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Prolonged coccidioidomycosis transmission seasons in a warming California: a Markov state transition model of shifting disease dynamics

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Coccidioidomycosis, an emerging fungal disease in the southwestern United States, exhibits pronounced seasonal transmission, yet the influence of current and future climate on the timing and duration of transmission seasons remains poorly understood. We developed a distributed-lag Markov state transition model to estimate the effects of temperature and precipitation on the timing of transmission season onset and end, analysing reported coccidioidomycosis cases (n = 72 125) in California from 2000 to 2023. Using G-computation substitution estimators, we examined how hypothetical changes in seasonal meteorology impact transmission season timing. Transitions from cooler, wetter conditions to hotter, drier conditions were found to significantly accelerate season onset. Dry conditions (10th percentile of precipitation) in the spring shifted season onset an average of 2.8 weeks (95% CI: 0.43–3.58) earlier compared with wet conditions (90th percentile of precipitation). Conversely, transitions back to cooler, wetter conditions hastened season end, with dry autumn conditions extending the season by an average of 0.69 weeks (95% CI: 0.37–1.41) compared with wet conditions. When dry conditions occurred in the spring and autumn, the transmission season extended by 3.70 weeks (95% CI: 1.23–4.22). With prolonged dry seasons expected in California with climate change, our findings suggest this shift will extend the period of elevated coccidioidomycosis risk.

1. Introduction

Coccidioidomycosis, also known as Valley fever, is a fungal infection caused by inhalation of soil-dwelling *Coccidioides* spp. Infection typically results in respiratory illness with symptoms including cough, fever and fatigue, and in severe cases may result in meningitis or death [1]. In recent years, coccidioidomycosis incidence has been rising across the southwestern USA [2], including in California, where incidence increased over eightfold between 2000 (2.5 per 1 00 000 population) [3] and 2021 (20.1 per 1 00 000 population) [4]. Coccidioidomycosis—like most infectious diseases [5–7]—exhibits seasonal trends in

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incidence, generally rising in the mid- to late summer, peaking in the autumn and winter, and returning to baseline levels in the spring months [8–10]. However, this pattern is variable across years, with some years displaying a seasonal rise and fall in incidence while others displaying stable high or low incidence throughout the year, and across geographies [9], with some regions displaying more consistent seasonal patterns than others, and the role of climate variability in structuring transmission seasons remains unclear [8–13]. Recent work found that counties in California's southern San Joaquin Valley exhibit relatively earlier coccidioidomycosis seasons than those in the northern San Joaquin Valley, Central Coast and Southern Coast regions [13]. Determination of the precise onset and duration of—and heterogeneity in—coccidioidomycosis transmission seasons, however, would enable targeted risk communication and efforts to mitigate seasonal increases in disease incidence and associated healthcare utilization [14,15].

Seasonal shifts in temperature and precipitation initiate *Coccidioides*' transition from mycelia to arthroconidia—the latter of which is more readily aerosolized and inhaled—probably contributing to seasonal differences in human incidence rates [8–10]. Arthroconidia form when alternating cells within the filamentous mycelia differentiate to form spores, partly in response to environmental stress such as increased temperatures and moisture deficits [16]. What is more, arthroconidia can become aerosolized through wind erosion or soil disturbance and disperse via dust, and precipitation deficits are known to promote mineral dust and arthroconidia dispersal [16–19]. Accordingly, hot, dry conditions in the summer have been linked to an increased incidence in the autumn in California [9,10,12], probably due to increased arthroconidia formation and aerosolization. Earlier onset of these conditions—as is expected under climate change [20]—may lead to an earlier onset of the coccidioidomycosis transmission season. In contrast, precipitation may remove airborne arthroconidia via wet deposition [21] and may limit the aerosolization of arthroconidia by increasing soil resistance to wind erosion due to higher interparticle capillary forces [22]. Delayed onset of rainy seasons—such as is indicated by climate projections in California [20,23]—may therefore permit continued aerosolization of *Coccidioides* spores, extending the transmission season. California's climate has exhibited substantial intra- and inter-annual variability in recent decades, including changing frequencies and intensities of phenomena such as droughts and atmospheric rivers that have important implications for coccidioidomycosis transmission [10]. However, little is known about how meteorological conditions influence the timing and duration of coccidioidomycosis transmission seasons.

Here, we leverage fine-scale coccidioidomycosis incidence data to investigate how meteorological factors influence coccidioidomycosis season timing in California. We estimate the associations between temperature and precipitation and the timing of the coccidioidomycosis season onset and end using a multi-state distributed-lag Markov modelling approach. We test the hypotheses that: (i) hotter, drier conditions in the spring shift the onset of the coccidioidomycosis transmission season earlier and (ii) hotter, drier conditions in the autumn, corresponding to a delayed onset of the rainy season, prolong the coccidioidomycosis transmission season. Improved understanding of meteorological influences on the seasonal timing of *Coccidioides immitis* infections in California can strengthen public health campaigns by improving the accuracy and timing of risk communication and supporting the projection of intra-annual incidence patterns in the context of anticipated climate changes in California in the coming decades [24].

2. Methods

2.1. Epidemiological and meteorological data

We obtained data on confirmed coccidioidomycosis cases reported in California between 1 January 2000 and 1 April 2023, from the California Department of Public Health's reportable disease surveillance system [3]. Since 1995, healthcare providers and laboratories have been required to report confirmed coccidioidomycosis cases—along with patient information, including residential address—to local public health authorities through this system. We calculated weekly incident cases at the census tract level based on the estimated date of disease onset and offline geocoding of each case's residence [25]. Approximately 98% of cases could be geocoded to the tract level. To reduce exposure misclassification resulting from case geolocation to census tracts of residence, we restricted our analysis to census tracts located in areas with more than 500 total cases and average annual incidence rates greater than eight cases per 100 000 population. In most cases, these areas corresponded to counties, but some counties spanning divergent geographical and meteorological profiles were split into sub-counties along 500 m elevational isoclines (figure 1A), as done previously [10]. We obtained daily, 4 km gridded precipitation and temperature estimates between 2000 and 2023 from the precipitation-elevation regressions on independent slopes model (PRISM) [26], and calculated weekly total precipitation and average temperature for each census tract (figure 1C,D).

2.2. Classifying seasonal transmission years

We defined the coccidioidomycosis transmission year as spanning the average annual minima of coccidioidomycosis incidence (1 April–31 March). To restrict our analysis to transmission years exhibiting a seasonal pattern, we first classified each census tract-transmission year as seasonal or aseasonal. To do so, we fit models of weekly incidence as a function of linear time excluding and including additional harmonic terms with 52-week periods (capturing annual seasonality between 1 April and 31 March) to the incidence time series for each census tract and transmission year. We used Akaike's information criterion (AIC) [27] to determine whether each tract-year's data were better described by the model excluding or including harmonic terms, classifying as seasonal all tract-years where the harmonic model was preferred (figure 1B). We excluded from further analysis 685 census tracts (53%) where no years were classified as seasonal during the study period.

