Supplemental Material

Supplemental Information

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Economic valuation of coccidioidomycosis (Valley fever) projections in the United States in response to climate change

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Tables

Table S1. Endemicity screen options for the number of counties to include within our Valley fever incidence model (county sample size), resulting in the total number of observations across selected counties and 16 sample years (2000-2015).

	Preferred endemicity screen	**No screen**	**Alternate screen #1**	**Alternate screen #2**
Precipitation	-0.012***	-0.008***	-0.016	-0.013
Temperature	3.56***	2.296***	4.063***	3.971***
Constant	-36.017**	-16.547**	-41.724**	-40.013**
R-squared	0.173	0.154	0.169	0.159
County sample size	109	152	109	78
Total observations	1,744	2,432	1,211	1,248

*** denotes statistical significance at the 95th percentile*

**** denotes statistical significance at the 99th percentile*

Note: We considered several different endemicity screen options, where the endemicity threshold is defined as mean annual temperature above 10.7°C and total annual precipitation below 600 mm: our preferred approach which selects counties that meet endemicity screen in any year between 2000 and 2015, no screen (rejected because the relationship between incidence and climate is not supported in places that do not meet endemicity levels, suggesting that incidence is more likely the result of travel to endemic counties), alternate screen #1 which selects observations that meet the endemicity screen in a given year (rejected because it results in an unbalanced panel at the county level), and alternate screen #2 which selects counties that have mean annual temperature and precipitation levels averaged from 2000-2015 that meet endemicity thresholds (rejected because averaging across sixteen years likely minimizing important variation, including counties that only meet endemicity levels in more recent years). All models include year fixed effects and clustered standard errors.

Table S2. Summary of alternative Valley fever incidence (VFI) model specifications

	Preferred model specification	No year fixed effects	No clustering standard errors	With lags added	With only lags	Log(VFI) as outcome variable
Precipitation	-0.012***	-0.011***	-0.012***	-0.007***		-0.001*
Lagged precipitation				-0.008***	-0.013***	
Temperature	3.562***	3.449***	3.562***	0.591		0.493***
Lagged temperature				3.127***	3.734***	
Constant	-36.017**	-34.047**	-36.017***	-37.747**	-38.536**	-7.654***
R-squared	0.1726	0.137	0.173	0.179	0.177	0.250
Total observations	1,744	1,744	1,744	1,635	1,635	1,744

** denotes statistical significance at the 90th percentile*
*** denotes statistical significance at the 95th percentile*
**** denotes statistical significance at the 99th percentile*
Note: Coefficients and R-squared values cannot be compared across linear and semi-log models. All models include year fixed effects, clustered standard errors, and endemicity screen consistent with our preferred approach unless otherwise mentioned.

Table S3. Number of endemic counties and states (in parenthesis) in the US predicted for the RCP4.5 climate scenario for each Earth system model for years 2030, 2050, 2070, and 2090.

PRISM Reference (2000-2015)							217 (12)
	CanESM2	**CCSM4**	**GFDL-CM3**	**GISS-E2-R**	**HadGEM2-ES**	**MIROC5**	**Multimodel mean**
2030	308 (17)	293 (16)	290 (16)	239 (15)	286 (16)	351 (16)	295 (16.0)
2050	333 (18)	325 (16)	334 (18)	274 (15)	357 (18)	385 (17)	335 (17.9)
2070	352 (18)	377 (16)	310 (18)	273 (16)	366 (19)	444 (19)	354 (17.7)
2090	332 (18)	405 (19)	382 (18)	282 (16)	414 (20)	413 (19)	371 (18.3)

Table S4. Number of millions of people living in endemic counties in the US based on the ICLUSv2 future population estimates and 2010 constant population (in parenthesis) projected for the RCP4.5 climate scenario for each Earth system model for years 2030, 2050, 2070, and 2090.

PRISM Reference (2000-2015)							48.8
	CanESM2	**CCSM4**	**GFDL-CM3**	**GISS-E2-R**	**HadGEM2-ES**	**MIROC5**	**Multi-model mean**
2030	59.6 (47.5)	65.3 (52.2)	64.9 (51.9)	61.8 (49.4)	66.9 (53.4)	66.1 (52.8)	64.1 (51.2)
2050	77.8 (53.5)	78.1 (53.2)	81.0 (55.8)	75.6 (51.5)	79.3 (54.4)	77.4 (52.9)	78.2 (53.6)
2070	78.0 (47.7)	87.8 (53.2)	89.6 (55.3)	82.3 (50.1)	92.1 (56.8)	93.3 (57.0)	87.2 (53.3)
2090	89.1 (50.8)	93.2 (53.4)	100.8 (57.6)	84.0 (47.1)	99.7 (57.2)	101.6 (58.1)	94.8 (54.0)

Table S5. The total number of Valley fever cases in the US based on the ICLUSv2 future population estimates and 2010 constant population (in parenthesis) projected for the RCP4.5 climate scenario for each Earth system model for years 2030, 2050, 2070, and 2090.

