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Review article

Valley fever under a changing climate in the United States

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ABSTRACT

This review summarizes studies on the relationships between climate change and Valley Fever (VF), also termed Coccidioidomycosis, a potentially fatal upper-respiratory fungal infection caused by the pathogenic fungi, *C. immitis* or *C. posadasii*. The intensified onset of climate change has caused frequencies and possibly intensities of natural hazard events like dust storms and drought to increase, which has been correlated with greater prevalence of VF. These events, followed by changes in patterns of precipitation, not only pick up dust and spread it throughout the air, but also boost the growth and spread of *Coccidioides*. In California alone, cases of VF have increased fivefold from 2001 to 2021, and are expected to continue to increase. From 1999 to 2019, there was an average of 200 deaths per year caused by VF in the United States. The number of deaths caused by VF fluctuates year to year, but because more infections are predicted to occur due to a changing climate, deaths are expected to rise; thus, the rising prevalence of the disease is becoming a larger focus of the scientific community and poses an increased threat to public health. By reviewing recent and past studies on Coccidioidomycosis and its relationships with climate factors, we categorize future impacts of this disease on the United States, and highlight areas that need more study. Factors affecting the incidence of VF, such as modes of dispersal and the optimum environment for *Coccidioides* growth, that could potentially increase its prevalence as weather patterns change are discussed and how the endemic regions could be affected are assessed. In general, regions of the United States, including California and Arizona, where VF is endemic, are expanding and incidences of VF are increasing in those areas. The surrounding southern states, including Nevada, New Mexico, Utah, and Texas, are experiencing similar changes. In addition, the entire endemic region of the United States is predicted to spread northward as drought is prolonged and temperatures steadily increase. The findings from the keyword search from eight databases indicate that more studies on VF and its relation to dust and climate are needed especially for endemic states like Nevada that are currently not adequately studied. Overall, results of this survey summarize mechanisms and climate factors that might drive spread of VF and describes trends of incidence of VF in endemic states and predicted likely trends that might occur under a changing climate. Through reviewing recent and past studies of Coccidioidomycosis and its relationships with climate factors, future impacts of this disease have been categorized and speculated on effects it might have on the United States. Better understanding of how climate factors affect VF as well as identifying regions that require more research could inform both environmental managers and medical professionals with the resources needed to make more accurate predictions, design better mitigation strategies, send timely warnings, and protect public health.

Shortened version

This review explores how climate change affects Valley Fever (VF), a dangerous fungal infection caused by *C. immitis* or *C. posadasii*. Climate change has increased natural hazard events such as dust storms and droughts, which have caused the spread of VF. Cases of the disease have increased fivefold between 2001 and 2021 in California alone, and it poses an increasing threat to public health. The review summarizes mechanisms that drive the spread of VF and highlights trends in endemic states under a changing climate. It recommends more studies on VF and its relation to dust and climate, especially for states like Nevada. Identifying regions that require more research can help make more accurate predictions, design better mitigation strategies, send timely warnings, and protect public health.

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1. Introduction

Valley Fever (VF), also known as Coccidioidomycosis, is becoming a prevalent public health issue. It is a potentially fatal upper respiratory illness with flu-like symptoms such as fatigue, cough, fever, shortness of breath, and headaches (Centers for Disease Control and Prevention, 2022b). VF is caused by the fungus *Coccidioides immitis* (*C. immitis*) or *Coccidioides posadasii* (*C. posadasii*) (Mayo Clinic, 2022). When dust particles carrying spores of *Coccidioides* are inhaled, they can infect mammals (including humans), reptiles, and birds.

C. immitis and *C. posadasii* are found in the soils of the Southwestern United States, Washington state, and parts of Mexico, Central America, and South America (Mayo Clinic, 2022). The semi-arid climates in these areas contribute to the term "endemic region" (College of Medicine Tucson, 2021). The fungus thrives in extremely dry soils, rich in salts with sparse xerophytic vegetation (Luxem, 2017; Reyes-Montes, 2016). The two significant factors contributing to the growth and spread of *C. immitis* and *C. posadasii* spores are wind and rain (Matlock et al., 2019). Climates marked with distinct weather patterns, such as rainy and dry seasons, provide optimal growing conditions for *Coccidioides*. The fungus flourishes in areas with hot and dry summers, cold winters, and little rainfall (Luxem, 2017). Seasonality allows for proliferation of the fungus during cool, wet seasons and increased dispersal of the spores during dry seasons (Reyes-Montes, 2016).

The increase in temperature due to climate change has shifted the weather patterns and caused an increase in the severity of droughts across the Southwest (US EPA, 2016). When the soil is dry, endospores present in dust can be picked up by wind. Wind serves as a dispersing agent in carrying the spores of *Coccidiodes* on dust particles. These spores are usually located near the soil surface, approximately 10 cm deep (Matlock et al., 2019). Disruption of these soils is frequent, often due to wind, soil composition, and climate of the area (Reed & Nugent, 2018). Wind aerosolizes the dust particles and spores, transporting them through the air and promoting subsequent inhalation (Matlock et al., 2019). Altered wind patterns and increased frequency and severity of dust storms due to climate change could contribute to spreading spores; thus, VF has become more prominent (Mirsaeidi et al., 2016).

Dust storms, such as the one in Kern County in 1977, cause a spike in cases of VF (Pappagianis & Einstein, 1978). In the last decade, there has been an increase in dust storms under a changing climate (Freedman et al., 2018; Jones & Driscoll, 2022). In the Southwestern United States, dust storms increased 240% from 1990 to 2000 (Tong et al., 2017). The frequency of dust storms seems to correlate with the incidence of VF. From 1998 to 2011, VF increased in the same areas in the United States where dust storms increased (Tong et al., 2017). As temperature and drought increase under a changing climate, the area of land that can accommodate *Coccidioides* is spreading rapidly (Gorris et al., 2019; Head et al., 2022).

From 1999 to 2019, there was an average of 200 deaths per year caused by VF in the United States alone (Centers for Disease Control and Prevention, 2022a). However, incidence rates continue to rise as the world experiences the rapid onset of the effects of climate change (Gorris et al., 2018). This review outlines the increased prevalence of VF incidence and the spread of the endemic region for the fungus, driven by

