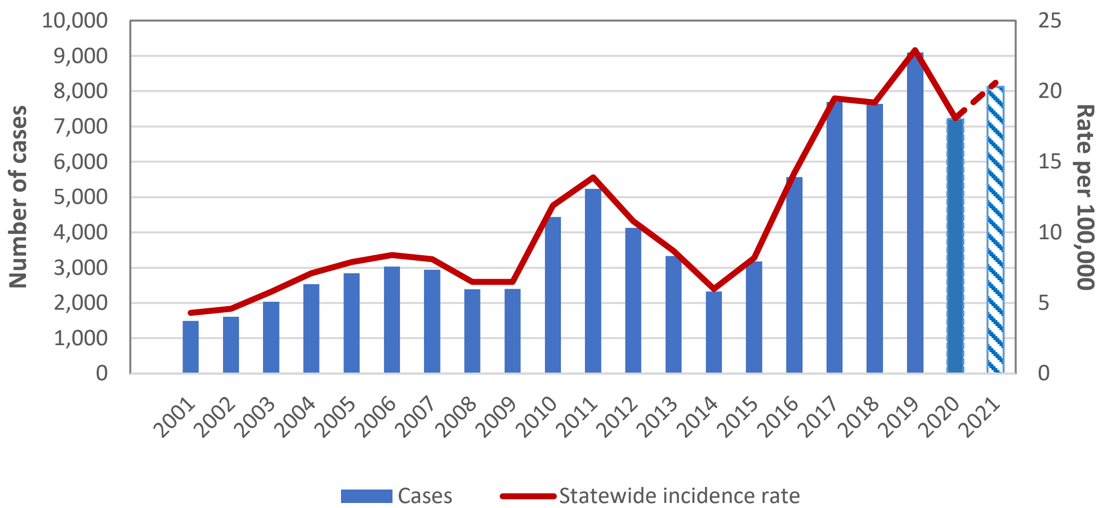
VALLEY FEVER (COCCIDIOIDOMYCOSIS)

The incidence of Coccidioidomycosis, commonly known as Valley fever, has increased over the past 20 years. Valley fever is caused by inhaling spores of the Coccidioides fungus that is endemic in the soil in parts of southwestern United States, including California. The fungus usually infects the lungs, causing respiratory symptoms.

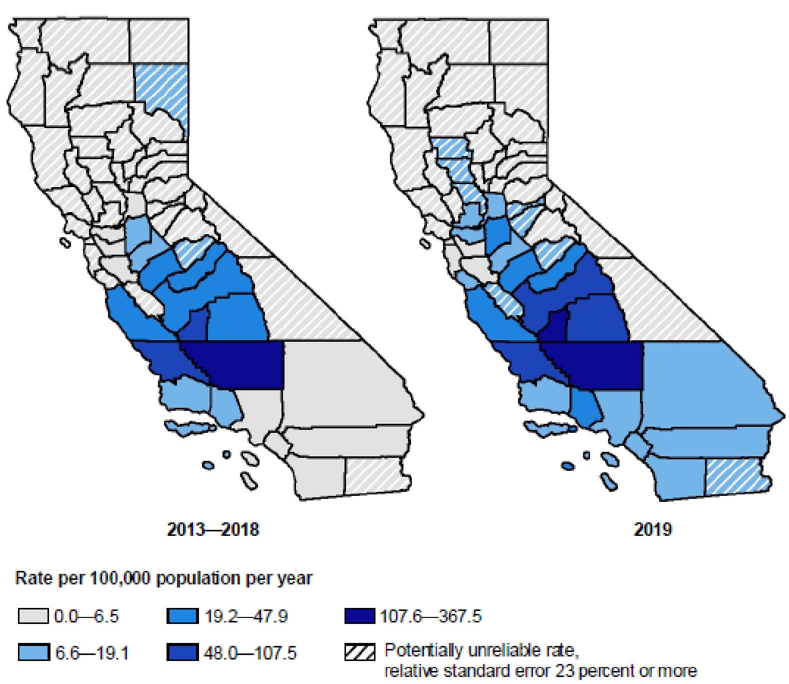
Figure 1. Valley fever cases and incidence rates by year of estimated illness onset in California (2001-2021*)



Source: CDPH 2020a; CDPH 2022a,b

**Note: 2021 values are provisional.*

Figure 2. Coccidioidomycosis, annual incidence rate by county, California, 2013-2019



Source: CDPH 2020a

What does the indicator show?