PRISM Reference (2000-2015)							9,621
	CanESM2	**CCSM4**	**GFDL-CM3**	**GISS-E2-R**	**HadGEM2-ES**	**MIROC5**	**Multi-model mean**
2030	14,547 (11,522)	13,807 (10,924)	14,930 (11,816)	12,694 (10,046)	14,641 (11,594)	14,160 (11,201)	14,130 (11,184)
2050	19,316 (13,021)	18,317 (12,308)	19,982 (13,459)	16,726 (11,263)	19,161 (12,887)	18,502 (12,450)	18,667 (12,565)
2070	21,142 (12,551)	20,526 (12,224)	23,699 (14,179)	18,350 (10,951)	23,667 (14,158)	22,832 (13,610)	21,703 (12,945)
2090	24,507 (13,576)	23,023 (12,728)	28,046 (15,482)	19,452 (10,687)	26,717 (14,824)	25,646 (14,186)	24,565 (13,580)

Table S6. Total annual cost of Valley fever in the US based on the ICLUSv2 future population estimates and 2010 constant population (in parenthesis) predicted for the RCP4.5 climate scenario for each Earth system model for years 2030, 2050, 2070, and 2090.

PRISM Reference (2000-2015)							$3.86
	CanESM2	**CCSM4**	**GFDL-CM3**	**GISS-E2-R**	**HadGEM2-ES**	**MIROC5**	**Multi-model mean**
2030	$6.62 ($5.24)	$6.28 ($4.97)	$6.79 ($5.38)	$5.78 ($4.57)	$6.66 ($5.27)	$6.44 ($5.10)	$6.43 ($5.09)
2050	$9.80 ($6.61)	$9.29 ($6.24)	$10.14 ($6.83)	$8.48 ($5.71)	$9.72 ($6.54)	$9.39 ($6.32)	$9.47 ($6.37)
2070	$11.92 ($7.07)	$11.57 ($6.89)	$13.36 ($7.99)	$10.34 ($6.17)	$13.34 ($7.98)	$12.87 ($7.67)	$12.23 ($7.30)
2090	$15.20 ($8.42)	$14.28 ($7.89)	$17.39 ($9.60)	$12.06 ($6.63)	$16.57 ($9.19)	$15.90 ($8.80)	$15.23 ($8.42)

Table S7. Average economic costs by outcome, overall, and cost per case with premature mortality valuation (VSL) and wage rates held constant at base values (2015$ millions) – for comparison with Table 5 in main text

Outcome	**Future scenario**	**2030**	**2050**	**2070**	**2090**
Hospitalization	RCP4.5	$61.8	$81.7	$95.0	$107.5
	RCP8.5	$64.5	$87.8	$107.9	$130.6
ER to discharge	RCP4.5	$3.2	$4.2	$4.9	$5.5
	RCP8.5	$3.3	$4.5	$5.5	$6.7
ER to hospital	RCP4.5	$83.2	$110.0	$127.9	$144.7
	RCP8.5	$86.9	$118.2	$145.3	$175.8
Physician's visit	RCP4.5	$3.0	$4.0	$4.6	$5.2
	RCP8.5	$3.1	$4.3	$5.2	$6.3
Premature Mortality	RCP4.5	$5,516.0	$7,287.3	$8,472.2	$9,589.6
	RCP8.5	$5,755.1	$7,833.5	$9,626.7	$11,651.0
Total cost	RCP4.5	$5,667.2	$7,487.1	$8,704.5	$9,852.6
	RCP8.5	$5,912.9	$8,048.3	$9,890.7	$11,970.5
Total cost per case	RCP4.5	$0.40	$0.40	$0.40	$0.40
	RCP8.5	$0.40	$0.40	$0.40	$0.40

Note: Average across the six Earth system models with population growth scenario (ICLUSv2). Each outcome includes both direct and indirect (i.e., productivity losses) costs.