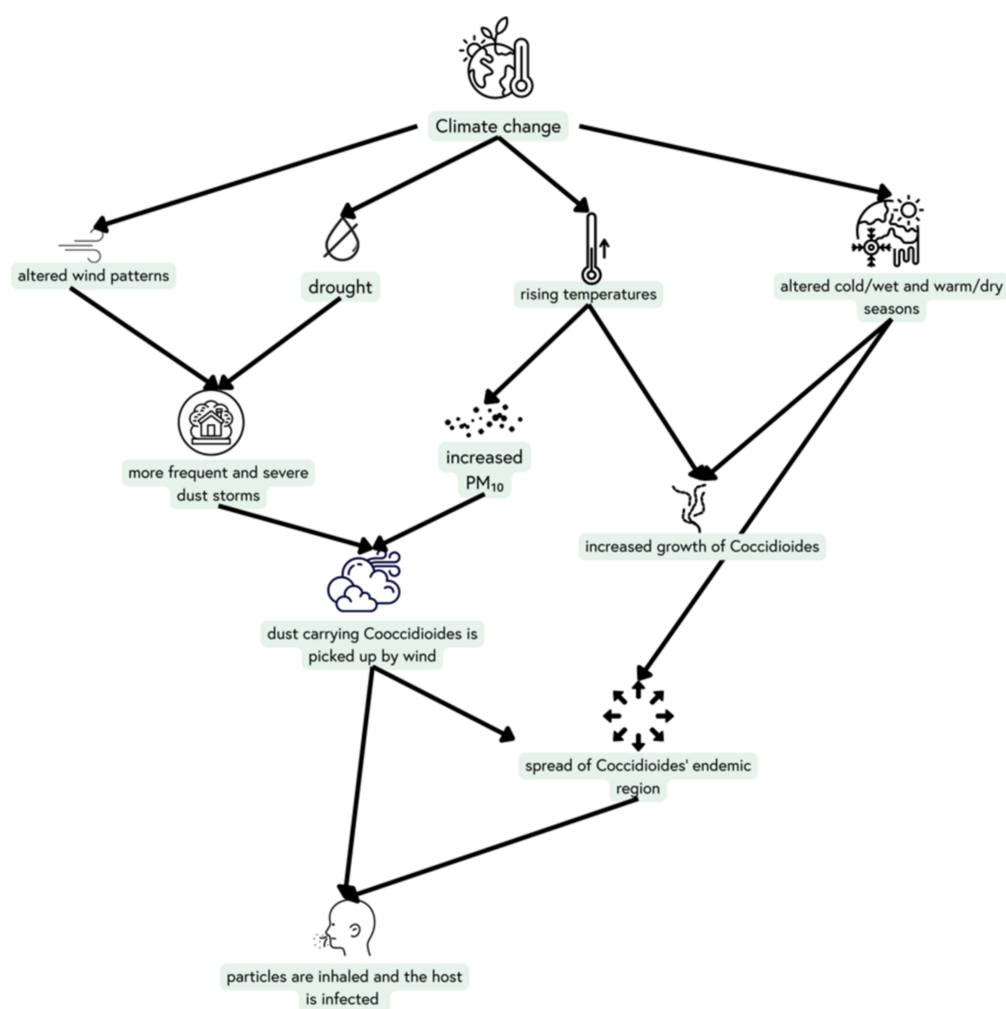

Fig. 1. Climate change is increasing dust occurrence and the growth of Coccidioides, leading to higher human exposure to VF.

climate change, with key pathways representing how climate change enhances dust storms and *Coccidioides* growth and human exposure (Fig. 1). The focus of the discussion is on the role of a changing climate on the past, recent, and predicted changes in VF, all of which are essential in preparing humans for a potentially detrimental encounter with this disease.

2. Biology of Coccidioidomycosis and Valley Fever in humans

With the increased incidence and spread of the region endemic to *Coccidioides*, it is crucial to know the fungi's life cycle. The inhalation of dust-carried *C. immitis* and *C. posadasii* spores begins the parasitic cycle. Genetic analyses show that *Coccidioides* heavily rely on a host, and several types of animals serve as effective growth reservoirs and dissemination paths for the fungi (Reyes-Montes, 2016). Although Coccidioidomycosis is not contagious, countless spores are released through decomposition when an infected host dies, enabling further infection cycles. When soil contaminated with *Coccidioides* spores is disturbed by wind, agricultural practices, and construction, the dust particles that carry the fungi are released into the air. The spores are inhaled and cause infection in the lungs. After deposition, the spores transform into larger multicellular structures called spherules (College of Medicine Tucson, 2021). These structures grow and undergo nuclear division for the first two to three days and mature into large cells containing endospores (Lewis et al., 2015). The spherules burst on days four and five, releasing between 100–300 endospores per spherule (Hernandez et al., 2019). Then, the parasitic cycle begins again (College of Medicine Tucson, 2021a).

Several cases of VF are asymptomatic. However, roughly 40% of individuals develop symptoms consisting of a pulmonary infection (Williams & Chiller, 2022). Individuals contracting Coccidioidomycosis show symptoms around 1–3 weeks after initial exposure to the airborne fungus (Lucero-Obusan et al., 2023). Coccidioidomycosis is characterized by its high morbidity and can include severe pulmonary infections, dissemination, or death (Lucero-Obusan et al., 2023).

VF usually occurs as an acute, benign, asymptomatic, or self-limited respiratory infection with the spectrum of disease ranging from acute pneumonia to disseminated extrapulmonary disease, including meningitis. Symptoms, if present, are those of lower respiratory infection or low-grade nonspecific disseminated disease, which occurs when the infection caused by *Coccidioides* migrates from the lungs to elsewhere in the body (Nakhla, 2018). Dissemination occurs in 1 to 5% of infected people and usually develops weeks to months after the initial infection (Crum et al., 2004). About 1 in 100 people experience the spread of the fungal infection to nerves, skin, bones, and joints (Centers for Disease Control and Prevention, 2021a). There are two types of disseminated VF, *i.e.*, meningeal and non-meningeal. A meningeal infection can lead to central nervous system (CNS) vasculitis, which can cause cerebral ischemia, infarction, and hemorrhage (Galgiani et al., 2005). The non-meningeal form usually requires surgery, as these cases are marked by continuously enlarging abscesses, bone sequestrations, spine instability, or impingement of organs and tissues.

Approximately 75% of people who contract VF miss work and school days, and about 40% must be hospitalized (Centers for Disease Control and Prevention, 2022b). It is estimated that there are approximately 2000–3000 hospitalizations and 160–200 deaths attributed to Coccidioidomycosis per year in the United States (Lucero-Obusan et al., 2023). As much as 80% of patients with VF are given more than one round of antibiotics before receiving the correct diagnosis of the fungal infection and appropriate treatment. Diagnosis is based on clinical and epidemiologic characteristics and confirmed by use of chest x-ray, microbiological culture, and serologic testing.

Current treatment methods are limited and exhibit adverse effects, such as intolerance or drug failure (O'Shaughnessy et al., 2022). Treatment, if needed, is usually with antifungal medications, such as fluconazole, itraconazole, newer triazoles, or the antibiotic amphotericin B. As case numbers increase, there is a need to find an effective treatment for VF. There have not been any new treatment options for VF approved in the United States for nearly 40 years.

The rate of recovery from infections with Coccidioidomycosis after receiving treatment can vary, depending on the type of Coccidioidomycosis being treated. For uncomplicated respiratory infections, treatment usually lasts 3 to 6 months (Williams & Chiller, 2022). Individuals may undergo lifelong treatment or surgery if they experience severe or chronic forms of Coccidioidomycosis. In some cases, lifetime treatment of antifungal drugs is required (Martinez-del-Campo et al., 2017).

