Title
Mouldy Planet: Fungi and One Health

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Mouldy Planet: Fungi and One Health

Fungi are among the most diverse and versatile organisms on earth. Pathogenic fungi cause diseases in animals, humans and plants. They spread and survive long in the environment through spores. This case focuses on *Coccidioides imitis*, a pathogen that causes diseases in humans and animals, and survives in soils, thereby exemplifying the need for a One Health approach toward preventive strategies.

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Summary

Prevention of diseases caused by pathogenic fungi exemplifies the need for a One Health approach because a fungal species can cause similar disease in humans and animals and can survive long in the environment. This case study of coccidioidomycosis (valley fever) illustrates the power of integrative surveillance for One Health.

Abstract

Fungi belong to a taxonomically distinctive group of organisms that are among the most diverse, widely distributed and metabolically versatile organisms on earth. Physically, fungi range in size from microscopic yeasts, visible mould with colourful spores, and mushrooms, which may be larger than a human palm. Through their genetic profile and heterotrophy, fungi are more related to animals than to plants. Fungi can cause disease in humans, animals and plants, and they produce infectious forms such as lightweight spores, which can survive long in natural environments. Therefore, many diseases caused by pathogenic fungi are better understood and controlled through a transdisciplinary One Health approach. Fungi produce antibiotics such as penicillin, and they are also capable of developing resistance to many medications used to treat infections, making them a major threat to global health. This case study focuses on coccidioidomycosis (valley fever), an illness that develops from inhaling spores of the fungus *Coccidioides imitis* or *Coccidioides posadasii*, which are commonly found in soils of the south-western USA and in Central and South America, where the disease has been long recognized as a threat. Communities of people, pets and farm animals inhabiting periodically dry environmental conditions are particularly vulnerable, and investigators have suggested that the current incidence of the disease and the geographical expansion of zones of vulnerability are linked to climate change.[1] Improved understanding of the One Health context of valley fever should inform public communication strategies for preventing the disease.

What Is the Incremental Value that Makes This a One Health Case?

This case illustrates the significance of translational and implementation sciences in the One Health approach toward effective engagement of the public sector to prevent fungal diseases. Government agencies responsible for implementing risk reduction activities regarding climate-sensitive disease that affects people and pets need to carefully tailor public communication messages to include scientific uncertainties at the intersection of animal, human and environmental health, while advocating precautionary measures that support population-level behaviour change to lower vulnerability to infection by fungal pathogens.

Learning Outcomes

1. Demonstrating relationships among occupational and environmental risk factors for fungal diseases that affect humans and animals, which requires integration of qualitative and quantitative information across multiple disciplines and societal sectors.
2. Designing communication tools for preventing diseases in the One Health context requires framing messages that appeal to various audiences within vulnerable populations.
3. Projecting the temporal trend of fungal diseases is challenging because the environmental, human and animal parameters may not necessarily converge to predict future disease incidence, but long-term, integrative surveillance and interdisciplinary collaboration between veterinarians, human healthcare providers, environmental health and planetary scientists can lead to improvements in the predictive models.

Background and Context

Rationale

Human-related activities which release greenhouse gases into the atmosphere have abruptly accelerated the degree of climate change. As a result, the integrity of natural ecosystems and their interrelated functions are being compromised. Climate change is currently seen as an existential threat to all life forms on our planet. The public health threat is manifesting in part as a surge in emerging and resurging infectious diseases caused by bacterial, viral and fungal pathogens.[2] In the case of pathogenic bacteria, the growing threat of infections that are resistant to antibiotic therapy has long been recognized[3] and it is widely accepted that it cannot be contained without a One Health approach to solve the multi-faceted problem because of the abuse of antibiotics in healthcare and agriculture.[4] In the case of pathogenic viruses, the probable zoonotic origin of COVID-19 has exemplified a quintessential One Health challenge that demands co-ordination of intersectoral solutions. Until recently, pathogenic fungi have not been very visible in the context of health impacts of climate change, which demand improved understanding through the One Health approach. Increasingly, fungal pathogens have also become more resistant to traditional antifungal agents, and the zone of vulnerability to fungal infections appears to be expanding. For example, a new urgent threat of a pandemic is associated with *Candida auris*, a multi-drug-resistant yeast that causes invasive infection and death to humans.[5] *C. auris* was first identified in 2009, appearing simultaneously on three continents, and is considered a key example of a pathogen emerging from global climate change.[6] Curbing the pandemic potential of *C. auris* demands a One Health approach, considering the influence of environments at the interface of human and animal habitats, and demands improvements in the co-ordination of local and international strategies for pandemic prevention.