Figure 1 presents the number cases of Valley fever reported in California each year, from 2001 through 2021, along with the statewide incidence rate. The annual incidence of reported cases of Valley fever has increased almost fivefold from 2001 (with a rate of 4.3 cases per 100,000 population) to 2021 (rate of 20.6, based on preliminary data). The number of new cases reported in 2019 is the highest reported in a given year since reporting began in 1995.

Figure 2 compares the change in Valley Fever rates from 2013-2018 and 2019, with a number of new counties reflecting substantial increase in cases in 2019. Regionally, Valley fever incidence has consistently been highest in the counties of Fresno, Kern, Kings, Madera, Merced, Monterey, San Luis Obispo, and Tulare. Kern County historically had the highest number of new cases, with 338 cases reported in 2019 (CDPH, 2020b). A recent regional analysis of surveillance data from 2000 to 2018 suggested that, despite the consistent high rates of Valley fever in the Southern San Joaquin Valley, the largest increases in incidence have occurred outside of that region, primarily in Northern San Joaquin Valley, Central Coast, and Southern Coast regions (Sondermeyer Cooksey et al, 2020).

The California Department of Public Health (CDPH) has an established surveillance system to track Valley fever cases and has been collecting individual case data since 1995 (Tabnak et al., 2017). Because Valley fever may occur as a chronic condition and be reported more than once, only the first report of the onset of illness is counted (CDPH, 2020). Valley fever is likely underdiagnosed and under-reported, as symptoms are similar to many other respiratory illnesses, such as influenza, COVID-19, or bacterial pneumonia.

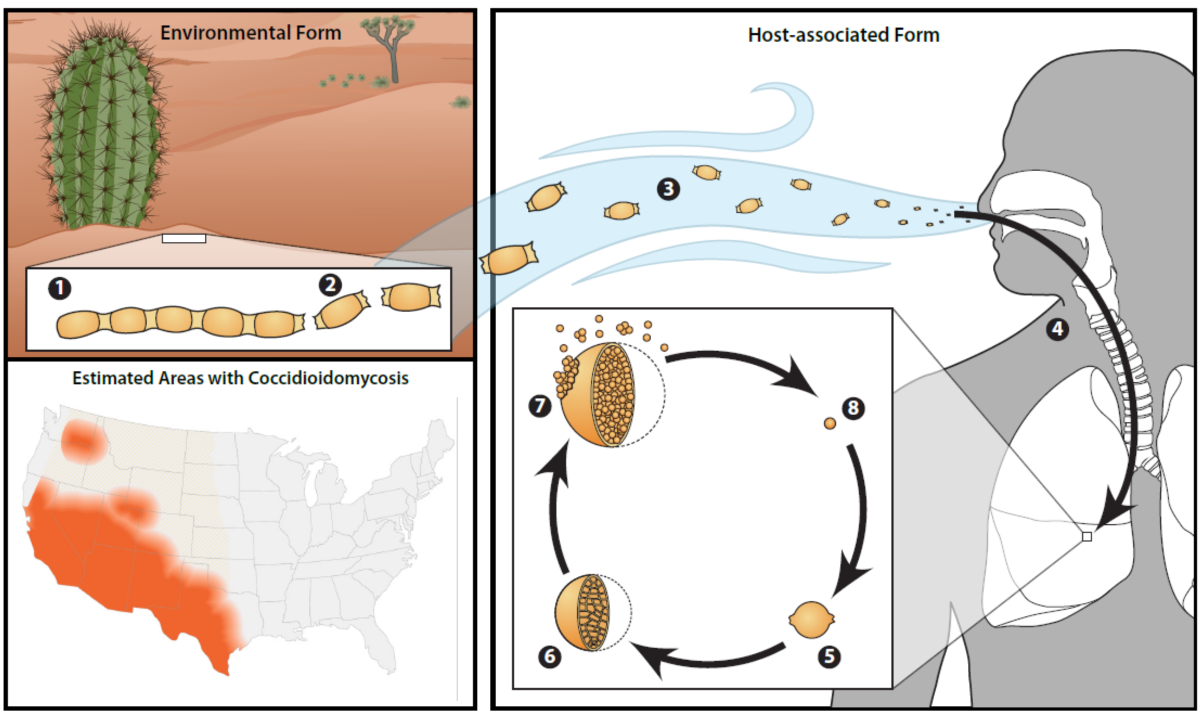
Why is this indicator important?