3. Analysis of the distribution of reported studies examining Valley Fever per U.S. State

Eight scientific databases are explored (*i.e.*, EBSCOhost Academic Search Complete, Web of Science Core Collection, BioOne, Wiley, Environmental Science Index ProQuest, PubMed, Science Direct, and Scopus). A keyword search is conducted for the terms "state name" (e.g., California) and "Valley Fever or Coccidioidomycosis" (Table 1). A second ("state name", "dust", and "Valley Fever or Coccidioidomycosis") and third ("state name", "dust", "climate" and "Valley Fever or Coccidioidomycosis") keyword searches are also performed. Finally, a keyword search only in the abstract or title for the words "state name", "dust", "climate," and "Valley Fever or Coccidioidomycosis" is performed. The publications' highest (green highlight) and lowest amounts (red highlight) are tabulated. Orange highlighting indicates no data available for the database.

4. Soil and dust properties that contribute to the spread of Valley Fever

One crucial aspect of the survival and reproduction of *Coccidioides* fungi is soil type (Kollath et al., 2019). The fungus *Coccidioides* thrives in dry, warm soils with high salt levels, making semi-arid regions with high salinity the optimal growing space (Chow et al., 2021). *Coccidioides* also require soil with a sandy loam texture consisting of sand and silt with lesser amounts of clay (Kollath et al., 2019). These conditions allow for quick drainage and drying of soil particles, enhancing the lifecycle of *Coccidioides*. Sandy-loam textured soils comprise homogenous particles with large pores, allowing water and air to flow rapidly (Fisher et al., 2007). These soils do not hold much water due to increased porosity and permeability, which largely determines *Coccidioides*' survival in nature (Dobos et al., 2021; Fisher et al., 2007). Textures of soils favored by *Coccidioides* also make them susceptible to wind erosion (Fisher et al., 2007).

Coccidioides can be found in various desert soils, as they can survive extreme temperatures and low pH (Fisher et al., 2007). Southwest regions of the United States endemic to *Coccidioides* typically experience extreme air temperatures ranging from −40° to 48.8°C. Soil temperatures can vary widely, ranging from below freezing to temperatures exceeding 26°C on average. Although *Coccidioides* have been known to survive in extreme temperatures, the optimal range for their growth is between 20°–40°C (Weaver & Kolivras, 2018). The fungus also thrives in areas of greater salinity, specifically those with increased soluble salts, such as sodium, calcium, sulfate, and chlorine (Elconin et al., 1964). The harsh conditions for which *Coccidioides* can survive serve as an advantage to the fungus because several predators or competitors cannot function in this environment (Dobos et al., 2021). Antagonists in the soil with *Coccidioides* include several bacterial species, such as *Streptomyces, Pseudonocardia, Nocardiopsis,* and *Bacillus* (Lauer et al., 2019). Due to the various antagonists, *Coccidioides* favor alkaline environments or soils with greater salinities (Lauer et al., 2019). Competing bacteria are not prevalent in regions endemic to *Coccidioides* because the soil temperatures and moisture levels are too extreme (Fisher et al., 2007). Without an abundance of competition, *Coccidioides* can prey on organic matter in these soils, usually consisting of iron, calcium, and magnesium, which

Table 1
Scholarly sources in the number of publications available per state for each keyword search performed.

Keywords	**State OR State Abbreviation + Valley Fever OR Coccidioidomycosis OR Coccidioides**							
Databases	**EBSCOhost Academic Search Complete**	**Web of Science Core Collection**	**BioOne Complete**	**Environmental Science Collection ProQuest**	**PubMed**	**Embase**	**Scopus**	**Biosis**
California	4767	1950	310	6284	1037	1983	7564	283
Arizona	1282	932	42	1263	723	1119	2181	227
Nevada	644	50	33	860	18	52	232	11
New Mexico	2290	264	147	4001	68	120	1290	37
Utah	734	110	38	938	70	140	566	12
Texas	1779	797	131	2204	419	825	2725	58
United States OR North America OR USA	6986	4582	425	9137	2645	7289	21,666	955
Total	9,512	8,106	527	12,553	7,112	10,453	29,455	6,624
Keywords	**State OR State Abbreviation + Valley Fever OR Coccidioidomycosis OR Coccidioides + dust**							
Databases	**EBSCOhost Academic Search Complete**	**Web of Science Core Collection**	**BioOne**	**Environmental Science Collection ProQuest**	**PubMed**	**Embase**	**Scopus**	**Biosis**
California	371	56	14	809	47	53	658	25
Arizona	189	33	4	353	22	25	357	14
Nevada	71	5	7	288	2	5	79	0
New Mexico	179	10	13	596	4	4	129	0
Utah	87	5	8	312	5	5	153	1
Texas	156	11	8	398	6	9	209	2
United States OR North America OR USA	442	74	18	968	55	88	914	46
Total	519	81	22	1099	80	100	1015	62
Keywords	**State OR State Abbreviation + Valley Fever OR Coccidioidomycosis OR Coccidioides + dust + climate**							
Databases	**EBSCOhost Academic Search Complete**	**Web of Science. Core Collection**	**BioOne**	**Environmental Science Collection ProQuest**	**PubMed**	**Embase**	**Scopus**	**Biosis**
California	159	18	8	552	12	10	364	3
Arizona	96	16	3	279	12	8	205	5
Nevada	35	3	4	241	1	0	61	0
New Mexico	92	4	6	446	1	0	82	0
Utah	51	3	4	252	4	0	105	0
Texas	91	2	3	304	1	1	137	0
United States OR North America OR USA	194	22	11	666	17	19	473	5
Total	213	24	13	701	26	22	506	9
Keywords	**Searched in the abstract and title ONLY: State OR State Abbreviation + Valley Fever OR Coccidioidomycosis OR Coccidioides + dust + climate**							
Databases	**EBSCOhost Academic Search Complete**	**Web of Science. Core Collection**	**BioOne**	**Environmental Science Collection ProQuest**	**PubMed**	**Embase**	**Scopus**	**Biosis**
California	2	6	0	5	7	5	10	3
Arizona	3	5	0	8	8	5	11	5
Nevada	0	1	0	1	1	0	1	0
New Mexico	0	2	0	1	1	0	1	0
Utah	0	1	0	1	1	0	1	0
Texas	1	0	0	0	0	1	0	0
United States OR North America OR USA	3	6	1	6	5	6	18	2
Total	7	12	1	14	14	12	29	8

= state with the highest % of scholarly sources
= state with the lowest % of scholarly sources
= no data

are required nutrients for survival (Dobos et al., 2021; Fisher et al., 2007). Temperature fluctuations also contribute to thriving *Coccidioides*. When temperatures are high during summer, competitors of *Coccidioides* in the soil die, allowing for increased growth when the temperatures and precipitation return to normal (Weaver & Kolivras, 2018). Greater temperatures and altered seasonality driven by climate change remove predators and competitors of *Coccidioides* with lower heat resistance, allowing the fungus to flourish and benefit from a changing climate.