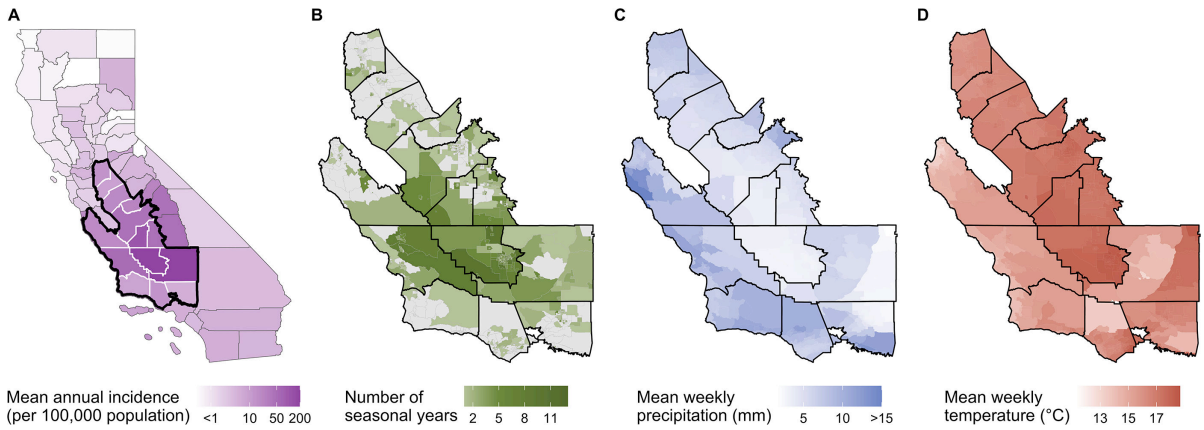

Figure 1. (A) County-level mean annual incidence of coccidioidomycosis between 2000 and 2023; counties outlined in black met the inclusion criteria (greater than 500 cases and greater than 8 cases per 100 000 population between 2000 and 2023) and sub-region designations are outlined in white. (B) Census tracts within the study area, coloured by the number of transmission years exhibiting a seasonal incidence pattern over the study period; grey census tracts did not exhibit a seasonal pattern in incidence over the study period and were excluded from further analysis. (C) Average weekly precipitation (mm) over the study period among census tracts in the study area. (D) Average weekly temperature (°C) over the study period among census tracts in the study area.

2.3. Estimation of season onset and end

Among census tract-transmission years classified as seasonal, we estimated the week of season onset and end using segmented regression [28,29], which has been previously applied to influenza and other seasonal infectious diseases [14,28,29]. The segmented regression approach involves partitioning transmission years into pre-peak and post-peak periods, then fitting piecewise linear trend lines to the incidence time series with a single breakpoint each. The location of the breakpoint that achieves the best model fit marks the estimated onset or end of the transmission season (electronic supplementary material, figure S1B). As the results of our analysis may be sensitive to this method of season onset and end estimation, we also estimated onset and end dates using the maximum curvature method [14], which estimates season onset and end as the point of maximum curvature (reciprocal of the radius of the osculating circle) in the increasing and decreasing phases of the weekly time series, respectively (electronic supplementary material, figure S1A), and conducted our analysis using estimates from both methods. To limit the influence of noise on season onset and end estimation, we applied a kernel smoothing function to the incidence time series with the bandwidth set to 8, as this bandwidth was the smallest value at which changes in estimates stabilized below 1 week on average compared with the next smallest bandwidth value (electronic supplementary material, figure S2).

2.4. Markov models of meteorological effects on coccidioidomycosis season onset and end

To analyse the effects of temperature and precipitation on the timing of season onset and end, we modelled all weeks of each census tract's coccidioidomycosis incidence time series as a Markov process governed by two seasonal states: (i) an aseasonal state where cases are stable over time and (ii) a seasonal state where incidence increases to a seasonal peak before declining back to stable levels (figure 2). Using estimates of season onset and end timing (see above), we classified each week as belonging to state 1 if it occurred either before season onset or after season end and state 2 if it occurred between season onset and season end (electronic supplementary material, figure S3). All weeks in aseasonal transmission years were classified as belonging to state 1, such that the entire time series for each census tract was modelled as a continuous Markov process.

Per the Markov assumption, the current state of a Markov process is dependent only upon the state of the previous time step [30]. Time-inhomogeneous Markov models relax this assumption by allowing the instantaneous probability of transition between states to vary in relation to time (t) and time-varying predictors ($z(t)$) [30]. For our analysis, transitions are governed by the transition probability matrix

$$P = \begin{pmatrix} p_{11}(t \mid z(t)) & p_{12}(t \mid z(t)) \\ p_{21}(t \mid z(t)) & p_{22}(t \mid z(t)) \end{pmatrix}, \tag{2.1}$$

where p_{11} represents the instantaneous probability of a week that was previously in state 1 staying in state 1; p_{12} represents the instantaneous probability of a week that was in state 1 during the previous week transitioning to state 2 and so on. We modelled each transition probability using a proportional hazard model with the following general form:

$$p_{rs}(t|z(t)) = p_{0rs}(t)e^{\boldsymbol{\beta}_{rs}^{T}\mathbf{z}(t)}. \tag{2.2}$$

Here, the instantaneous probability of transition from state r to state s (p_{rs}) at time t is calculated as the product of the baseline transition probability (p_{0rs}) and a log-linear function of time-varying and time-invariant covariates ($\mathbf{z}(\mathbf{t})$) with a vector of coefficients for each pair of states ($\boldsymbol{\beta}_{rs}$) (electronic supplementary material, figure S3). Our set of covariates included lagged temperature and precipitation as well as terms for county and year. Due to the incubation period of coccidioidomycosis (1–3 weeks) [31] and delays in case reporting [32,33], we anticipated individuals to be exposed for 1–12 weeks before appearing