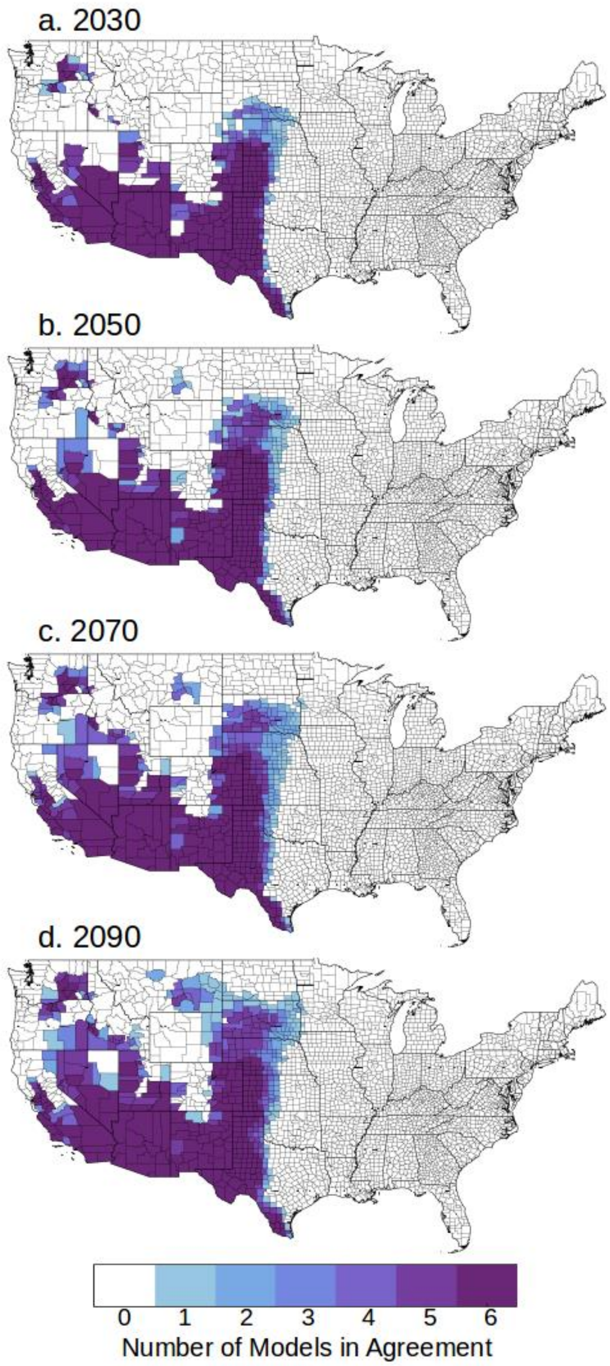


Figure S1. The number of Earth system models from the CIRA framework (*n* = 6) in agreement that each county may be endemic to Valley fever for the RCP4.5 climate scenario in years (a) 2030, (b) 2050, (c) 2070, and (d) 2090, defined by meeting both the mean annual temperature and mean annual precipitation thresholds following Gorris et al. (2019). The northward expansion of endemicity is limited compared to the RCP8.5 climate scenario.