Soil types suitable for the survival and growth of *Coccidioides* are found in centralized endemic regions, including a large part of the Southwestern United States (Dobos et al., 2021), as soils in California, Arizona, Nevada, New Mexico, Texas, and Utah meet the climatic and physical requirements to support the growth of Coccidioidomycosis and are the source of sand and dust storms across America (Crum, 2022; Tong et al., 2023). Climate change has resulted in earlier starts and lengthier durations of dry periods, and these trends are expected to continue (National Park Service, 2023). Under a changing climate, larger soil areas are drying out, and the frequency and intensity of dust storms are increasing, making more extensive soil areas receptive to erosion, which have the potential to expand the endemic region of *Coccidioides*.

Although soils that house *Coccidioides* can be identified in endemic regions, the characteristics and distributions of fungi in the air are still unknown, and few studies describe the nature of the particulate matter that holds *Coccidioides* and how it is distributed across endemic regions (Gade et al., 2020). Endospores of *Coccidioides* measuring at 2 to 5 μm in primary particle diameter reside on the surfaces of particulate matter smaller than 10 μm (PM_{10}) (Akram & Koirala, 2023; Kollath et al., 2022). Particles with which the spores are associated are small enough to be inhaled and deposited into the respiratory zones of the lungs (Brown et al., 2013; Kim et al., 2015). If these particles are abundant, there are sufficient surface sites on the particles to hold and support the transportation of *Coccidioides* spores through the air, thus, the amount of particulate matter is associated with the number of cases of environmental diseases such as VF (Kollath et al., 2022). An increasing amount of PM_{10} could be correlated with enhanced number of VF cases, which explains why the number of VF cases are greater in winter and spring months when airborne particulates are at a maximum (e.g., Kollath et al., 2022). In recent years, there has been an increase of 22% in PM_{10} across the Southwestern region of the United States (US EPA, 2022). However, ambient PM_{10} are not the sole indicator of *Coccidioides.* PM_{10} is emitted into the atmosphere from a variety of sources such as wind-blown dust from open lands, construction, road dust, agricultural fields, and smoke from fires (US EPA, 2023), and the enhanced activities of all these sources could contribute to the increases of PM_{10} concentrations (Weaver & Kolivras, 2018). In addition, the increase in ambient temperature due to climate change could also enhance PM_{10} in the air (Leão et al., 2023). Analyzing both particle properties and climate conditions might result in a good predictive relationship for incidence of VF.

4.1. Climate change and the spread of Valley Fever

It is important to recognize what could be the causative factors of the rapid rise in VF cases. Climate change causes increased temperatures, altered durations and intensities of hot and cold seasons, and increased frequencies and severities of drought and dust storms. This can result in area expansions of regions in which VF is endemic and can increase the incidence of VF in those regions (Gorris et al., 2019; Reyes-Montes, 2016; Weaver & Kolivras, 2018).

The increase in temperature due to climate change has shifted the weather patterns and caused an increase in the severity of droughts across the Southwest (US EPA, 2016). When the soil is dry, endospores present in dust can be picked up by wind. Wind serves as a dispersing agent in carrying the spores of *Coccidioides* on dust particles. These spores are usually located near the soil surface, approximately 10 cm deep (Matlock et al., 2019). Disruption of these soils is frequent, often due to wind, soil composition, and climate of the area (Reed & Nugent, 2018). Wind aerosolizes the dust particles and spores, transporting them through the air and promoting subsequent inhalation (Matlock et al., 2019).

The Southwest region has been in a megadrought since 2000; the largest to occur in at least 1200 years (US EPA, 2016). The area affected by drought in the United States is quickly expanding outward from the states that have traditionally been drier. Expansion of dry conditions and higher temperatures could facilitate the spread of *Coccidioides* spores and thus VF infections (Gorris et al., 2019).

Altered wind patterns and increased frequency and severity of dust storms due to climate change could contribute to spreading spores; thus, VF has become more prominent (Mirsaeidi et al., 2016). Dust storms, such as the one in Kern County in 1977, cause a spike in cases of VF (Pappagianis & Einstein, 1978). In the last decade, there has been an increase in dust storms under a changing climate (Freedman et al., 2018; Jones & Driscoll, 2022). In the Southwestern United States, dust storms increased 240 % from 1990 to 2000 (Tong et al., 2017). The frequency of dust storms seems to correlate with the incidence of VF. From 1998 to 2011, VF increased in the same areas in the United States where dust storms increased (Tong et al., 2017). As temperature and drought increase under a changing climate, the area of land that can accommodate *Coccidioides* is spreading rapidly (Gorris et al., 2019; Head et al., 2022). The endemic region of VF is predicted to spread northward and become more severe by 2090. The endemic region covers several states and the changes in VF cases in these states especially indicate a rapid increase over the recent decades (Fig. 2).

5. Valley Fever and climate change in California

The state for which there are the greatest number of publications on VF is California, which also has one of the highest incidence rates in the U.S. (Table 1). In 2019, 95% of cases were in California and Arizona (National Academies of Sciences, Engineering, and Medicine, 2023). The fungus *C. immitis* affects the majority of the endemic region of California, in which VF cases are increasing at alarming rates (roughly 800% since the year 2000) (National Academies of Sciences, Engineering, and Medicine, 2023). Kern County repeatedly reports the most cases in California (Dobos et al., 2021). The original endemic region for VF in California is located in the San Joaquin Valley, which includes Fresno, Kern, Kings, Madera, Merced, Monterey, San Luis Obispo, and Tulare counties (Cooksey & Pearson, 2022). However, the areas experiencing the greatest increase in cases of VF are now located in the northern parts of the San Joaquin Valley, the Central Coast, and much of the Southern Coast regions (Cooksey & Pearson, 2022). The increase in numbers of cases is non-linear and is influenced by shifts in weather patterns due to climate change-derived drought, aridity, and drastic weather swings between dry and wet periods (Cooksey & Pearson, 2022). Distinctive climatic regions in California are affected differently and are developing contrasting sensitivities (Head et al., 2022). In hot and dry regions of California, climate change is causing greater amounts of precipitation during the winter, contributing to the increase in cases of VF. Increased precipitation promotes the rapid growth of *Coccidioides* species in the