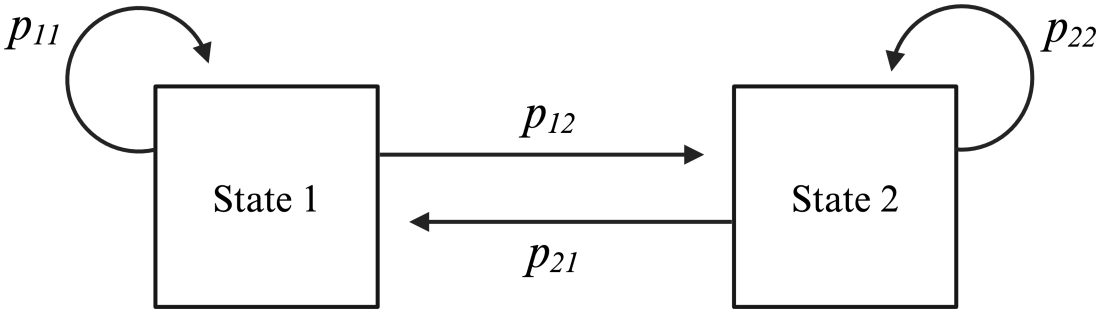

Figure 2. Schematic of Markov state transition process. p_{12} indicates the transition from an aseasonal state to a seasonal state (i.e. season onset), and p_{21} indicates the transition from a seasonal state to an aseasonal state (i.e. season end).

in the surveillance record. Thus, to estimate the immediate and delayed effects of temperature and precipitation on season onset and end, we used a distributed-lag nonlinear (DLNM) modelling approach to estimate the effect of temperature and precipitation lagged by 2–26 weeks [34]. Our model of season onset and end took the following form for $z(t)$ in equation (2.2):

$$\boldsymbol{z}(\boldsymbol{t}) = \left[\boldsymbol{cb}(P_{t,j}), \boldsymbol{cb}(T_{t,j}), \text{year}_t, \text{county}_j\right], \tag{2.3}$$

where the primary environmental exposures of interest, $T_{t,j}$ and $P_{t,j}$, are the mean temperature and total precipitation in week t in census tract j. Here, $\boldsymbol{cb}$ indicates a matrix of cross-basis functions, in which we modelled the exposure–response relationships between lagged environmental covariates and the outcome as linear, and constrained the lag–response relationship (2–26 weeks) to follow a natural cubic spline with three degrees of freedom. Models were adjusted for county and year to account for secular trends across the study area and study period, respectively.

2.5. Estimating changes in seasonal onset and duration under counterfactual scenarios

We estimated the effects of hypothetical changes in seasonal meteorological conditions on transmission season timing using G-computation substitution estimators derived from our fitted Markov models [22,35]. To test our hypotheses, we estimated the expected coccidioidomycosis season onset timing under wet versus dry spring conditions and the expected season duration under wet versus dry autumn conditions. These scenarios were selected because climate projections in California indicate a sharpening of the rainy season (i.e. reductions in both autumn and spring precipitation alongside increases in winter precipitation), resulting in a prolonged dry season [20,23]. We simulated dry and wet spring conditions by first calculating the cumulative distribution of observed spring (March–May) precipitation for each census tract and identifying the years in our study period where each census tract experienced the 10th and 90th percentile of spring precipitation. We then deterministically set the precipitation and temperature for each week to their observed values for the transmission year following a dry spring (10th percentile) or a wet spring (90th percentile). We simulated dry and wet autumn conditions by calculating the cumulative distribution of observed autumn (September–November) precipitation for each census tract and identifying the years in our study period where each census tract experienced the 10th and 90th percentile of autumn precipitation. We then deterministically set the precipitation and temperature for each week to their observed values for the transmission year that experienced a dry autumn (10th percentile) or a wet autumn (90th percentile).

To estimate the expected time of coccidioidomycosis season onset and end (T) from instantaneous transition probabilities, we first calculated cumulative probabilities of transition prospectively from the start of the transmission year, for season onset, and from the estimated season onset, for season end (equation (2.4)), with precipitation and temperature, $\boldsymbol{A_{i,t}}$, and other covariates, $\boldsymbol{W_{i,t}}$, deterministically set to their observed values during dry and wet conditions

$$\Pr(T \le t | p_{0rs}(t), \boldsymbol{A_i}, \boldsymbol{W_i}) = 1 - \prod_{t=1}^{t} 1 - p_{rs}(t, p_{0rs}(t), \boldsymbol{A_{i,t}}, \boldsymbol{W_{i,t}}). \tag{2.4}$$

We derived distributions of census tract onset times and season durations as the inverse, or quantile function, of onset and end cumulative probabilities over time. For each counterfactual contrast, we Monte Carlo simulated 10 000 onset times and durations for each condition, then empirically estimated the 2.5th, 50th and 97.5th percentiles of the distribution of the mean differences in timing between conditions of interest across census tracts.

2.6. Sensitivity analyses

Because case data are over-dispersed such that zero cases were recorded in many weeks in many census tracts, reducing our ability to reliably detect season onset, we replicated our analysis after aggregating cases and covariates to the county (or sub-county) level and assessed the congruity of county-level and census tract-level results. To examine the sensitivity of our results to the methods of estimating season onset and end timing (i.e. segmented regression and maximum curvature), we compared results generated using timing estimates from both methods at census tract and county (sub-county) spatial

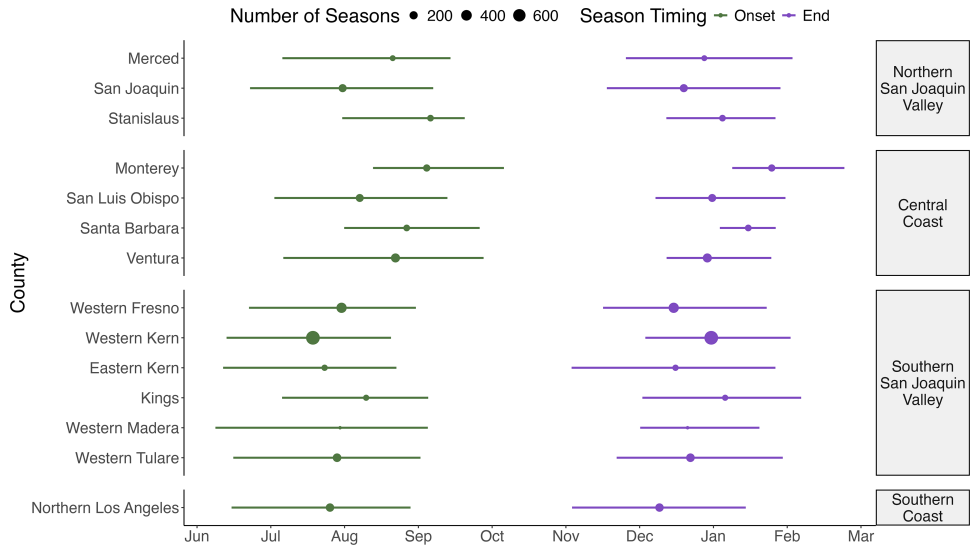

Figure 3. Comparison of transmission season timing across counties. Points represent average season onset (green) and end (purple) times within each county, nested within regions. Whiskers indicate the interquartile range of the estimated distributions. The size of the points corresponds to the number of seasonal tract-years within each county.

resolutions. Lastly, to assess the robustness of our results to confounding by other factors that fluctuate seasonally, we replicated our analysis after including a periodic B-spline for a week in our models.

