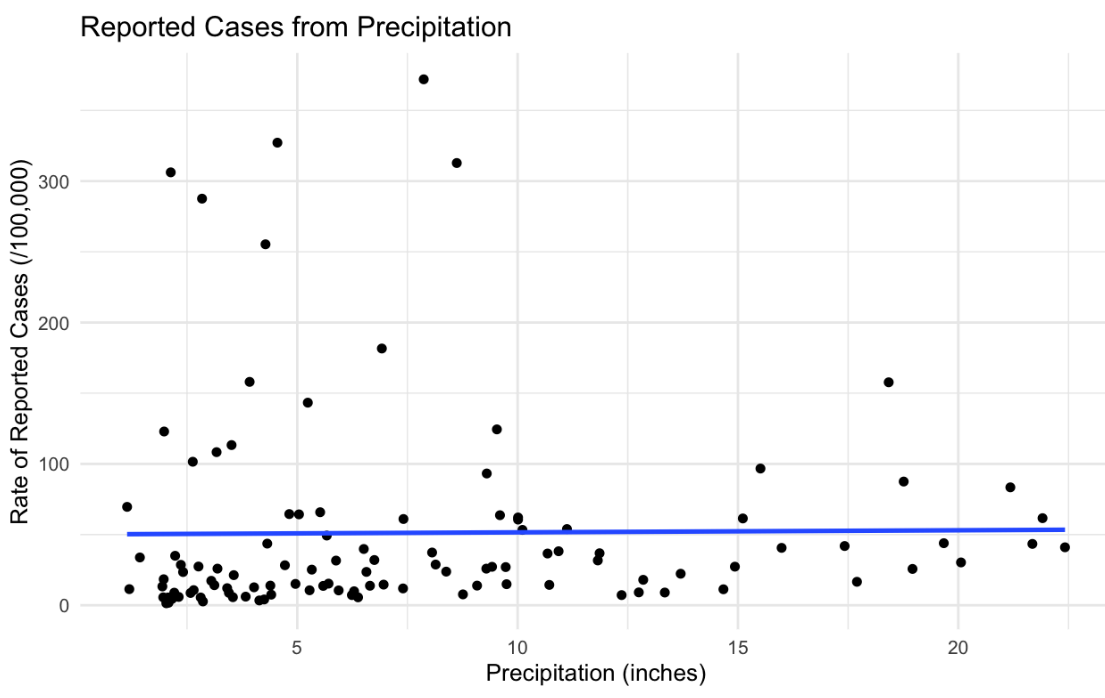


Figure X. Scatterplot of precipitation in inches and reported cases of coccidioidomycosis as a rate per 100,000 people across the San Joaquin Valley, Coastal California, and Southern California ($r = 0.2972157$; $p = 0.001461$)

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