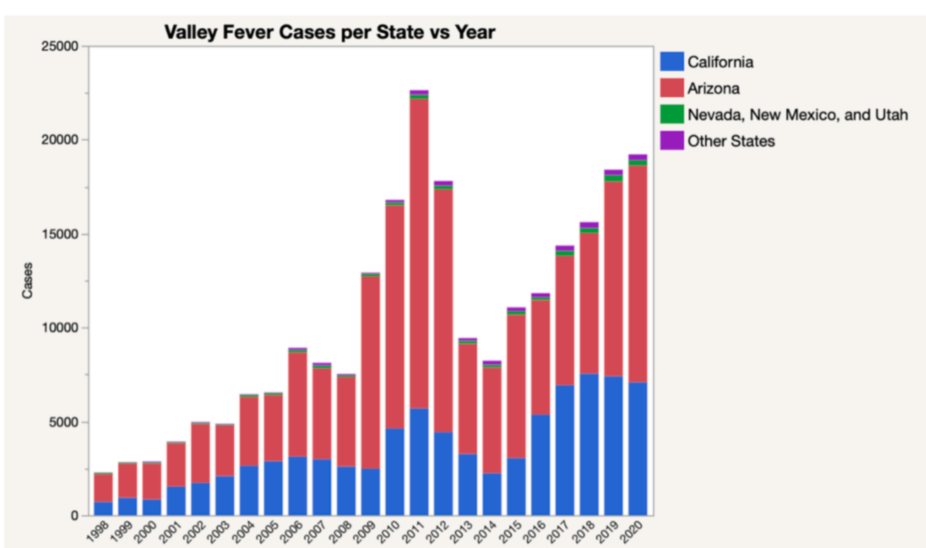

Fig. 2. Variations in annual cases of VF for each state from 1998 to 2020. Data obtained from the Centers for Disease Control and Prevention (Centers for Disease Control and Prevention, National Notifiable Diseases Surveillance System, 2020 Annual Tables of Infectious Disease Data; Centers for Disease Control and Prevention, 2022a; Centers for Disease Control and Prevention., 2023).

soil (Head et al., 2022). As the soil dries during the summer, more spores become available to be carried by the wind. In California regions typically considered wet and cool, rising temperatures have led to a surge VF cases (Head et al., 2022). Warmer conditions cause the soils to dry quickly, making *Coccidioides* spores more vulnerable to wind erosion and aerosolization. This "grow and blow" hypothesis explains why cool, wet areas, like coastal regions, are seeing more VF cases compared to arid regions due to the cyclical hot-to-cold, dry-to-wet weather patterns (Head et al., 2022). The fungi in this area are proliferating exponentially due to the heat and, consequently, disperse the *Coccidioides* into individual spores, making them more respirable and spiking infection rates (Head et al., 2022). VF is expected to become endemic in normally cool and wet regions at faster rates than potentially neighboring regions that are typically more arid (Head et al., 2022). Rates of increasing cases of VF in these regions have already been recorded 15-fold greater in the San Joaquin Valley than two decades ago (Head et al., 2022). In California and across the United States, the incidence of VF depends on climate change, and the increasing number of cases is likely to continue progressing rapidly (Linh Anh Cat et al., 2019).

6. Valley Fever and climate change in Arizona

Like California, the endemic region of VF in Arizona is expanding, and incidence rates are increasing (Mead et al. 2022). Arizona has a different species of *Coccidioides* than California, *C. posadasii,* which is also present in Texas and parts of Mexico and South America (Kollath et al., 2019). Although genotypically different, this species functions clinically in the same ways as *C. immitis* (Kollath et al., 2019). The main difference between *C. immitis* and *C. posadasii* is their geographic distributions, which could be due to geological barriers between the ancestors of these species (Kirkland & Fierer, 2018). It has been found that *C. posadasii* species grow slower than *C. immitis* on high-salt media, indicating physiological differences between the two species (Fisher et al., 2002). *C. posadasii* is a large, much more diverse population than *C. immitis* (Kirkland & Fierer, 2018). There are several smaller subpopulations of *C. posadasii* in different geographic areas (Kirkland & Fierer, 2018). The population of *C. posadasii* in Arizona is distinct from those in Texas, Mexico, and South America (Kirkland & Fierer, 2018; Kollath et al., 2019).

Arizona typically has the most diagnosed cases in the United States, except in 2018 when California exceeded its incidence (Mead et al., 2022). The endemic region in Arizona is marked by the southernmost counties, including Maricopa, Pima, and Pinal counties, where 94 % of infection occurs in the state (National Academies of Sciences, Engineering, and Medicine, 2023). Like California, the area affected by VF is expanding due to climate change and the "grow and blow" hypothesis (Roach et al., 2017). One study in Arizona found that abnormal precipitation fluctuations in the fall and winter months explained the increase in incidence seen from 1995 to 2006 (US EPA, 2009). Much like California, just as the incidence rates increase, Arizona's endemic regions are expanding. The northern counties are experiencing an increase in VF cases due to the expansion of areas that can hold and support the fungus that causes VF (Mead et al., 2022). The incidence of VF in northern counties such as Mohave, Yavapai, and Apache has doubled since 2019. Although these soils are not the preferred habitat for the fungus, it is projected that they will soon be able to hold and support the growth of *Coccidioides* (Mead et al., 2022).

7. Valley Fever and climate change in other Southwestern U.S. States

California and Arizona are considered high-endemic regions, while the surrounding southern states, including Nevada, New Mexico, Utah, and Texas, are all considered "established" or "suspected" endemic, also termed low-endemic regions (Gorris et al., 2019). These regions have a case rate of 2.1% in the United States combined (Smith et al., 2022). The fungus *C. posadasii* is present in all low-endemic regions (National Academies of Sciences, Engineering, and Medicine, 2023).

Although not considered highly endemic for VF, Nevada is the third-ranking state with the highest case levels despite the evidence that Nevada has the least number of publications on Coccidioidomycosis (Fig. 2). This raises the question of why more research is not being done on VF in this area. Cases of VF have been reported from all four corners of Nevada, although most of the endemic region is in the southern parts (Centers for Disease Control and Prevention, 2021b; Crum, 2022). The hospitalization rate for Nevada is 1.6%, and an upward trend in hospitalizations has been recorded, as much as a 150% increase from 2005 to 2011, as the endemic region continues to expand and the disease becomes more prevalent (Luo et al., 2017).

The endemic region of New Mexico is found in the southern areas of the state due to the physical environment being very similar to the endemic regions of Arizona and California (Hamm et al., 2019). Although most of New Mexico's environment is fit for the growth of the fungus, the annual case numbers are much lower than in California and Arizona. This is due to the state's low population and population density. The population is more spread out and distributed sparsely throughout the southern parts of the state. However, with continued climate warming conditions, the endemic region of VF in New Mexico is projected to spread northward through the Great Plains (Gorris et al., 2019).

Utah, more northern than the other states mentioned, is also considered endemic for VF. The southwestern regions, along with the northeastern corner of Utah, have the state's highest endemicity and case number, with Washington County having the highest incidence (Carey et al., 2021; Centers for Disease Control and Prevention, 2021c). The increase in cases in Washington County and other surrounding counties in Utah may be due to population growth, tourism, and climate change (Carey et al., 2021). When modeling the endemic region's spread by considering climate change and population growth, researchers found that the northeastern corner may be at risk (Carey et al., 2021).

VF is also found in Texas along the Rio Grande (Centers for Disease Control and Prevention, 2021c). Texas' endemic region has not been clearly defined but is described as being throughout the western and southwestern parts of the state (Gautam et al., 2013). This is due to a lack of studies and surveillance of the disease in Texas; Coccidioidomycosis is only reportable in El Paso (Benedict et al., 2019).