All analyses were conducted in R v. 4.2.2 [36]. Piecewise linear regressions were fit using the *segmented* package [37], distributed-lag cross-bases were created using the *dlnm* package [38] and multi-state Markov models were fit using the *msm* package [30].

3. Results

3.1. Spatial and temporal patterns of transmission season timing

Between 1 January 2000 and 31 March 2023, there were a total of 72 269 cases of coccidioidomycosis recorded in the study region. Among the counties included, western Kern County had the highest average annual incidence rate (227 per 100 000 population), while Santa Barbara County had the lowest (8.6 per 100 000 population). Only census tract-years with at least two cases (29.1%) exhibited a seasonal pattern, and of those, we identified 1592 seasonal tract-years (18.5%).

On average, season onset and end occurred on weeks 17 (approx. 29 July, s.d. = 7.8 weeks) and 38.4 (approx. 26 December, s.d. = 6.9 weeks) of the transmission year (1 April– 31 March), respectively, and mean season duration was 22.4 weeks (approx. 5.2 months, s.d. = 7.3). There was substantial heterogeneity in transmission season timing over the study period, with average season onsets ranging from week 10.0 (approx. 10 June) in 2002 to week 19.2 (approx. 14 August) in 2013, and season ends ranging from week 31.7 (approx. 9 November) in 2002 to week 40.8 (approx. 12 January) in 2005. Average annual season durations ranged from 17.5 weeks (approx. 4.0 months) long in 2000 to 24.0 weeks (approx. 5.5 months) long in 2005. The number of census tracts classified as seasonal varied substantially over time, with a minimum of 19 in 2000 and a maximum of 206 in 2017.

Spatially, western Kern had the earliest average season onset (week 15.5 (approx. 19 July)), whereas Stanislaus had the latest (week 22.4 (approx. 5 September); figure 3). Northern Los Angeles had the earliest average season end (week 35.8 (approx. 8 December)), whereas Monterey had the latest (week 42.4 (approx. 24 January); figure 3). Stanislaus had the shortest average season duration (18.2 weeks (approx. 4.2 months)), while western Kern had the longest (24.4 weeks (5.6 months)). There was substantial spatial variation in the number of tract-years classified as seasonal across the study period, with Stanislaus having the fewest (19) and western Kern having the most (648).

3.2. Effects of precipitation and temperature on transmission season onset

Census tract-level distributed-lag inhomogeneous Markov state models indicated that temperature and precipitation had distinct, lag-specific influences on transmission season timing (figure 4; electronic supplementary material, table S1). Increases in precipitation (adjusted for temperature) were associated with decreased onset probability at shorter lags and increased probability at longer lags. Increases of 10 mm in precipitation were associated with decreased onset probability at 2–14 week lags (minimum hazard ratio (HR) at 2 week lag: 0.94; 95% CI: 0.91–0.97) and increased onset probability at 19–26 week lags (maximum HR at 26 week lag: 1.06; 95% CI: 1.04–1.06). In other words, we estimated that a 10 mm increase in precipitation reduced the instantaneous probability of the coccidioidomycosis season starting two weeks later by 6%. The effects of increasing temperature (adjusted for precipitation) were roughly opposite to that of precipitation; higher temperatures were associated with increased onset probability at short lags and reduced onset probability at longer lags. A 1°C increase in temperature was

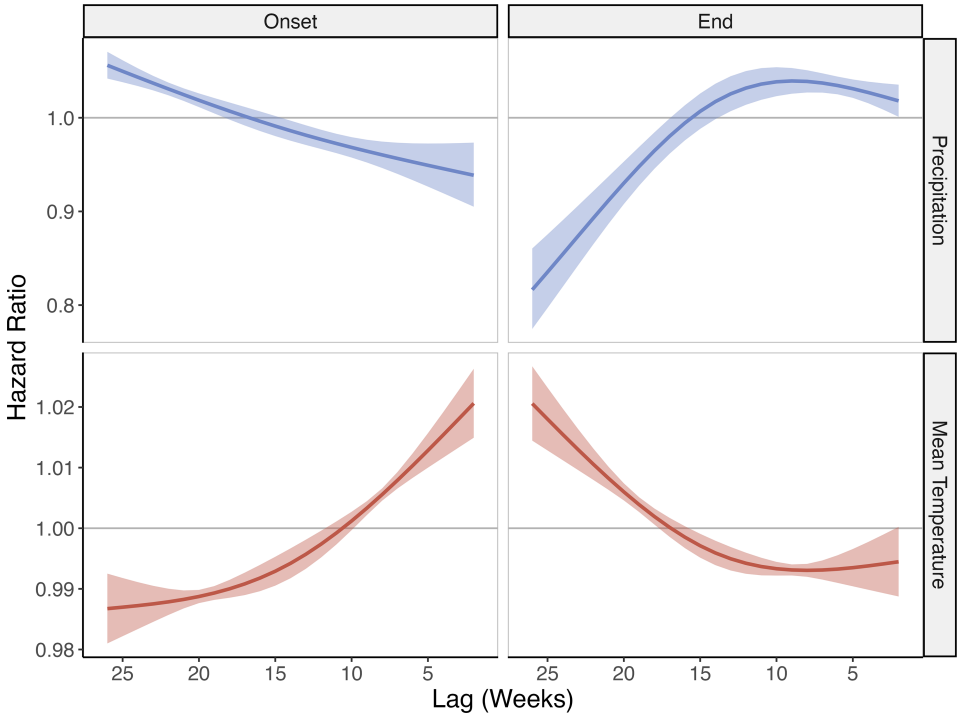

Figure 4. Hazard ratios associated with 10 mm increases in precipitation and 1°C increases in temperature on coccidioidomycosis season onset (left column) and end probabilities (right column) at 2–26 week lags from distributed-lag inhomogeneous Markov models. Shaded regions represent 95% confidence intervals.