Approximately 97% of coccidioidomycosis cases in the United States are reported from California and Arizona. The disease usually manifests as a mild self-limited respiratory illness or pneumonia. While most people recover fully, experiencing only mild symptoms, up to five percent exhibit more serious health consequences, including severe respiratory, disseminated disease - where the infection has spread from the lungs to the skin, bones and central nervous system, or meningitis (Ampel et al., 2010; CDPH, 2015). Severe Valley fever can lead to hospitalization, and in the most severe cases, death. Even in those with milder disease, days lost to low productivity and poor health create significant burdens for the patients and the economy at large. Those of Black or Filipino background, pregnant women, older adults, and people with weakened immune systems are at increased risk for severe disease (CDPH, 2020).

Robust CDPH surveillance of Valley fever over the last couple of decades indicates an increase in disease burden. Each year in California, around 80 deaths and over 1,000 hospitalizations are attributed to Valley fever. It is not transmitted directly from person to person, but rather from the direct inhalation of fungal spores. Pets and other animals can also be infected (CDPH, 2020).

Two species of the soil-dwelling *Coccidioides* fungus cause coccidioidomycosis: *C. immitis*, which is found primarily in California, and *C. posadasii*, which is found primarily in Arizona, other parts of the southwestern United States as well as Central and South America (CDPH, 2015; Tintelnot et al., 2007). The life cycle of the fungus is illustrated in Figure 3. Since there is no commercially available test to determine whether the fungus is growing in the soil in an area, the current understanding of the geographic risk for infection is largely based on human surveillance data. As mentioned above, most cases of Valley fever in California are reported in people who live in the Central Valley and Central Coast regions.

Figure 3. The life cycle of *Coccidioides*



Modified from: CDC, 2020

The *Coccidioides* fungus exists in different forms in the environment (left) and in the host (right). In the environment, the fungus exists as filaments or chains divided into cellular compartments (1). These compartments can fragment into spores called arthroconidia (2), which measure only 2-4 µm in diameter and are easily aerosolized when disturbed (3). Arthroconidia are inhaled by a susceptible host (4) and settle into the lungs, where they become spherules (5). Spherules divide internally until they are filled with endospores (6). When a spherule ruptures (7), the endospores are released and disseminate within surrounding tissue. Endospores are then able to develop into new spherules (6) and repeat the cycle. The map in the lower left shows where the Valley fever fungi live in the United States.

Population influx into endemic areas, increased construction and other soil-disturbing activities, and climatic changes that induce fungal proliferation and dissemination through air could be factors working in unison to increase Valley fever incidence in California. Tracking the incidence and geographic distribution of Valley fever therefore provides valuable information to inform public health decisions, particularly given projected changes in climate-related factors. There is currently no vaccine to prevent Valley fever, but antifungal medications are available for treatment, particularly for severe disease (CDPH, 2015). Understanding the dynamics among climatic, ecological niche, lifestyle and demographic factors could help control the spread of the disease (Pearson et al., 2019). Informing people whether their occupation, residence or travel destination could expose them to the spores could help in preventing disease propagation or help identify early disease symptoms before they get worse, disseminate in the body, or even lead to death. Fact sheets and other information help communicate the potential association between high wind events, like the Santa Anas, wildfire and Valley fever infection (CDPH, 2013; Ventura County DPH, 2018).