Recent assessments show that fungi are widely distributed in habitats jointly populated by people and animals, and the extent of species diversity in the fungal domain suggests a deep pandemic potential and disruptions to global health security.[7] Posing a threat of a recalcitrant disease in people and animals in susceptible environments is another fungal disease, valley fever (coccidioidomycosis), which exhibits all the features of a disease influenced by climate and demands a One Health approach to securing population health (Fig. 1). Presently, valley fever disease is prevalent in geographic zones limited to the western part of the USA and in Central and South America. The disease is common in arid regions where people and animals encounter and breathe in air-borne fungal spores. Humans and animals may manifest different symptoms of the disease. The factors that limit the range of the disease are not fully understood and there is evidence that the range is expanding, partly due to climate change.[8,9] Data on human coccidioidomycosis are incomplete because of variations in testing practices, misunderstanding of the disease symptoms, and gaps in epidemiological reporting. It is estimated that 10–50% of those living in endemic areas have been exposed to some form of the pathogenic fungi. The symptoms of coccidioidomycosis are similar to influenza in humans and might even be confused with COVID-19, although some differences may manifest in various patients depending on their immune status and trajectory of infection. Co-infection of coccidioidomycosis

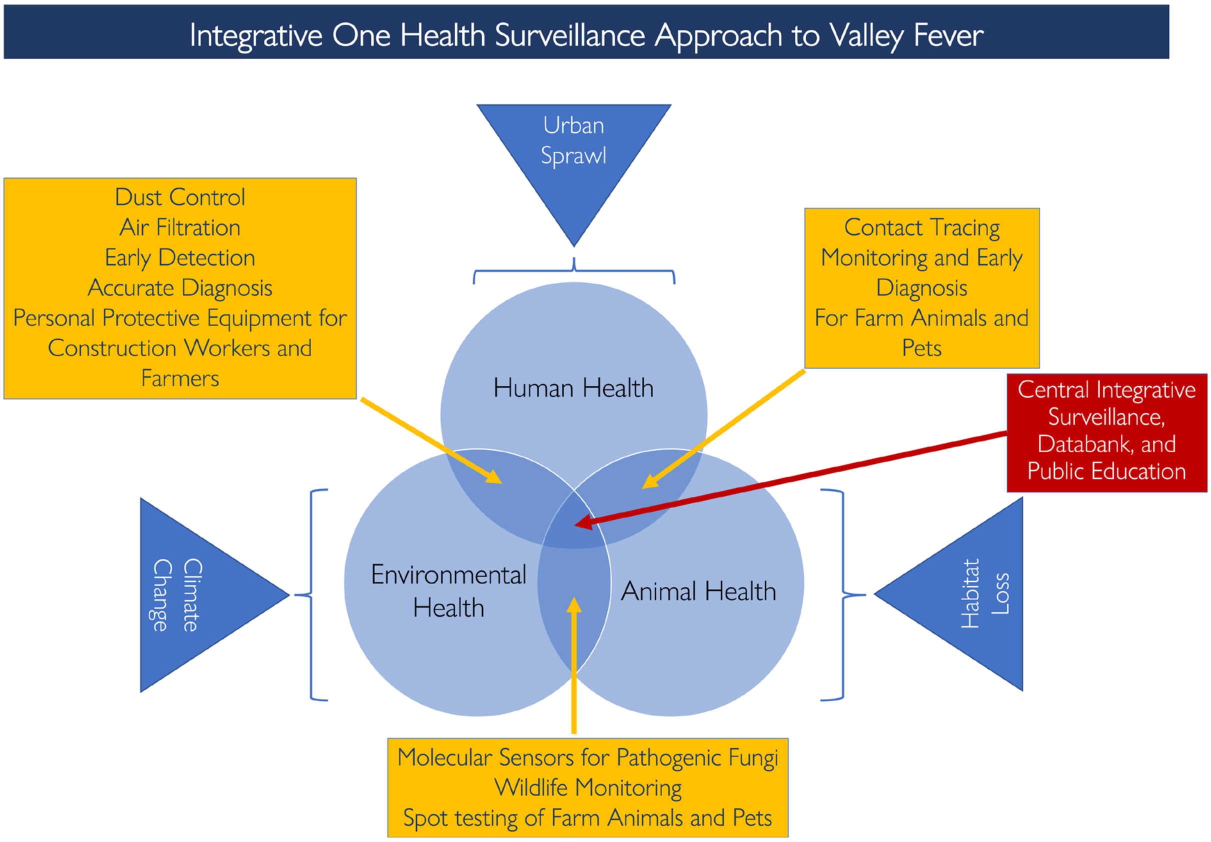

Fig. 1. A One Health approach to understanding the risk factors underlying vulnerability to Valley Fever in humans and animals includes integration of disease surveillance data and environmental monitoring data to generate predictive models of vulnerability and opportunities for preventive strategies including health communication and education campaigns targeted to stakeholders such as farmers, pet owners, construction workers, and municipal and regional healthcare agencies.