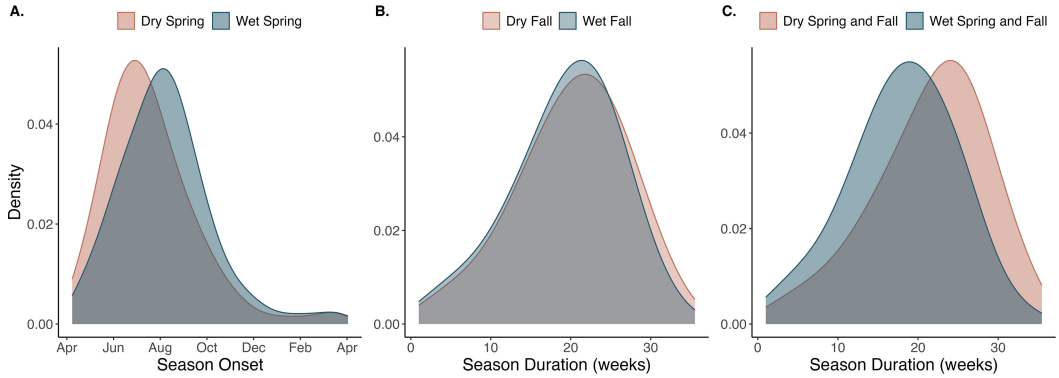

Figure 5. Distributions of (A) simulated season onset times given dry (brown) and wet (blue) spring conditions, (B) simulated season durations given dry (brown) and wet (blue) autumn conditions and (C) simulated season durations given both dry (brown) and wet (blue) spring and autumn conditions based on G-computation substitution estimators.

associated with increased onset probability at 2–9 week lags (maximum HR at 2 week lag: 1.02; 95% CI: 1.01–1.03) and decreased probability at 12–26 week lags (minimum HR at 26 week lag: 0.98; 95% CI: 0.98–0.99; figure 4). In other words, we estimated that a 1°C increase in temperature increased the instantaneous probability of the coccidioidomycosis season starting two weeks later by 2%.

Based on G-computation substitution estimators, we estimated that dry spring conditions (10th percentile of precipitation) shifted the transmission season onset 2.80 weeks earlier on average (95% CI: 0.43–3.58 weeks; figure 5A) compared with wet spring conditions (90th percentile of precipitation). Dry spring conditions reduced the probability that a given year would be seasonal; the maximum cumulative probability of season onset was lower when the spring was dry (9.3%) compared with when it was wet (7.7%).

3.3. Effects of precipitation and temperature on transmission season end

For each variable, trajectories of lagged effects on transition probabilities were roughly opposite for season end compared with onset (figure 4). Increases in precipitation (adjusted for temperature) were associated with increased end probability at shorter lags and decreased probability at longer lags. Increases of 10 mm in precipitation were associated with increased end probability at 2–13 week lags (maximum HR at 9 week lag: 1.04; 95% CI: 1.03–1.05). Conversely, at lags of 17–26 weeks, 10 mm increases in precipitation were associated with reduced end probability (minimum HR at 26 week lag: 0.82, 95% CI: 0.77–0.86). The effects of increasing temperature (adjusted for precipitation) were roughly opposite; hotter temperatures were associated with reduced end probability at short lags and increased end probability at longer lags. A 1°C increase in temperature was

associated with reduced end probability at 2–15 week lags (minimum HR at 8 week lag: 0.993; 95% CI: 0.992–0.994) and increased probability at 18–26 week lags (maximum HR at 26 week lag: 1.02; 95% CI: 1.01–1.03; figure 4).

Based on G-computation substitution estimators, we estimated that dry autumn conditions (10th percentile of precipitation) prolonged the coccidioidomycosis transmission season by 0.69 weeks on average (95% CI: 0.37–1.41 weeks; figure 5B) compared with wet autumn conditions (90th percentile of precipitation). Combined, dry spring and autumn conditions extended the transmission season by 3.70 weeks (95% CI: 1.23–4.22 weeks) compared with wet spring and autumn conditions (figure 5C).

3.4. Sensitivity analyses

Seasonal transitions detected via segmented regression and maximum curvature methods were comparable, reporting concordant transition times (onset r = 0.70; end r = 0.65) (electronic supplementary material, table S3). While transmission seasons were slightly longer at the county level, with earlier onsets and later ends, estimates of mean onset and end times across counties differed by less than three weeks from census tract level estimates (electronic supplementary material, table S2). Varying the transition detection method, spatial scale and including a periodic spline to represent seasonal effects acting through mechanisms other than temperature and precipitation resulted in similar lag–response relationships and did not qualitatively change Markov model interpretation (electronic supplementary material S4–S7).

4. Discussion

We found evidence that temperature and precipitation influence the onset and duration of coccidioidomycosis transmission seasons in California. Notably, shifts from cooler, wetter conditions to hotter, drier conditions—a transition typically occurring in spring—accelerated the onset of the transmission season. When the spring season was dry, the transmission season started an average of 2.8 weeks earlier compared with when the spring was wet. Conversely, shifts from hotter, drier conditions to cooler, wetter conditions—a transition typically occurring in autumn—accelerated the end of the transmission season. When the autumn season was dry, the transmission season was extended by an average of 0.69 weeks compared with when the autumn was wet. Combined, both dry spring and autumn seasons extended the length of the transmission season by a total of 3.7 weeks.

Temperature and precipitation have been previously shown to influence coccidioidomycosis incidence in California [9–12]. Our results suggest that part of their influence on incidence may be explained by their curtailing or shifting of the coccidioidomycosis transmission season. The climate cycling associated with season onset—cool, wet conditions followed by hot, dry conditions—has been previously shown to increase coccidioidomycosis incidence [8–10,12], probably as a result of increased growth and subsequent dispersal of *Coccidioides* spores. Here, we build upon these studies by demonstrating that climate cycling additionally influences the timing of transmission season onset, with drier spring conditions leading to earlier increases in seasonal coccidioidomycosis transmission. Further, wet spring conditions increased the overall probability that a transmission season would occur, possibly due to increased *Coccidioides* growth in the presence of additional spring moisture, leading to a higher abundance of spores circulating during the following dry season.

In contrast, hot, dry conditions followed by cool, wet conditions were associated with an earlier end of the transmission season. This result probably arises because hot, dry conditions following transmission season onset continue promoting *Coccidioides* dispersal by facilitating arthroconidia aerosolization via wind erosion and dust generation, heightening transmission. Subsequent transition to cooler, wetter conditions probably leads to a reduction in *Coccidioides* exposure, as precipitation may directly remove spores from the air [21] or increase soil moisture and suppress dust emissions [18]. Due to delays between pathogen exposure and disease reporting, declines in *Coccidioides* exposure may not be reflected in the coccidioidomycosis surveillance record for many weeks [39,40], probably why the strongest effect of precipitation occurs at a nine-week lag. Previous studies have found negative associations between concurrent precipitation and coccidioidomycosis incidence [8–10]. Our findings concur with these and suggest that precipitation is a key factor determining when the transmission season concludes, with drier autumn conditions resulting in a delayed season end and prolonged transmission of coccidioidomycosis.