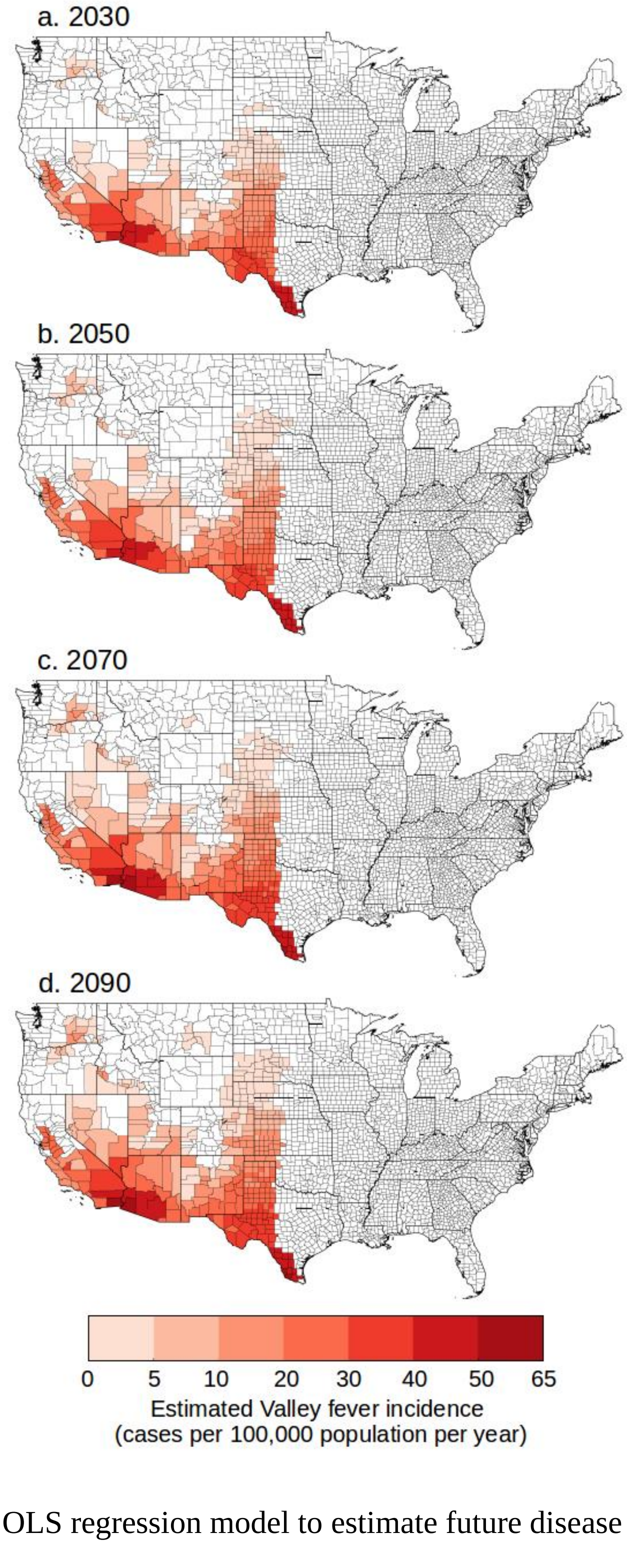


Figure S2. We used an OLS regression model to estimate future disease incidence for the counties projected to be endemic. We averaged the incidence projections between the six Earth system models and applied the incidence value to counties in which at least four of the six models agree will be endemic in that time period. Incidence for the RCP4.5 climate scenario for years (a) 2030, (b) 2050, (c) 2070, and (d) 2090 is highest in the extreme southwestern US.