and COVID-19 have been reported, further complicating the categorization of common symptoms, including fatigue, cough, fever, headache, shortness of breath, muscle ache or joint pain, and resulting in similar post-exposure incubation periods.[10,11] There is no vaccine to prevent coccidioidomycosis, and diagnosed patients are typically prescribed antifungals for up to six months to relieve symptoms and clear the infection. In the continental USA, surveillance data show a clustering of coccidioidomycosis in the south-west region and a record number of cases in 2011 in Arizona, while a record number of cases in California were recorded in 2019 (Fig. 2).

Data on animal coccidioidomycosis is even more sparse than for human cases of the disease. In endemic regions, dogs are the most frequently reported animals to have the disease and to show severe symptoms. However, all animals, including horses, cattle and other livestock, can be affected when they breathe in an environment where fungal spores are aerosolized through disturbance of soil during farming operations or construction of infrastructure such as roads and buildings in urban regions. Among wildlife, coccidioidomycosis has been documented broadly, including in marine organisms.[12,13,14,15] Important to the One Health context is the potential role of rodents and small animals, which may move between human habitats and wildlife in perpetuating the fungus in environmental reservoirs.[16,17,18] Evidence is mounting that progressive climate change is fuelling more intense wildfires in regions inhabited by fungal pathogens associated with coccidioidomycosis. Frequent wildfires have increased the vulnerability of firefighters and first responders in the health sector. Additionally, scientists exploring the relatively new research field of pyroaerobiology are documenting the role of wildfires in dissemination of the fungal pathogens over wide geographic areas because the spores can survive the heat and they are sufficiently light to be transported in the smoke plume.[19,20]

People and animals develop valley fever after they breathe in dust from soil that contains fungal spores. Climate change causes increasingly frequent droughts, which create more dust. Earthquakes and building construction also mobilize dust to spread widely. Together, these factors increase people's vulnerability to valley fever. Public health education and communication campaigns are essential in strategies to reduce vulnerability to valley fever. For example, in the south-western USA, a case study on data collection and interpretation is underway to better predict pandemic threats posed by fungal pathogens, particularly valley