Our central hypotheses were formulated based on the theory of how changes in temperature and precipitation impact *Coccidioides* through their effects on the aerosol transmission efficiency of spores [41,42], fungal growth and spore viability [39,40]. However, other climate-driven processes may affect the seasonal timing of *Coccidioides* transmission. For instance, *C. immitis* may be affected by soil microbial community dynamics [43], as fungi and bacteria in soils have been shown to have differential responses to seasonal shifts in soil moisture and temperature [44]. Under certain conditions, intra-annual shifts in climate may affect rodent host dynamics, with subsequent effects on *Coccidioides* spore production and the timing of coccidioidomycosis season onset [45,46]. Seasonality in coccidioidomycosis incidence may additionally follow from seasonal changes in human behaviour or host immune defences [7,41]. For example, seasonal infection risk may mirror seasonal outdoor activity, including recreational (e.g. hiking [47]) and occupational (e.g. agricultural work [48]) activities that can increase exposure to ambient airborne spores as well as disturb soils (e.g. via tilling) and aerosolize the pathogen. Seasonal changes in host airway mucosal surface defences have been associated with changes in temperature and relative humidity [41], which may affect the clearance of pathogens in susceptible hosts and induce seasonality in coccidioidomycosis.

Climate projections for California indicate that temperatures will continue to increase in the coming decades. These warmer temperatures are anticipated to increase moisture loss from soils, resulting in dry soil conditions that last longer into the autumn and winter rainy season, even accounting for potential increases in extreme winter rain events, leading to sharper

rainy seasons [20,23,24]. According to our estimates, these changes may result in substantially longer coccidioidomycosis transmission seasons, as drier spring conditions may lead to earlier season onsets and drier autumn and winter conditions may delay the end of the season. Climate change is also expected to increase the frequency of drought in the southwestern USA in the 21st century [24,49]. These future droughts may disrupt the seasonal pattern of coccidioidomycosis transmission, as recent findings suggest that seasonal incidence patterns are suppressed during drought years [13].

There are several limitations of this study. First, coccidioidomycosis cases were aggregated to census tracts based on patient home residence. This may lead to exposure misclassification and distorted seasonal timing estimates if cases were exposed to *Coccidioides* while at work or travelling in other census tracts, particularly for cases geolocated to small urban census tracts, for which movement outside of the home residence census tract is more likely. However, sensitivity analyses comparing findings at the tract level with those using a county-level spatial aggregation suggest minimal impact of small-area effects. Our seasonal transition detection methods assumed a unimodal seasonal incidence pattern. While previous work has found that coccidioidomycosis incidence in California follows a unimodal seasonal pattern on average [7,11], multiple seasonal peaks may be possible in some areas due to anthropogenic soil moisture alterations, such as through irrigation related to agriculture. This assumption also limits the translatability of our methods to settings where bimodal incidence patterns are observed, such as Arizona. It is hard to disentangle seasonally varying confounders (e.g. anthropogenic activities that may impact *Coccidioides* exposure, such as agricultural or construction practices [50,51]) from seasonal variation in temperature and precipitation. Including a periodic spline to control for such seasonally varying factors attenuated the estimated effects of meteorological variables in our models. However, it did not qualitatively change associations between seasonal transitions and the exposures of interest (electronic supplementary material, figure S7). Finally, our analysis did not account for small-scale landscape factors, such as soil composition and rodent burrows, which are important determinants of *Coccidioides* presence in soil and air [52,53] and may modify the relationship between meteorology and coccidioidomycosis season onset and duration.

This study also has several strengths. We investigated variation in seasonal timing of coccidioidomycosis incidence at finer spatial scales than prior work, allowing for a more detailed understanding of climate factors influencing intra-annual differences in seasonality. We developed a novel Markov state transition model to estimate how spatial and temporal variation in seasonal climate patterns impact the timing and duration of coccidioidomycosis transmission seasons, leveraging a distributed-lag nonlinear modelling approach to capture the effects of climate on *Coccidioides* exposure while accounting for the delays between exposure and diagnosis inherent in surveillance data.

5. Conclusion

Our findings suggest that meteorological factors regulate seasonal incidence patterns of coccidioidomycosis in California. By identifying how temperature and precipitation influence the onset and end of coccidioidomycosis transmission seasons, this work provides initial steps towards improved capacity to anticipate and prepare for transmission seasons based on observed or anticipated conditions. Such information could inform real-time disease surveillance efforts, public health risk assessment and awareness campaigns targeting both the public and diagnosing physicians [54] as well as enhance efforts to predict coccidioidomycosis incidence, particularly in the context of climate change. Future work should investigate changes to fungal growth and dust concentrations as potential mediators of the impact of meteorological conditions on coccidioidomycosis seasonal patterns to further mechanistic understanding, as well as multi-annual and multi-year coccidioidomycosis incidence periodicities. Climate change is expected to increase the frequency of extreme precipitation and heat events in California [24], and thus future work should also examine how extreme events influence coccidioidomycosis seasonal dynamics.

Ethics. This study received approval from the Committee for Protection of Human Subjects of the California Health and Human Services Agency (protocol no. 17-05-2993). Approval by the University of California, Berkeley is provided by reliance on the California State approval.

Data accessibility. The R scripts used to conduct the data analysis are available in a publicly accessible Zenodo repository [55]. The coccidioidomycosis surveillance data are protected health information (PHI) with access restricted to authorized California Department of Public Health (CDPH) staff. County-level human case data are available at [56]. More complete human disease data can be obtained for approved purposes by submitting a formal request to the CDPH, Infectious Diseases Branch, Surveillance and Statistics Section. The meteorological data can be obtained at https://prism.oregonstate.edu/.

Supplementary material is available online [57].

Declaration of AI use. We have not used AI-assisted technologies in creating this article.

Authors' contributions. S.K.C.: conceptualization, data curation, formal analysis, investigation, methodology, project administration, validation, visualization, writing—original draft, writing—review and editing; J.R.H.: conceptualization, funding acquisition, methodology, project administration, supervision, visualization, writing—review and editing; P.A.C.: conceptualization, investigation, methodology, supervision, validation, writing—review and editing; A.K.W.: conceptualization, investigation, methodology, supervision, visualization, writing—review and editing; A.K.H.: conceptualization, funding acquisition, supervision, writing—review and editing; K.A.C.: formal analysis, writing—review and editing; A.B.: conceptualization, writing—review and editing; G.S.-C.: conceptualization, data curation, resources, writing—review and editing; D.J.V.: conceptualization, resources, writing—review and editing; S.J.: conceptualization, resources, writing—review and editing; J.V.R.: conceptualization, funding acquisition, investigation, methodology, project administration, resources, software, supervision, validation, writing—review and editing.

All authors gave final approval for publication and agreed to be held accountable for the work performed therein.

Conflict of interest declaration. We declare we have no competing interests.