8. Climate-linked Valley Fever incidence: 2011 and future predictions

The increasing trend of VF incidence could be due to climate change. Several factors are affected by changing climate conditions, one being the increased longevity and frequency of drought (Trenberth et al., 2013). The Southwestern U.S. experienced a megadrought around 2000 (Szejner et al., 2021). Megadroughts typically last two decades, so in 2011, nearly 11 years of drought had already occurred, resulting in soil drying (Szejner et al., 2021).

Another extreme weather event that could aid in explaining the increased incidence is the heatwave of 2011 (Climate Scientists Say Human Link Evident in Extreme Weather Events, 2017). The heatwave began the warmest five years ever recorded, starting in 2011 and lasting until 2015 (Look back at the decade: Extreme weather, 2019). During July of 2011, a monsoon caused a massive dust storm to erupt (Sprigg et al., 2014). When the thunderstorm came through, it picked up large amounts of dust and caused a haboob to hit Phoenix, Arizona (Sprigg et al., 2014). These events, followed by precipitation, not only pick up dust and spread it throughout the air but also boost the growth and spread of *Coccidioides* (Sprigg et al., 2014). All these events in 2011 could have combined to provide suitable living conditions for *Coccidioides* and allowed it to expand its endemic region, causing the spike in 2011.

Similar conditions are present in the last recorded annual case count in 2020. In 2020, drought continued to worsen, and temperatures hit record highs in the Southwestern region of the United States. From January 2020 to August 2021, this region received the lowest amount of precipitation ever recorded and experienced the third-highest average daily temperatures on record (Mankin et al., 2021). The intensified onset of climate change causes natural hazard events like dust storms and drought to increase in number and severity, resulting in the proliferation of VF. Climate change is causing an expansion in the area where *Coccidioides* can survive and reproduce while also playing a factor in the spread of Coccidioidomycosis to humans.

9. Climate change influencing human health mortality

Higher temperatures and intensified weather events under a changing climate also influence mortality induced by the fungus that causes VF (Linh Anh Cat et al., 2019). Understanding both the acute and chronic effects of Coccidioidomycosis is crucial to raising awareness and limiting exposure.

The crude mortality, or the general mortality rate for a certain population, in the U.S. for Coccidioidomycosis is 0.58 per 1 million person-years from 1990 to 2008 (Centers for Disease Control and Prevention, 2018a; Huang et al., 2012). The age-adjusted mortality, the mortality that is calculated when mortality is highest in certain age groups, is 0.59 per 1 million person-years from 1990 to 2008 (Centers for Disease Control and Prevention, 2018b; Huang et al., 2012). Focusing on the two most endemic states over the same time frame, the mortality rates in Arizona and California increase to 2.19 and 1.89 per 100,000 person-years, respectively (Noble et al., 2016).

Mortality due to Coccidioidomycosis is known to increase with age and this change is more associated with the male sex (Noble et al., 2016). In the United States, males have an average mortality rate of 0.93 and females have 0.31 (Noble et al., 2016). Higher rates of both infection and severity are present in males in humans and nonhuman primates, and veterinary animals (McHardy et al., 2022). The frequency of dissemination of the fungal infection is also greater in males than in females, roughly 80% greater (Smith and Beard, 1946). This difference is not likely due to behavioral differences between males and females (McHardy et al., 2022). In a study done by McHardy et al. (2022), the increase in infection and severity rates remained higher in the male species of all animals tested, one being canines that exhibited no difference in digging behaviors, which is the pathway would predispose them to VF exposure. Instead, this difference in severity and infection of VF might be due to estrogen inhibiting the fungus from progressing to the yeast form as hypothesized in *Paracoccidioides mycelium,* a close relative to *C. immitis* and *C. posadasii* (Drutz et al., 1981; Drutz et al., 1981; McHardy et al., 2022; Restrepo et al., 1984; Shankar et al., 2011; Sharpton et al., 2009).

The mortalities are identified to be the highest in immunocompromised individuals and those of the African-American, Filipino, Hispanic, and Native American racial and ethnic groups (Lucero-Obusan et al., 2023; Noble et al., 2016). Lucero-Obusan et al. (2023) calculated adjusted Risk Ratios (aRRs) for several racial and ethnic populations. They found that African Americans have an aRR of 1.029, Asians 1.060, Native Hawaiian/Pacific Islander 1.068, and American Indian/Alaskan Native 1.026.

The prevalence of VF has consistently risen in recent years (Williams & Chiller, 2022). The increase in reported cases could result from compounding factors. Climate change increases exposure to more individuals as the endemic region expands (Williams & Chiller, 2022). Population increase is also exposing previously unexposed individuals by the migration of people to endemic regions (Williams & Chiller, 2022). Improvements in disease surveillance and diagnoses are identifying cases more efficiently and accurately (Williams & Chiller, 2022).

10. Social and economic implications of the spread of Valley Fever

With the consequences of climate change in effect, it is crucial to know the impact VF could have on human society and the economy. VF can shorten the length and decrease the quality of life (Wilson et al., 2019). Pneumonia caused by VF infection can lead to residual pulmonary nodules which take extended amounts of time to disappear; some can last for years and raise concern for the onset of cancer (Crum et al., 2004). Treatments for Coccidioidomycosis can be extensive as well as costly on the body. Certain long-term anti-fungal medications may cause harm to the kidneys. Other treatment options require surgery.

VF is estimated to cost the United States approximately $3.9 billion every year due to annual medical costs, lost income, and economic welfare losses (Gorris et al., 2021). The individual cost of VF treatment ranges from $22,039 to $1,023,730 depending on health complications (Wilson et al., 2019). If the incidence rate of VF were to continue to increase at the rate seen today, the United States would experience approximately $18.5 billion in costs per year by 2090 simply because of the predicted tripling number of cases (Gorris et al., 2021).

11. Discussion

Coccidioidomycosis is a fungal disease becoming increasingly prevalent across the Southwestern United States as the climate changes. In this paper, a literature review study is conducted, and several databases are examined for information on VF with dust and climate change. California has the most scholarly sources on VF available out of all the states, and Nevada repeatedly has the least amount. While California has a high incidence of VF, it is second to Arizona. It is expected that Arizona would have the most significant number of publications due to having the highest incidence rates, but according to the databases examined, it does not. Secondly, Nevada's lack of publications is intriguing. Out of all low-endemic states described, Nevada has on average, the highest case rate, ranking third highest incidence in the United States. The percentage of sources that contain information on the United States roughly increases as the search narrows, indicating that information on climate and dust regarding VF mainly focuses on the states. To understand how this disease functions, it is crucial for information on every region susceptible to VF to be studied so scientists can more accurately depict how climate is affecting the transmission of the disease. Additional information on high-endemic areas also needs to be made readily available to the scientific community, as Coccidioidomycosis is a growing problem in America. There is a strong need for more data on VF to be obtained.