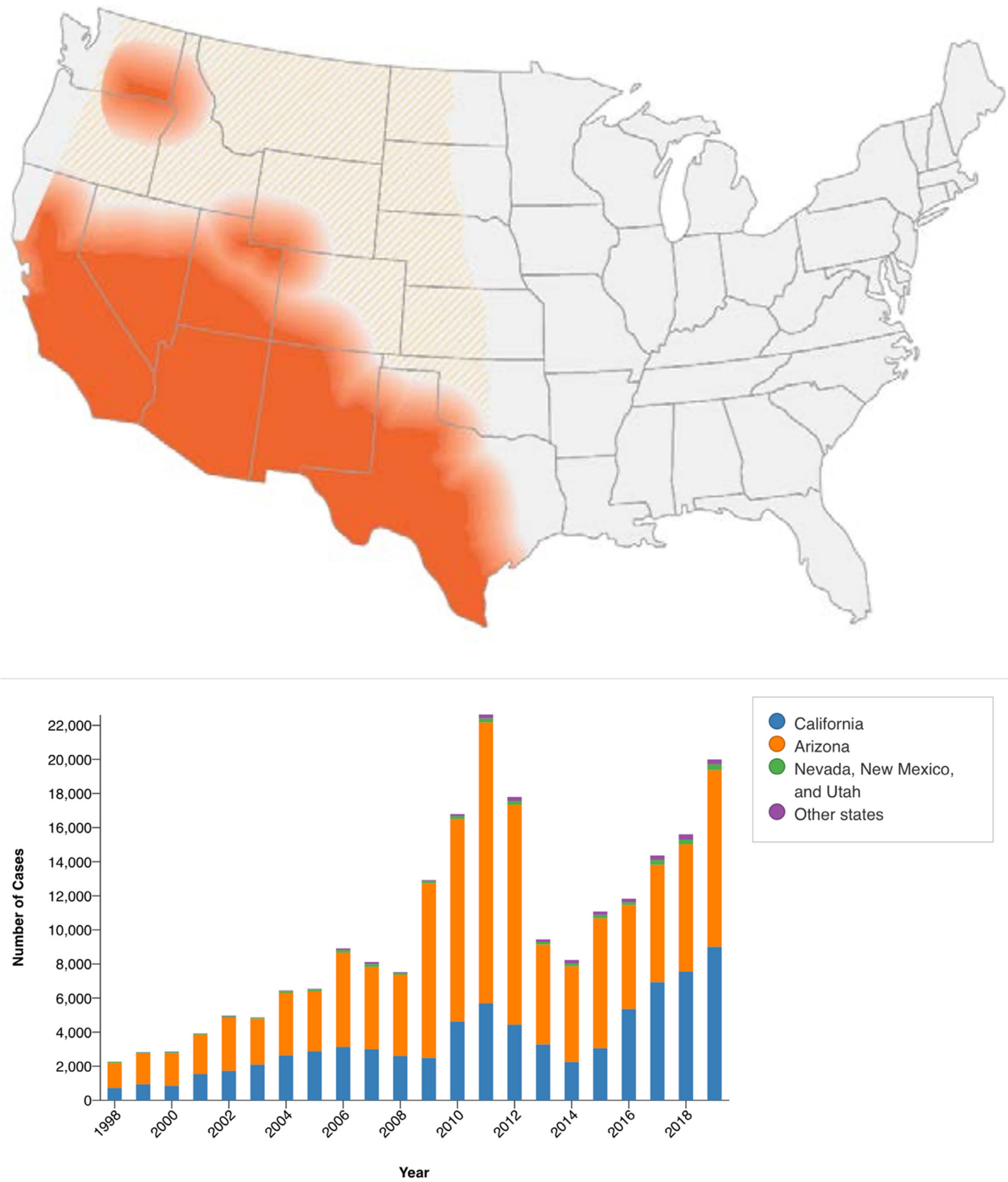

Fig. 2. Panel A: Current estimate of the geographic distribution of fungal etiologic agents of Valley Fever in environments within the United States. The global distribution of Valley Fever extends to northern Mexico, and parts of Central and South America; Panel B: The annual number of diagnosed Valley Fever cases in the U.S. is trending upward with expansion of the zone of vulnerability projected to increase due to the impacts of climate change. Change in the criteria for laboratory reporting was implemented in Arizona in 2009, which may be responsible in part for the rapid increase in the number of cases beginning that year (see: https://vfce.arizona.edu/sites/vfce/files/5-year-review-07-11.pdf). Map and data are from the U.S. Centers for Disease Control and Prevention.

fever, under the influence of climate change. The superimposition of epidemiologic data, climate data and social vulnerabilities is generating greater public awareness of the disease.[21,22]

Transdisciplinary Process

Cases of valley fever have increased steadily in the south-western USA, where the disease has been considered endemic for more than a decade. But the geographical scale of vulnerable populations is expanding as climate change enlarges the desert zones where *C. imitis* grows (Fig. 3). Valley fever disease exemplifies the need for a One Health approach to developing preventive strategies because it is important to co-ordinate assessment of environmental factors that enable the fungus to spread, while also monitoring the incidence of the disease in people and domestic animals, such as dogs, farm animals, such as horses,