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References

1. Galgiani JN, Ampel NM, Blair JE, Catanzaro A, Johnson RH, Stevens DA, Williams PL. 2005 Coccidioidomycosis. *Clin. Infect. Dis.* **41**, 1217–1223. (doi:10.1086/496991)
2. Centers for Disease Control and Prevention. 2022 Valley Fever (Coccidioidomycosis) Statistics. See https://www.cdc.gov/fungal/diseases/coccidioidomycosis/statistics.html (accessed 6 January 2023).
3. Centers for Disease Control and Prevention.2013 Increase in reported coccidioidomycosis—United States, 1998-2011. *MMWR Morb. Mortal. Wkly. Rep* **62**, 217–221.
4. Ghaly M, Aragón TJ. 2022 *Epidemiologic summary of valley fever (coccidioidomycosis) in California, 2020-2021*. Sacramento, CA: California Department of Public Health.
5. Fisman DN. 2007 Seasonality of infectious diseases. *Annu. Rev. Public Health* **28**, 127–143. (doi:10.1146/annurev.publhealth.28.021406.144128)
6. Martinez ME. 2018 The calendar of epidemics: seasonal cycles of infectious diseases. *PLoS Pathog*. **14**, e1007327. (doi:10.1371/journal.ppat.1007327)
7. Altizer S, Dobson A, Hosseini P, Hudson P, Pascual M, Rohani P. 2006 Seasonality and the dynamics of infectious diseases. *Ecol. Lett*. **9**, 467–484. (doi:10.1111/j.1461-0248.2005.00879.x)
8. Comrie AC. 2005 Climate factors influencing coccidioidomycosis seasonality and outbreaks. *Environ. Health Perspect*. **113**, 688–692. (doi:10.1289/ehp.7786)
9. Gorris ME, Cat LA, Zender CS, Treseder KK, Randerson JT. 2018 Coccidioidomycosis dynamics in relation to climate in the southwestern United States. *GeoHealth* **2**, 6–24. (doi:10.1002/2017gh000095)
10. Head JR *et al*. 2022 Effects of precipitation, heat, and drought on incidence and expansion of coccidioidomycosis in western USA: a longitudinal surveillance study. *Lancet Planet. Health* **6**, e793–e803. (doi:10.1016/s2542-5196(22)00202-9)
11. Coopersmith EJ, Bell JE, Benedict K, Shriber J, McCotter O, Cosh MH. 2017 Relating coccidioidomycosis (valley fever) incidence to soil moisture conditions. *GeoHealth* **1**, 51–63. (doi:10.1002/2016gh000033)
12. Weaver EA, Kolivras KN. 2018 Investigating the relationship between climate and valley fever (coccidioidomycosis). *EcoHealth* **15**, 840–852. (doi:10.1007/s10393-018-1375-9)
13. Heaney AK *et al*. 2024 Coccidioidomycosis seasonality in California: a longitudinal surveillance study of the climate determinants and spatiotemporal variability of seasonal dynamics, 2000–2021. *Lancet Reg. Health Am*. **38**, 100864. (doi:10.1016/j.lana.2024.100864)
14. Cai J, Zhang B, Xu B, Chan KKY, Chowell G, Tian H, Xu B. 2019 A maximum curvature method for estimating epidemic onset of seasonal influenza in Japan. *BMC Infect. Dis*. **19**, 181. (doi:10.1186/s12879-019-3777-x)
15. Won M, Marques-Pita M, Louro C, Gonçalves-Sá J. 2017 Early and real-time detection of seasonal influenza onset. *PLoS Comput. Biol*. **13**, e1005330. (doi:10.1371/journal.pcbi.1005330)
16. Barrera CR. 1986 Formation and germination of fungal arthroconidia. *Crit. Rev. Microbiol*. **12**, 271–292. (doi:10.3109/10408418509104431)
17. Achakulwisut P, Mickley LJ, Anenberg SC. 2018 Drought-sensitivity of fine dust in the US southwest: implications for air quality and public health under future climate change. *Environ. Res. Lett*. **13**, 054025. (doi:10.1088/1748-9326/aabf20)
18. Duniway MC, Pfennigwerth AA, Fick SE, Nauman TW, Belnap J, Barger NN. 2019 Wind erosion and dust from US drylands: a review of causes, consequences, and solutions in a changing world. *Ecosphere* **10**, e02650. (doi:10.1002/ecs2.2650)
19. Okin GS. 2022 Where and how often does rain prevent dust emission? *Geophys. Res. Lett*. **49**, L095501. (doi:10.1029/2021gl095501)
20. Swain DL, Langenbrunner B, Neelin JD, Hall A. 2018 Increasing precipitation volatility in twenty-first-century California. *Nat. Clim. Chang*. **8**, 427–433. (doi:10.1038/s41558-018-0140-y)
21. Rathnayake CM, Metwali N, Jayarathne T, Kettler J, Huang Y, Thorne PS, O'Shaughnessy PT, Stone EA. 2017 Influence of rain on the abundance of bioaerosols in fine and coarse particles. *Atmos. Chem. Phys*. **17**, 2459–2475. (doi:10.5194/acp-17-2459-2017)
22. Naimi AI, Cole SR, Kennedy EH. 2017 An introduction to G methods. *Int. J. Epidemiol*. **46**, dyw323. (doi:10.1093/ije/dyw323)
23. Luković J, Chiang JCH, Blagojević D, Sekulić A. 2021 A later onset of the rainy season in California. *Geophys. Res. Lett*. **48**, L090350. (doi:10.1029/2020gl090350)
24. Bedsworth L, Cayan D, Franco G, Fisher L, Ziaja S. 2018 Statewide summary report. California's fourth climate change assessment: California governor's office of planning and research. Scripps Institution of Oceanography, California Energy Commission, California Public Utilities Commission.
25. CDC. 2022 *How to use EpiWeek Function*. See https://www.cdc.gov/epiinfo/user-guide/check-code/epiweekfunctions.html.
26. PRISM Climate Group. *PRISM Gridded Climate Data*. Corvallis, OR: Oregon State University. October 10, 2021 https://prism.oregonstate.edu.
27. Akaike H. 1998 Information theory and an extension of the maximum likelihood principle. In *Selected papers of Hirotugu Akaike* (eds E Parzen, K Tanabe, G Kitagawa), pp. 199–213. New York, NY: Springer New York. (doi:10.1007/978-1-4612-1694-0_15)
28. Charu V, Zeger S, Gog J, Bjørnstad ON, Kissler S, Simonsen L, Grenfell BT, Viboud C. 2017 Human mobility and the spatial transmission of influenza in the United States. *PLoS Comput. Biol*. **13**, e1005382. (doi:10.1371/journal.pcbi.1005382)
29. Geoghegan JL, Saavedra AF, Duchêne S, Sullivan S, Barr I, Holmes EC. 2018 Continental synchronicity of human influenza virus epidemics despite climactic variation. *PLoS Pathog*. **14**, e1006780. (doi:10.1371/journal.ppat.1006780)
30. Jackson CH. 2011 Multi-state models for panel data: The msm package for R. *J. Stat. Softw.* **38**, 1–28. (doi:10.18637/jss.v038.i08)
31. McHardy IH, Barker B, Thompson GR III. 2023 Review of clinical and laboratory diagnostics for coccidioidomycosis. *J. Clin. Microbiol*. **61**, e0158122. (doi:10.1128/jcm.01581-22)
32. Benedict K *et al*. 2018 Enhanced surveillance for coccidioidomycosis, 14 US States, 2016. *Emerg. Infect. Dis*. **24**, 1444–1452. (doi:10.3201/eid2408.171595)
33. Tsang CA *et al*. 2010 Enhanced surveillance of coccidioidomycosis, Arizona, USA, 2007–2008. *Emerg. Infect. Dis*. **16**, 1738–1744. (doi:10.3201/eid1611.100475)
34. Gasparrini A, Armstrong B, Kenward MG. 2010 Distributed lag non-linear models. *Stat. Med*. **29**, 2224–2234. (doi:10.1002/sim.3940)
35. Robins J, Hernán M. 2009 Estimation of the causal effects of time-varying exposures. In *Longitudinal data analysis* (eds G Fitzmaurice, M Davidian, G Verbeke, G Molenberghs), pp. 553–597. Boca Raton, FL: Taylor & Francis Group.
36. R.Core Team. 2022 *R: a language and environment for statistical computing*. Vienna, Austria: R Foundation for Statistical Computing. See https://www.R-project.org/.
37. Muggeo VMR. 2008 Estimating regression models with unknown break-points. *Statist. Med* **22**, 3055–3071. (doi:10.1002/sim.1545)
38. Gasparrini A. 2011 Distributed lag linear and non-linear models in R: the package dlnm. *J. Stat. Softw* **43**, 1–20. (doi:10.18637/jss.v043.i08)