The findings from the keyword searches from eight different databases show that more information is needed from each endemic state, particularly on VF and its relation to dust and climate. Few scholarly sources are available as the search narrows down to Coccidioidomycosis, state, dust, and finally, climate. When searching for all the terms specifically in the title or abstract, there is an extreme reduction in the number of publications. For several of the databases observed, the number of sources is in the single digits.

Cases of VF have increased fivefold in California alone from 2001 to 2021, and are expected to continue to rise (Cooksey, 2022). The number of deaths caused by VF fluctuates year to year, but as more infections are predicted to occur due to a changing climate, deaths are expected to rise; thus, the rising prevalence of the disease is becoming a larger focus of the scientific community and poses an increased threat to public health (Gorris et al., 2021). In the western census region of the United States, there were 115 deaths due to VF in 2020–the highest ever recorded (CDC Wonder, 2020). In 1999, the beginning of the recording period, there were only 68 deaths in this region (CDC Wonder, 2020).

As climate change intensifies, it is crucial for public health officials to implement diverse strategies to prevent VF outbreaks. Although a live attenuated vaccine is currently in development, it is not yet available to the public (Kollath et al., 2019). In the meantime, other preventative measures include government policies, public and occupational education, prophylactic drug use, health recommendations for immunocompromised individuals, and warning systems. Employers in VF-endemic areas are advised to conduct a Job Hazard Analysis (JHA) to identify workers at risk, as recommended by the Occupational Safety and Health Administration (OSHA). Based on the results of the JHA, employers should implement protective measures such as engineering and administrative controls, personal protective equipment, and safe work practices. For high-risk occupations in endemic regions, the JHA should be integrated into site-specific health programs, as mandated by OSHA's 29 CFR 1926.20(b) Occupational Safety and Health Administration.

The increasing relocation of people to endemic areas such as California, Arizona, and Texas for work, education, or military service raises questions about institutional responsibility for medical costs related to VF. Some lawsuits have already been filed and settled in response to these concerns, underscoring the need for better public and institutional education to reduce potential liability (Galgiani, 1999). In high-risk endemic regions of California, outdoor workers are trained in dust control, equipment cleaning, and respiratory protection (Freedman, 2018). However, not all outdoor workers receive this safety training, making it imperative for health officials to ensure that information is accessible to everyone at risk.

Researchers are also exploring the use of antifungal prophylactics for immunocompromised individuals, as VF incidence continue to rise in endemic areas (Crum, 2022). Regular testing in these regions is also encouraged to improve disease surveillance and ensure accurate diagnoses (Crum, 2022). Specific prevention strategies are recommended for at-risk populations. For organ transplant recipients in endemic areas, a 6–12-month course of oral azole antifungal therapy is advised (Galgiani et al., 2016). Likewise, individuals undergoing biologic response modifier (BRM) therapy in these regions should be tested for VF before starting treatment (Galgiani et al., 2016). Public health officials are also working on implementing warning systems for dusty days, similar to poor air quality alerts (Matlock, 2019).

Few review papers are available on Coccidioidomycosis and its relation to climate change and dust. PubMed, ScienceDirect, and ProQuest are searched, and roughly 12 reviews are identified that are written over or include a section on VF and climate change or dust. An additional three papers are found but are not included in this study due to only including a very small section on the relationship between climate and dust or being written before 2007. The results of our review study and from these review articles are compared and summarized (Table 2). Most reviews on VF are written on the toxicology of the disease and not the epidemiology or ecology.

12. Conclusion

VF becomes more prevalent as the climate shifts (Roach et al., 2017). As areas with soils that support the growth and proliferation of *Coccidioides* expand due to climate change, the endemic region for VF is also spreading. In California and Arizona where VF is most prevalent, researchers are seeing an exponential increase in cases followed by an increase in the area affected (National Academies of Sciences, Engineering, and Medicine, 2023). The climate is altering dry and wet periods, causing an increase in the number of fungi in the soils (Cooksey, 2022). With projected increases in case numbers and expansion of endemic regions, the consequences of VF are imperative to be aware of, as the fungus may one day cost the country billions of dollars and the lives of countless individuals (Gorris et al., 2021).

Currently, there is no standardized, established warning system for VF outbreaks, and public education on the disease in endemic regions remains limited (Matlock, 2019). This poses a significant challenge as VF is projected to spread more rapidly in the coming years. Efforts are underway to create future risk messaging systems to notify the public of VF outbreaks, similar to existing alerts for poor air quality and flu risk (Matlock, 2019). Another challenge is the difficulty in accurately predicting future VF incidence. Factors such as population influx/growth, climate variations, especially fluctuations in precipitation and drying cycles, and activities that disturb dust all contribute to the unpredictability of VF cases. A county-level map illustrating the average VF incidence over the past 16 years has been made available to help identify endemic regions and enable faster diagnoses (Gorris et al., 2019). However, this analysis does not account for the impact of climate change or major weather events. Current models for predicting VF incidence suggest that long-term climate conditions are more important than short-term fluctuations (Kolivras & Comrie, 2003). Nonetheless, short-term events, such as localized wind or dust storms, may contribute to the unexplained variability observed in these models, as they are often excluded, creating limitations (Kolivras & Comrie, 2003). Developing a comprehensive predictive model that incorporates all relevant factors, both short- and long-term ones, is crucial for better preparing the public during high-risk periods.

Public health initiatives are increasingly focused on educating the public about VF prevention, as population growth exacerbates the impact of climate change on its spread; and this is particularly concerning as previously unexposed individuals mitigate to endemic regions, which heighten their risk (Gorris et al., 2019). Education efforts emphasize actions such as staying indoors on windy days, wetting dry soil, and wearing respirators to minimize exposure to the fungus (Matlock, 2019). However, some populations face unavoidable exposure due to natural disasters like dust storms, and many workers in high-risk areas also cannot avoid outdoor activities during these periods due to the nature of their jobs (Pearson, 2019; Matlock, 2019). For these at-risk groups, comprehensive education on coccidioidomycosis is being actively promoted. Despite these efforts, not all individuals in vulnerable occupations are receiving this critical information, highlighting the urgent need to expand outreach efforts to protect public health more effectively.

The spatial and temporal characteristics of the regions endemic to *Coccidioides* must be further evaluated to draw more accurate conclusions on the disease's expansion (Roach et al., 2017). Additional research needs to be conducted in this area to better understand how climate affects the endemic region and what can be done to help prevent the spread of VF. Information on the ecology of *C. immitis* and *C. posadasii* also needs to be gathered to better understand who it infects, how it is transmitted, and if there are underlying patterns in its life cycle. This information could help in understanding how this fungus could adapt to impending climate change and could aid in finding potential treatments for the disease.