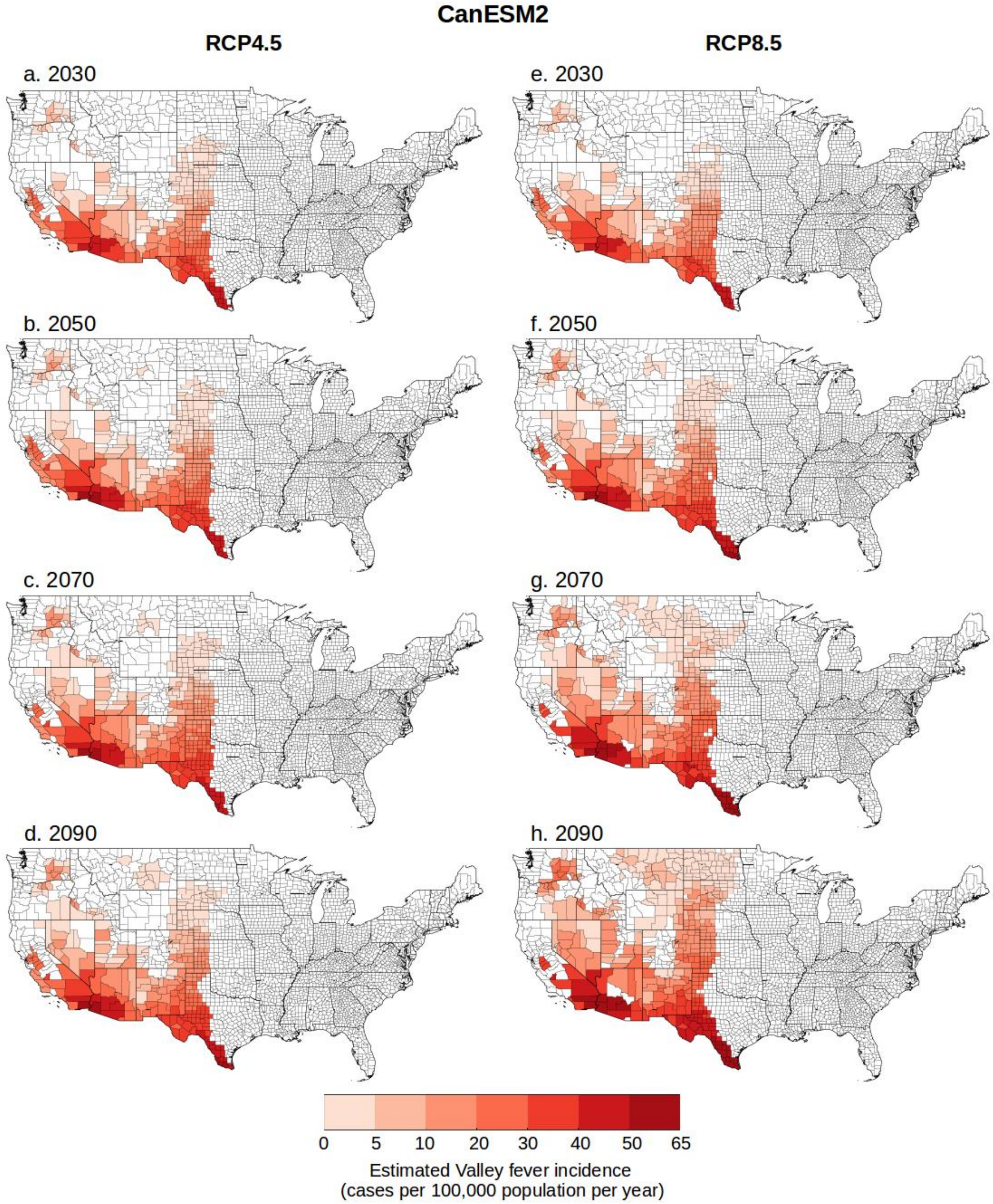


Figure S3. We used an OLS regression model to estimate future Valley fever incidence for the counties projected to be endemic using CanESM2 climate projections, shown for both the RCP4.5 climate scenario (a-d) and the RCP8.5 scenario (e-h) for years (a,e) 2030, (b,f) 2050, (c,g) 2070, and (d,h) 2090.