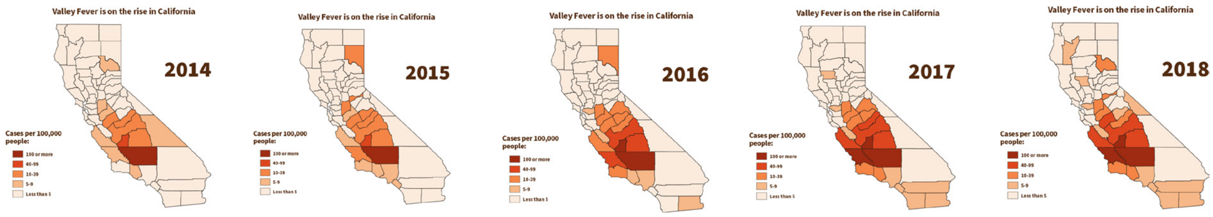

Fig. 3. The recently increasing geographic area of human population vulnerability to Valley Fever disease in California is attributable to climate change driving drought conditions which allow the fungal spores to spread. Maps collated from California Department of Public Health's public education campaign[i].California Department of Public Health. 2022. Valley Fever Basics. https://www.cdph.ca.gov/Programs/CID/DCDC/PublishingImages/Valley Fever/VF-Map.gif. Accessed 1 September 2022.

and wildlife. In addition to the technical skills and competencies needed by health personnel to understand the emergence and spread of valley fever, they also need functional skills and competencies such as risk communication, interprofessional collaboration, and partnerships to develop early-warning systems that can protect vulnerable populations and curb the spread of the disease. The ultimate goal of the case study is to identify information that could be used to create and establish early-warning systems including public communication campaigns targeting vulnerable populations and communities. The initial step is to explore the convergent influence of environmental variables hypothesized to increase population vulnerability in a designated region. The results of such explorations should help develop effective strategies for community engagement and communication toward changing behaviours that put individuals and animals at risk of infection.

Transdisciplinary technical competency activities: quantitative modelling of coccidioidomycosis and climate

Public health preparedness benefits from the development of location-specific models for disease outbreaks and the development of community-based education, and interventions that target vulnerable populations to decrease risk. The understanding of risks posed by coccidioidomycosis requires a transdisciplinary integration of quantitative data and qualitative information that (i) has seasonal environmental significance, such as climate; (ii) crosses government agency boundaries, such as dust; and (iii) involves a disease that manifests itself differently in animals and people and is often misdiagnosed. It is important to carefully select essential factors and methods to generate reliable determinants and trajectories of disease (Fig. 4). For example, through a review of published research we tested the strengths of association between various environmental factors and coccidioidomycosis incidence. The variables of interest can be divided into three main categories: ecological niche, risk factors related to human traits, and environmental/climate factors. The risk factors related to human traits include variables such as gender, ethnicity, age, immunosuppression and occupation (including working with animals, firefighting, construction and landscaping). The environmental/climate factors include precipitation, wind, dust, temperature, Palmer Drought Severity Index (PDSI), and the Normalized Difference Vegetation Index (NDVI). We investigated these variables across counties in California where the reported trends of disease have been on an upward trajectory.

Transdisciplinary functional competency activities: stakeholder engagement and communication strategies

The maps presented in Fig. 3 show that, by 2018, 25 of the total of 58 counties in California had 5–9 cases of valley fever per 100,000 people, while three counties had more than 100 cases per 100,000. The California Department of Public Health is responsible for collating disease incident data, statewide, and the department publishes information about the disease on its website. However, county-level agencies dedicated to public health are expected to develop strategies for stakeholders and community engagement strategies for communicating with vulnerable groups with the goal of modifying behaviour and risk factors to prevent the disease. The fact that the incidence of valley fever has been on the upward trajectory for more than a decade, and the number of counties reporting the disease has also increased, indicates that more needs to be done for prevention. In this case study, five counties were targeted to better understand barriers to communicating risk to their communities given the modelling data showing the possibility of predicting outbreaks. We investigated Fresno, Kern, Kings, San Luis Obispo and Tulare counties. We interviewed key personnel at the respective county public health agencies to assess their use of epidemiological data and the strategies they use to communicate disease information including

Fig. 4. Scatterplot of the Log of Valley Fever Cases by Diagnosis Date (Y-axis) by the Log of Climate Factors (X-axis) in Each County Included in the Case Study.

outbreaks and early warning systems. We also reviewed the public information available on the agency websites regarding currency and comprehensiveness of risk communication regarding valley fever (Fig. 5).