It is important to note that other factors, such as population increase, commercial activity, animal vectors, dust storms, wildfires, wind patterns, and distribution of the fungus, affect the spread of Coccidioidomycosis (Roach et al., 2017). Along with expanding the endemic region, climate change also alters dust storms, wildfires, and wind patterns, contributing to the spread of VF (Andersen et al., 2023). A holistic approach that encapsulates each contributing factor, especially those affected by climate change should be carried out to more accurately model future projections of the disease. All the research included in this review in predicting the future implications of VF agrees that the changing climate has a role in spreading this disease. It is a driving force behind not only the incidence of the disease but the spread of it to regions that can support its growth.

It is imperative for additional research to be conducted on climate change and its relation to VF. This research could give insight into ways in which the spread of VF could be prevented amid a changing climate. Achieving a better understanding of how increased drought, temperatures, and dust events affect VF could give scientists and medical professionals alike the resources they need to make more precise predictions, send timely warnings, and protect public health in the Southwest US.

Table 2
This table lists and summarizes review papers on the relationship between climate change, dust, and VF or review papers with sections on the relationship between climate change, dust, and VF.

First Author, Year	Location	Year Range	Data Type	Exposure Source	Outcome	Results
This study	SW US	1998—2020	Review	Dust, climate change	Climate change is causing endemic regions to expand and the fungus to proliferate.	Climate change is impacting the spread of VF across and outside of endemic regions.
Michael D. Schweitzer, 2018	30° N and 30° S of equator	–	Review	Dust, dust storms, climate change	Larger dust particles can negatively impact health during dust storms. For instance, in Barcelona, Sahara dust storms were linked to an 8.4% increase in daily mortality for every 10 $\mu g/m^3$ rise in PM levels.	Dust storms are increasing due to climate change, and dust exposure may affect immunity to VF.
Daniel R. Kollath, 2019	Arid and semi-arid soils of SW US, Mexico, Central, and South America	–	Review	Drought, weather pattern, increased temperature, climate change	The rise in VF cases is associated with both the presence of certain animals and the desert climate. Endemic counties typically have average surface temperatures of at least 10 °C, while those with more than 6 cases per 100,000 people often experience temperatures exceeding 16 °C.	The drying of endemic regions, changing precipitation patterns, and warming trend may contribute to the increase spread of endemic regions and VF incidence.
Andrew C. Comrie, 2007	Southern Arizona	1992—2005	Sensitivity analysis	Dust, precipitation patterns	While climate variability does not fully account for the overall rise in VF cases, it did explain much of the year-to-year fluctuations in incidence between 1992 and 2005.	There is a strong relationship between climate change and VF incidence, but climate does not account for all of the increase.
Jorge Talamantes, 2007	Kern County, CA	1961—2002	Review and simple linear correlation analysis	Human activities, PM_{10}	In Arizona, VF incidence strongly correlates with climate, but this is not the case in California. The rising VF cases there are likely due to human activities, as 81% of PM_{10} in summer and 89% in winter are from anthropogenic sources.	The increase in VF incidence is due to human activities and not climate.
Andrew C. Comrie, 2021	Phoenix area of Maricopa County, AZ and Bakersfield area of Kern County, CA	2006—2020	Review and compositing analysis	Inhalation of spores from disturbed soil	An analysis of dust storms from 2006 to 2020 found no significant difference in VF cases between dust storm and non-dust storm conditions.	No relationship between VF and dust storms.
Daniel Q. Tong, 2022	AZ and CA	2006—2018	Review and quantitative trend analysis	Dust storms	In response to Comrie (2021), correcting data errors from Tong's (2017) study improved the correlation between dust storm frequency and VF cases, but the p-value remained below 0.001, leaving Tong's original conclusion unchanged.	Dust storms put people at risk for VF.
Dharshani Pearson, 2019	California	1940—2017	Review	Occupation location, natural disaster, drought and precipitation, human activities/land use	The increase in VF cases is due to climate change, shifting demographics, land use, and natural events. From 2008 to 2011, 19 out of 24 health districts in Kern County experienced VF a 100% to 1500% increases in VF cases compared to the 2000–2003 period.	Climate change, population movement, winds, and increased wildfires are contributing to the increase in VF cases.
Rafael Laniado-Laborin, 2012	Between 40° N and 40° S latitudes	–	Review	Human migration, human soil disturbance, precipitation pattern	VF affects more males than females, likely due to occupational exposure. In Arizona, 54% of VF cases from 2006 to 2008 were in males, and 46% in females.	Soil exposure is a major risk factor. This can be achieved by large groups of people moving to endemic states and increased soil disturbances caused by construction.
Chinh Nguyen, 2013	SW US, Mexico, Central America	–	Review	Precipitation, rodents	Precipitation pattern and rodent burrowing may impact the rise in VF more than dust storms. Endemic regions can shift over time, as shown by spherules found in a bison jaw from Nebraska about 8,500 years ago.	Wind and dust storms do not always correlate with the increase in VF cases. Precipitation patterns and rodent burrows may aid in spreading VF.
Jennifer Brown, 2013	CA, AZ, Mexico, Central America	–	Review	Changing climate (e.g., precipitation, drought), rodents, construction,	*Coccidioides*' life cycle is closely tied to climate patterns, leading to rising of VF cases outside traditional endemic areas.	Due to the increasing reach and infection rate of VF, more research is needed in order to better determine prevention measures that should be

(*continued on next page*)

Table 2 (*continued*)

First Author, Year	Location	Year Range	Data Type	Exposure Source	Outcome	Results
				human activity, natural disasters, windstorms	Isolated cases have been reported beyond these regions, including 23 in Ohio (1980–1998), 161 in New York State (1992–1997), two in Chicago with musculoskeletal involvement, and four in New Orleans.	taken to reduce the number of VF cases.
Nancy Crum, 2022	SW U.S. and parts of Mexico, Central America, and South America	–	Review	Earthquakes, dust storms, fires, construction, recreational activities, agriculture, military	Climate change and population movement are driving the increase in VF cases. From 1940 to 2015, 47 VF outbreaks occurred, with 25 (53%) linked to occupational exposure, half of which were related to construction work. Climate change could potentially increase VF cases by 164% by 2050.	Climate change and population movement are increasing VF incidence. The endemic region is expanding and the search for treatment and a vaccine is ongoing.
Ziad M. Shehab, 2010	SW US, Northern Mexico, parts of South and Central America	–	Review	Travelers, migration, climate, dust storms, natural disasters	Precipitation, dust index, wind, and drought all increase VF incidence. In Arizona, VF cases rose from 37 to 91 per 100,000 people between 1999 and 2006. In California, cases increased from 2.4 to 8.0 per 100,000 people from 2000 to 2006.	Coccidioidomycosis is underrecognized in highly endemic regions. Increased travel to endemic regions is causing VF to be seen outside of endemic regions.Climate explains a lot of the variability in VF incidence.

CRediT authorship contribution statement

Madelynn H. Howard: Writing – original draft, Visualization, Methodology, Investigation, Formal analysis, Data curation. **Christie M. Sayes:** Writing – review & editing. **John P. Giesy:** Writing – review & editing. **Yang Li:** Writing – review & editing, Validation, Supervision, Project administration, Funding acquisition, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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