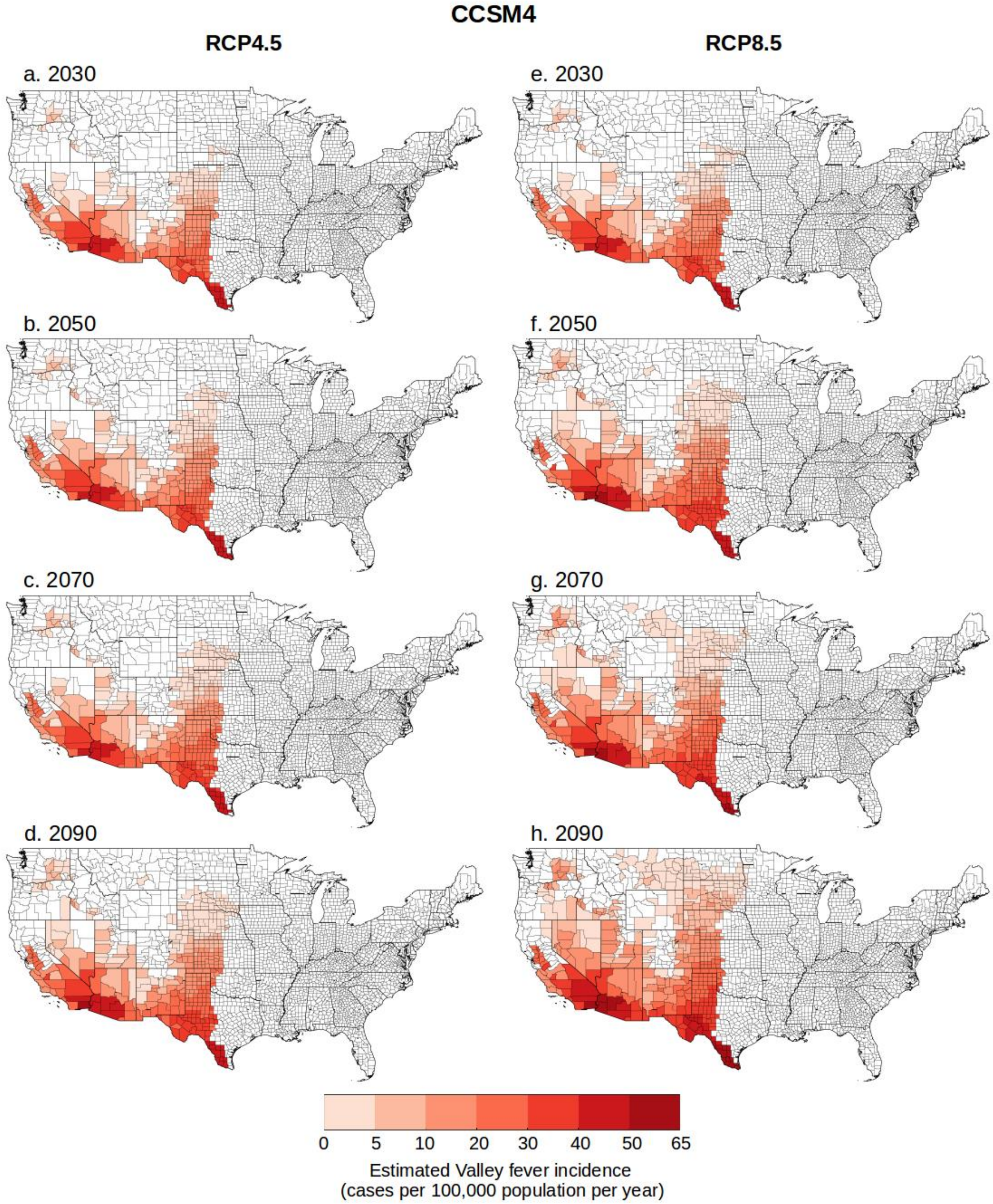


Figure S4. We used an OLS regression model to estimate future Valley fever incidence for the counties projected to be endemic using CCSM4 climate projections, shown for both the RCP4.5 climate scenario (a-d) and the RCP8.5 scenario (e-h) for years (a,e) 2030, (b,f) 2050, (c,g) 2070, and (d,h) 2090.