Valley fever presents an ongoing and increasing public health burden in California. Since mild cases are less likely to be diagnosed and reported, incidence data likely reflect cases with moderate or severe illness. Hence, impact on the economy and health costs are also grossly underestimated (Thompson et al., 2015). A study estimated that lifetime costs in 2017 from Valley fever in California were $94,000 per hospitalized person – with $58,000 in direct costs (including diagnosis, treatment, and follow-up) and $36,000 in indirect costs (including productivity losses) – totaling $700 million for the state (Wilson et al., 2019). At the same time, severe infections have costly implications: from 2000 to 2011, patients hospitalized with Valley fever in California spent a median of six days receiving care at a median charge of $6,800 per day ($55,062 per stay). For the same time period, the total charge for all Valley fever-associated hospitalizations in the state was $2.2 billion (Sondermeyer et al., 2013).

What factors influence this indicator?

People are more likely to get Valley fever if they live, work, or visit in areas where the fungus grows in the soil or is in airborne dust. The majority of outbreaks in California have been associated with dirt-disturbing work settings, including construction, military, archeologic sites, wildland firefighting, and correctional institutions, where high attack rates have been seen even among relatively young people. Drought, aridity, dust storms and wildfires – all related to climate change in California and projected to increase in frequency and severity over the years (Abatzoglou et al., 2016; Cook et al., 2015; Prein et al., 2016; Seager et al., 2007; Tong et al., 2017) – could directly or indirectly affect fungal proliferation and spore dissemination, and eventual human and animal infection with Valley fever. These and other climate-related phenomena can work together to spread *Coccidioides* infection to people who live beyond the historically-endemic Central Valley (Pearson et al., 2019). Valley fever cases have been increasing, although not linearly, likely due to the complex interaction between various climatic and environmental factors that impact *Coccidioides,* changes in work or recreational travel patterns that influence exposure, changes in population susceptibility, and testing and reporting practices.

<u>Geography, drought and precipitation</u>

"Valley" in Valley fever refers to the disease being endemic to the Central Valley of California where most cases in the state have been consistently reported. However, over the last decade, increasing cases have been detected in surrounding counties and even more northerly locations, like eastern Washington State (Johnson et al., 2016). The geographic niches within California that are hospitable to *Coccidioides* also appear to be expanding, as evidenced by increasing rates of Valley fever outside of the Central Valley, particularly in the Northern San Joaquin Valley and Central Coast (Sondermeyer et al., 2020). Central Coast counties like Monterey and Santa Barbara, where numerous large fires have recently occurred, are seeing more cases, particularly among firefighters who participate in ground-disrupting fire prevention activities (Bubnash 2017; Laws, et al., 2021; Wilson 2017). There is also some evidence indicating cases are increasing in geographic range around Los Angeles County. One study found that compared with 2000 through 2003, 19 of 24 health districts in Los Angeles County had a 100% to 1,500% increase in overall cases during 2008–2011 (Guevara et al., 2015). Although the reasons for these increases are likely multifactorial, drought and aridity and other climatic changes likely play a major role. In the Antelope Valley, a high desert area containing parts of San Bernardino, Los Angeles, and eastern Kern County, researchers found the fungal pathogen in 40% of soil samples; they also found an association between the incidence of Valley fever and both land use and particulate matter of 10 micrometer (µm) or less in air (Colson et al., 2017).

Drought desiccates soil, creating dust and coarse particulate matter in endemic areas containing *Coccidioides* spores, which escape deeper into the soil (Gorris et al., 2018). Because the *Coccidioides* fungus is quite hardy, it can become dormant deep in parched soil whereas other organisms would have succumbed to drought and lack of nutrients. When rain and more ideal conditions return, the dormant fungus becomes active, growing in soil and often multiplying in larger numbers than usual since competing organisms have become less plentiful (Coates and Fox, 2018; Fisher et al., 2000; Kirkland and Fierer, 1996; Zender et al., 2006). Then, when dry, hot conditions return, infections fragments called arthroconidia (refer to Figure 3) can be released into air when soil is disturbed (Gorris et al., 2018; Johnson et al., 2014; Lewis et al., 2015).