Public information provided by the counties varied in the extent to which they capture the One Health approach, including human health, animal health and environmental factors, and on the presentation of epidemiological data, geographic information systems data, and qualitative textual information. For example, Fresno and Kings counties made no reference to animals and included air quality and dust as environmental factors. Kern county noted that people and animals can get sick when they breathe in dust that contains the fungus that causes valley fever, and refers to dust exposures. Tulares county noted that valley fever is not contagious and cannot be contracted from another person or from animals, while referencing inhabiting dry desert zones as a risk factor. San Luis Obispo county provided the most One Health-oriented information, with clear statements about dry, windy and dusty environmental conditions, while also providing the most extensive statements regarding the vulnerability of animals to the disease through responding to the question of whether people can contract valley fever from their dog:

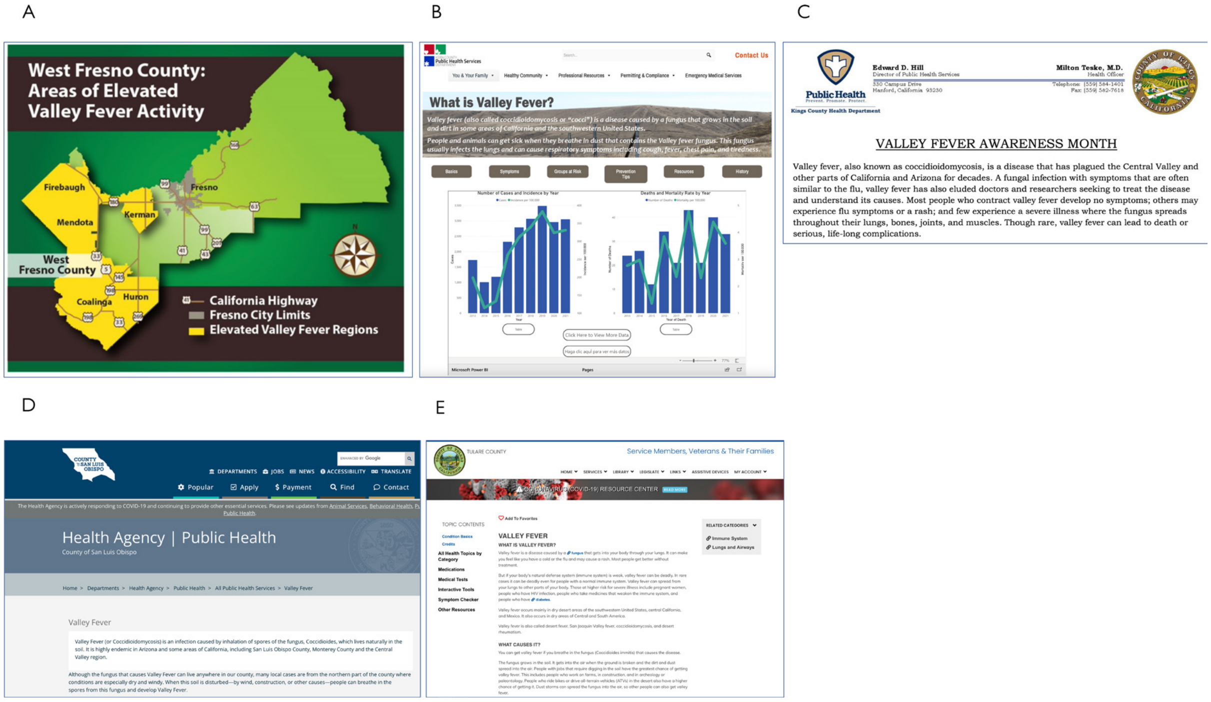

Fig. 5. Public information to communicate risks of Valley Fever in five counties in California show variations reflecting target audiences, and gaps in adoption of the One Health framework to include animal health, environmental health, and human health. Information provided to the public also varies in the use of quantitative data, geographic visualization, and qualitative text. Panel A: Fresno County[i]. Panel B: Kern County[ii]. Panel C: Kings County[iii]. Panel D: San Luis Obispo County[iv]. Panel E: Tulare County[v]. All websites were accessed on 23 September 2022.