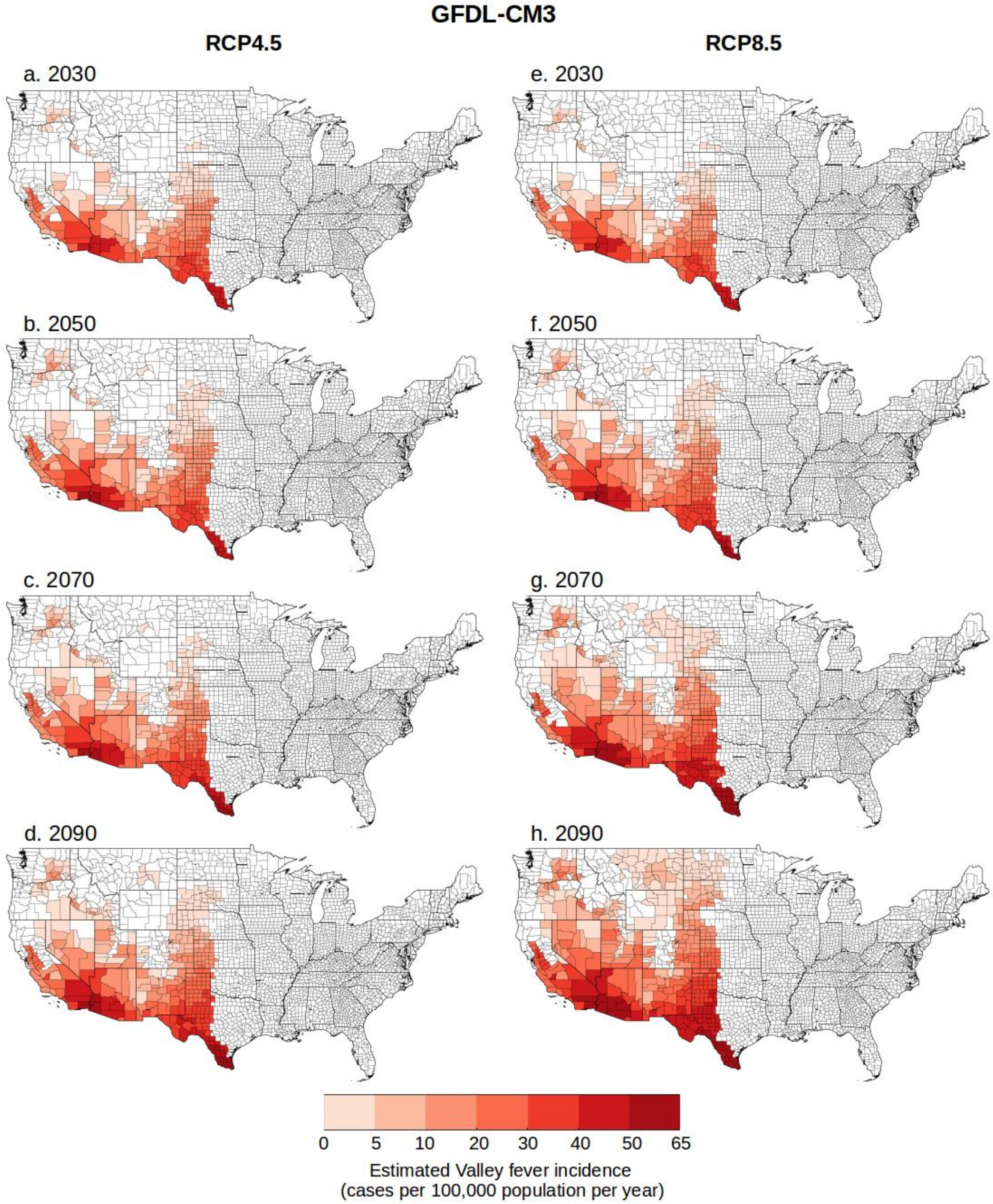


Figure S5. We used an OLS regression model to estimate future Valley fever incidence for the counties projected to be endemic using GFDL-CM3 climate projections, shown for both the RCP4.5 climate scenario (a-d) and the RCP8.5 scenario (e-h) for years (a,e) 2030, (b,f) 2050, (c,g) 2070, and (d,h) 2090.

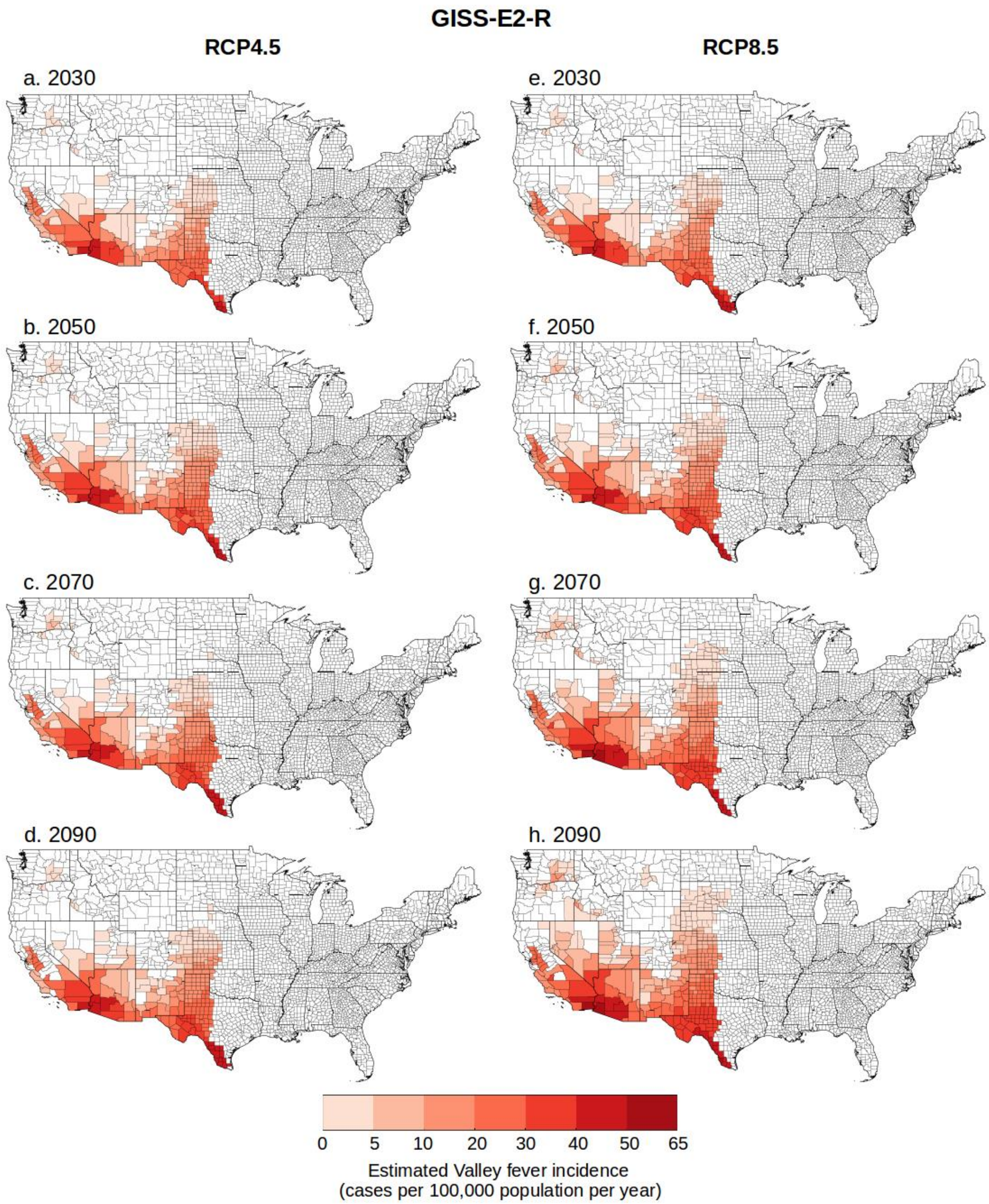


Figure S6. We used an OLS regression model to estimate future Valley fever incidence for the counties projected to be endemic using GISS-E2-R climate projections, shown for both the RCP4.5 climate scenario (a-d) and the RCP8.5 scenario (e-h) for years (a,e) 2030, (b,f) 2050, (c,g) 2070, and (d,h) 2090.