Patterns of Valley fever incidence and drought have been consistently observed in California, with large increases occurring following periods of drought. After several years of drought, increased rainfall in California in early 2016 might have resulted in more favorable conditions for *Coccidioides* and, consequently, more infections (Benedict et al., 2019). In another study, both temperature and drought variability were positively correlated with Valley fever vulnerability based on case incidence in California from 2000 through 2014 (Shriber et al., 2017). Researchers have predicted that prolonged dryness and drought in the American Southwest will render much of the area west of the Rocky Mountains hospitable to *Coccidioides* (Gorris et al., 2019). In fact, scientists have designated Arizona cases as being related to the effects of climate change (Park et al., 2005); cases in Arizona far outnumber those of California. Evidence of the expanding geographic range of *Coccidiodes* indicate a need for safety precautions aimed to limit Valley fever transmission when proceeding with development in these areas.

<u>Wind and dust storms</u>
Increased winds linked to global climate change (Tong et al., 2017) could also be driving Valley fever infections. There is evidence that a dust storm in 1978 in the Central Valley carried the pathogen hundreds of miles, infecting individuals in Sacramento County, for example (Williams et al., 1979). Dust storms, particularly those attributed to Santa Ana winds that take place in the fall in Southern California, could also help spread the spores to farther locations. Santa Ana winds and the ensuing dust storm that occurred after the 1994 Northridge earthquake have been linked to distributing *Coccidioides* spores to local communities after the earthquake, triggering an outbreak in Simi Valley (Schneider et al., 1997). In Arizona, researchers found a moderate correlation (r = 0.51) between frequency of dust storms and Valley fever incidence in Maricopa County (Tong et al., 2017).

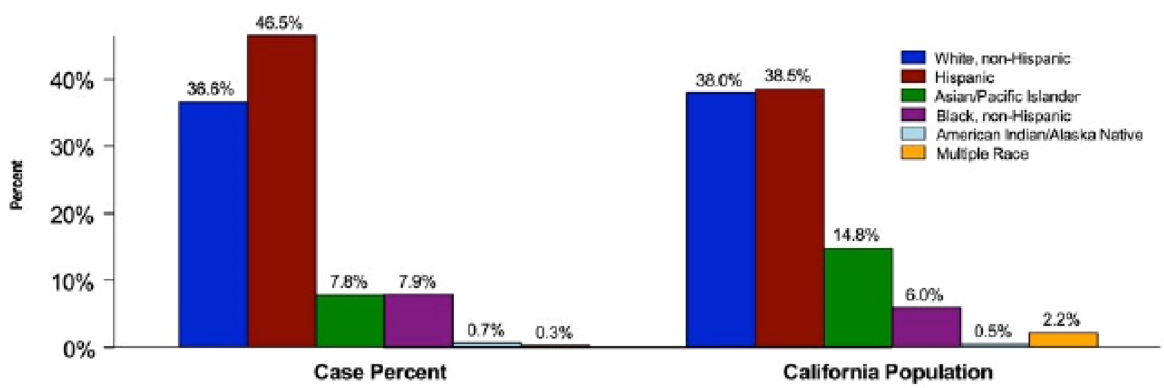
<u>Wildfire</u>
With the increasing risk of wildfires (see *Wildfires* indicator), research has begun investigating their potential influence on Valley fever. Anecdotal evidence and interviews with firefighters have provided insight into this relatively new area of research. Although these associations are not yet well understood and research is ongoing, wildfires can impact soil composition and ground cover. Firefighting can lead to soil disruption when firefighters create fire lines using hand tools for digging. These factors could impact the ability of *Coccidioides* to proliferate and spores to be dispersed through the air. Santa Ana winds, which occur in the fall, coincide both with the seasonality of Valley fever and when fire danger is also highest, particularly in coastal Central and Southern California. Valley fever outbreaks have occurred among wildland firefighters, particularly among those involved in soil disruptive activities used to contain wildfires (Laws et al., 2021).

<u>Seasonality</u>
The number of Valley fever cases have generally shown an uptick during the late summer and fall seasons in California since disease surveillance attempts began in the 1940s, indicating possible associations with season, temperature, precipitation, and/or wind (Smith et al., 1946). With climate change experts predicting an earlier start to summer and a later beginning for fall/winter (Wang et al., 2021), there is the potential for an extension of Valley fever season, leaving residents and summer visitors in endemic areas more vulnerable to infection for longer periods of time. Although most people become immune to the pathogen after a primary illness, newcomers moving into endemic areas and children born to current residents remain susceptible to infection. However, surveillance data indicate that people who have lived in highly-endemic areas for years without becoming sick can develop symptoms, which are sometimes very

severe. Compromised immunity, due to age or comorbidities, can lead to relapse (CDPH, 2018).