Dogs, cats, horses and other animals can become infected with Valley Fever the same way people can. Similar to people, most dogs do not experience any symptoms and naturally fight off the infection. Some dogs become sick – with symptoms such as coughing, weight loss, and fatigue – and some experience the more serious form of the disease that spreads throughout the body. After a diagnosis of Valley Fever, your veterinarian may prescribe a treatment of oral antifungal medication.

These variations in public communication provide the opportunity to refine communication approaches for fungal diseases within the One Health approach and to better integrate qualitative and quantitative information in public health communication strategies. The design of effective communication strategies has long been a subject of translational research to apply theoretical frameworks in the social sciences.[23,24,25] In general, certain principles underpin effective public health communication to influence behaviours toward disease prevention, namely: identification and characterization of the targeted behaviour; effective strategy for ensuring that people are exposed to the message; adopting an all-inclusive approach; and routinizing media exposure. In addition, lessons being learned from the failures of communication strategies deployed during the COVID-19 pandemic show that top-down unidirectional communication approaches are not effective and are subject to corruption and misinformation.[23] In the One Health approach, an important difference exists between health communication strategies for influencing behaviour depending on whether the targeted infectious diseases can be transmitted directly from person to person (for example, COVID-19) or diseases such a valley fever, which is associated with direct contact with environmental media such as dust and is not known to be contagious from infected to healthy individuals. Therefore, the stress levels associated with social distancing and quarantine may be relaxed in the case of valley fever, whereas the stress associated with the inability to work for prolonged periods in certain occupations, including farming, construction, landscaping, firefighting and veterinary medical practice, may be heightened for valley fever. Ideally, targeting vulnerable sub-populations with information about the risk of contracting valley fever and personal prevention strategies should be active dialogues with communities, including the social context of the disease, rather than passive presentations focusing only on the scientific facts of the disease. Communication in local languages and consideration for educational backgrounds and sociocultural factors are important, particularly in low-income and immigrant communities. Messages should be pre-tested in focus groups, and communication should be implemented frequently with clear opportunities for anonymous feedback.

Project Impact

As the geographical zone of vulnerability to valley fever expands due to prolonged and more extensive droughts related climate change, several more counties in California have had to develop strategies to be ahead of outbreaks through better use of predictive models. Counties have also had to refine existing public communication messages or develop new ones to emphasize the need to protect humans and animals in vulnerable environments. Inadequacy of funds needed to control fungal diseases was cited as an impediment, especially in comparison to the substantially larger public funds allocated to viral and bacterial diseases. With improved understanding of the long-term impacts of valley fever on communities, agencies are collaborating to ensure that resources necessary to curb the spread of the disease are provided at the state level.

Project Outlook

Increasing recognition that climate change is forcing the emergence of new diseases and the resurgence and spread of diseases previously marginalized will likely enhance the salience of fungal diseases such as valley fever.[8] The spread of drug-resistant fungal pathogens will also contribute to the level of importance of this topic among researchers and pharmaceutical companies. Gaps in the adoption of the One Health approach will require education targeting the public health workforce to keep fungal pathogens from causing another pandemic.

Conclusions

Pathogenic fungi are widely distributed in the environment. Human and animal exposure to fungi in spore forms has the potential for widespread distribution, particularly because changes in environmental factors are the most likely explanation for the geographical spread of the zone of vulnerability. This is the reason why diseases such as valley fever are ideal candidates for studying the impacts of climate change. Several climate variables correlate with the epidemiological data, and it is important to integrate quantitative and qualitative information for developing public health communication campaigns for effective disease prevention strategies.

Group Discussion Questions

1. Describe why disease outbreaks caused by fungal pathogens such as *Coccidioidomyces imitis* are likely to become more challenging to control under scenarios of abrupt climate change.
2. Describe the main reason to adopt a One Health approach in understanding the risk factors for fungal diseases such as valley fever. What are the possible limitations of the approach in disease prevention?
3. Describe the main components of effective public health education and communication campaigns to curb the incidence and spread of fungal diseases in the One Health approach. What are some limiting factors encountered by public health agencies in implementing effective communication?

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