39. Mead HL *et al*. 2020 Differential thermotolerance adaptation between species of *Coccidioides*. *J. Fungi* **6**, 366. (doi:10.3390/jof6040366)
40. Berman RJ, Friedman L, Pappagianis D, Smith CE. 1956 Survival of *Coccidioides immitis* under controlled conditions of temperature and humidity. *Am. J. Public Health Nations Health* **46**, 1317–1324. (doi:10.2105/ajph.46.10.1317)
41. Moriyama M, Hugentobler WJ, Iwasaki A. 2020 Seasonality of respiratory viral infections. *Annu. Rev. Virol*. **7**, 83–101. (doi:10.1146/annurev-virology-012420-022445)
42. Tang JW. 2009 The effect of environmental parameters on the survival of airborne infectious agents. *J. R. Soc. Interface* **6**, S737–46. (doi:10.1098/rsif.2009.0227.focus)
43. Chow NA *et al*. 2021 Factors influencing distribution of *Coccidioides immitis* in soil, Washington State, 2016. *mSphere* **6**, e00598-21. (doi:10.1128/msphere.00598-21)
44. Bell C, McIntyre N, Cox S, Tissue D, Zak J. 2008 Soil microbial responses to temporal variations of moisture and temperature in a Chihuahuan desert grassland. *Microb. Ecol*. **56**, 153–167. (doi:10.1007/s00248-007-9333-z)
45. Taylor JW, Barker BM. 2019 The endozoan, small-mammal reservoir hypothesis and the life cycle of *Coccidioides* species. *Med. Mycol*. **57**, S16–S20. (doi:10.1093/mmy/myy039)
46. Prugh LR, Deguines N, Grinath JB, Suding KN, Bean WT, Stafford R, Brashares JS. 2018 Ecological winners and losers of extreme drought in California. *Nat. Clim. Chang*. **8**, 819–824. (doi:10.1038/s41558-018-0255-1)
47. Natarajan P, Miller A. 2017 Recreational infections. *Infect. Dis.* 643–646. (doi:10.1016/B978-0-7020-6285-8.00071-X)
48. Finn DR *et al*. 2021 Agricultural practices drive biological loads, seasonal patterns and potential pathogens in the aerobiome of a mixed-land-use dryland. *Sci. Total Environ*. **798**, 149239. (doi:10.1016/j.scitotenv.2021.149239)
49. Williams AP, Cook BI, Smerdon JE. 2022 Rapid intensification of the emerging southwestern North American megadrought in 2020–2021. *Nat. Clim. Chang*. **12**, 232–234. (doi:10.1038/s41558-022-01290-z)
50. Das R *et al*. 2012 Occupational coccidioidomycosis in California: outbreak investigation, respirator recommendations, and surveillance findings. *J. Occup. Environ. Med*. **54**, 564–571. (doi:10.1097/JOM.0b013e3182480556)
51. Villarejo D, McCurdy SA, Bade B, Samuels S, Lighthall D, Williams D III. 2010 The health of California's immigrant hired farmworkers. *Am. J. Ind. Med*. **53**, 387–397. (doi:10.1002/ajim.20796)
52. Kollath DR, Teixeira MM, Funke A, Miller KJ, Barker BM. 2020 Investigating the role of animal burrows on the ecology and distribution of *Coccidioides* spp. in Arizona soils. *Mycopathologia* **185**, 145–159. (doi:10.1007/s11046-019-00391-2)
53. Fisher FS, Bultman MW, Johnson SM, Pappagianis D, Zaborsky E. 2007 Coccidioides niches and habitat parameters in the Southwestern United States. *Ann. NY Acad. Sci*. **1111**, 47–72. (doi:10.1196/annals.1406.031)
54. Benedict K, Li Y, Molinari NAM, Jackson BR. 2021 Health care providers' testing practices for coccidioidomycosis and histoplasmosis in patients with community-acquired pneumonia—United States, 2020. *Open Forum Infect. Dis*. **8**, ofab020. (doi:10.1093/ofid/ofab020)
55. simonkcampo. 2025 simonkcampo/cocci-season-timing: Releasing to Zenodo. Zenodo. (doi:10.5281/zenodo.14713930)
56. CDPH. Valley Fever in California Year-end Data Dashboard. See https://www.cdph.ca.gov/Programs/CID/DCDC/Pages/ValleyFeverDashboard.aspx.
57. Camponuri SK, Head JR, Collender PA, Weaver AK, Heaney AK, Colvin KA *et al*. 2025 Supplementary material from: Prolonged coccidioidomycosis transmission seasons in a warming California: a Markov state transition model of shifting disease dynamics. Figshare. (doi:10.6084/m9.figshare.c.7681909)