<u>Vulnerable Populations</u>
Different population groups in the state face additional risk of exposure to *Coccidioides* (e.g., outdoor workers) and of severe disease if infected (e.g., pregnant women, those 65 and older, and immunocompromised persons, including those who have diabetes) (Bercovitch et al., 2011; CDPH, 2018; Johnson et al., 2014; Nguyen et al., 2013). Black persons are consistently reported to have the highest rates of Valley fever throughout California and are known to have increased risk for severe and disseminated disease and hospitalization. Additionally, a higher proportion of Hispanics are reported among Valley fever cases than would be expected based on the California population. Racial-ethnic disparities (see Figure 4) in Valley fever cases are not well understood and are likely due to a variety of factors including occupation, genetics, and other factors, including the differential distribution of underlying health conditions across racial or ethnic groups.

Figure 4. Coccidioidomycosis, cases and population by race/ethnicity, 2013-2019



Source: CDPH 2020

34.5% (n=13363) of reported incidents of Coccidioidomycosis did not identify race/ethnicity and 5.6% (n=2176) of reported incidents identified as “other” race/ethnicity and are not included in the Case Percent calculation. Information presented with a large percentage of missing data should be interpreted with caution.

Outbreaks among incarcerated individuals imprisoned in endemic areas have been ongoing during the last twenty years. Many of these individuals have no previous exposure to Valley fever. In one outbreak, exposure stemmed from fugitive dust from building construction near where prisoners were housed or engaging in outdoor physical activity; despite mitigation efforts, such as planting vegetation, high Valley fever attack rates continued (Wheeler et al., 2015). (“Attack rate” refers to the proportion of persons in a population who experience an acute health event during a limited period, such as during an outbreak.) Black race was found to be a risk factor for disseminated disease.

Prisons include a continual rotation of new inmates who are likely immunologically naïve to Valley fever infection. California prisons house a disproportionately larger black population (Lofstrom et al., 2020), a group also identified as bearing a disproportionately poor health outcome burden from Valley fever. Again, many incarcerated individuals engage in wildland firefighting, putting them at greater risk.

Technical considerations

Data characteristics

California regulations require local health officers to report cases of Valley fever to CDPH. Up until 2019, a case was defined as a person who had laboratory and clinical evidence of infection that satisfied the most recent surveillance case definition published by the Council of State and Territorial Epidemiologists (CSTE). Effective January 1, 2019, CDPH changed its Valley fever case definition to require only laboratory confirmation of disease (CDPH, 2018). CDPH accepts all cases determined by the local health department as confirmed.

Strengths and limitations of the data

The number of reported cases of Valley fever shown in Figure 1 are likely to underestimate the true magnitude of the disease. Factors that may contribute to under-reporting include ill persons not seeking health care, misdiagnoses, failure to order diagnostic tests, and limited reporting by clinicians and laboratories. Asymptomatic or minor cases are likely not diagnosed and not reported and Valley fever is likely often misdiagnosed since it presents like many other respiratory illnesses such as influenza, COVID-19, and bacterial pneumonia. Factors that may enhance disease reporting include increased exposure and disease severity, recent media or public attention, and active surveillance activities. Surveillance data include serious cases, which are more visible and have been increasing, and are less likely to identify those with fewer symptoms but still lead to missed worked days and illness. Increased surveillance could explain some of the increased number of cases, though not all.

Because race/ethnicity information was missing or incomplete for 34.5 percent of all 2013-2019 cases (shown in Figure 4), incidence rates by race/ethnicity were not calculated for this indicator. However, the proportion of cases representing race/ethnicity categories are presented alongside statewide averages for these categories during the seven-year surveillance period. Nonetheless, race/ethnicity information based on a high percentage of missing data should be interpreted with caution. Data presented in this indicator may differ from previously published data due to delays inherent to case reporting, laboratory reporting, and epidemiologic investigation.

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