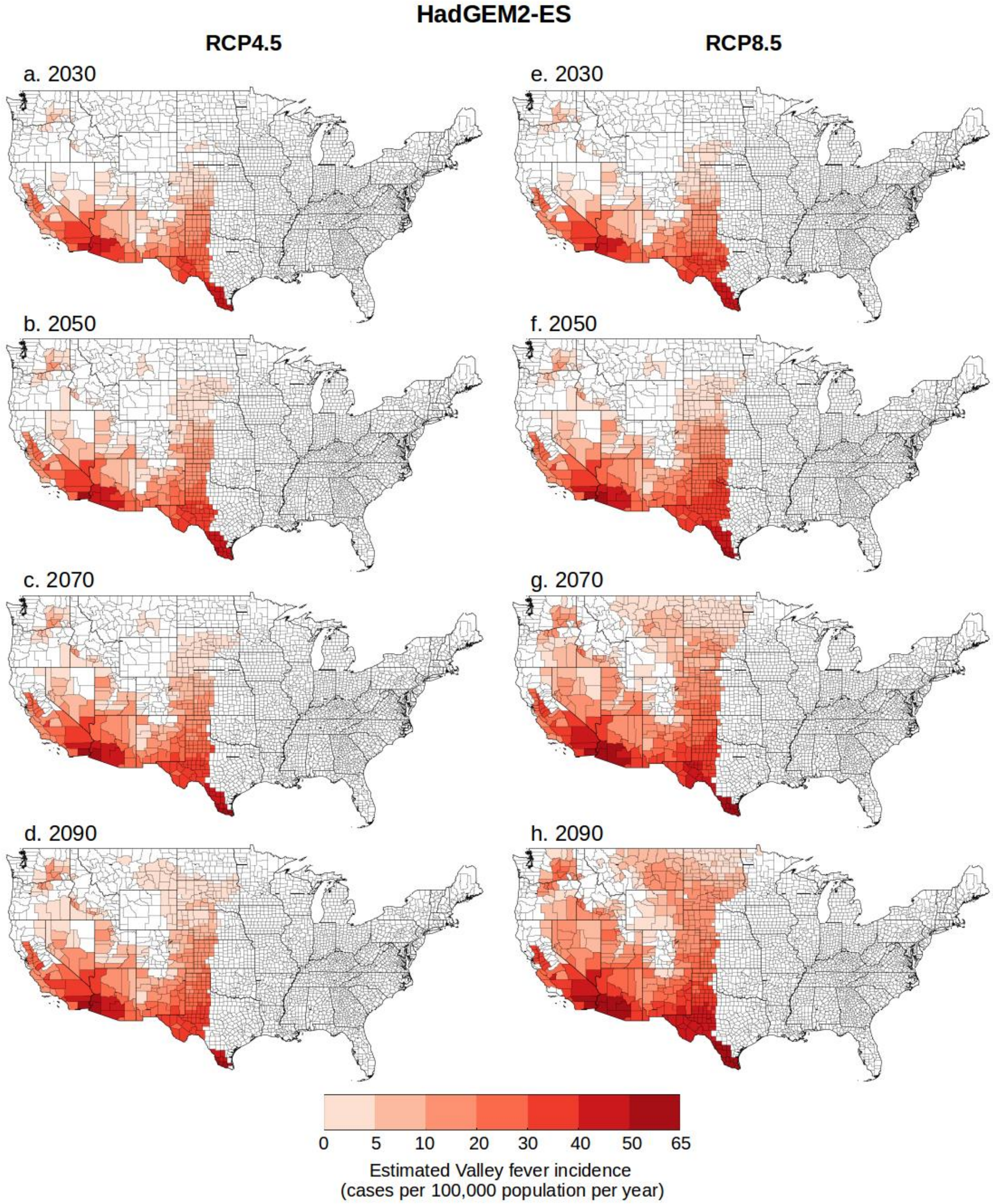


Figure S7. We used an OLS regression model to estimate future Valley fever incidence for the counties projected to be endemic using HadGEM2-ES climate projections, shown for both the RCP4.5 climate scenario (a-d) and the RCP8.5 scenario (e-h) for years (a,e) 2030, (b,f) 2050, (c,g) 2070, and (d,h) 2090.

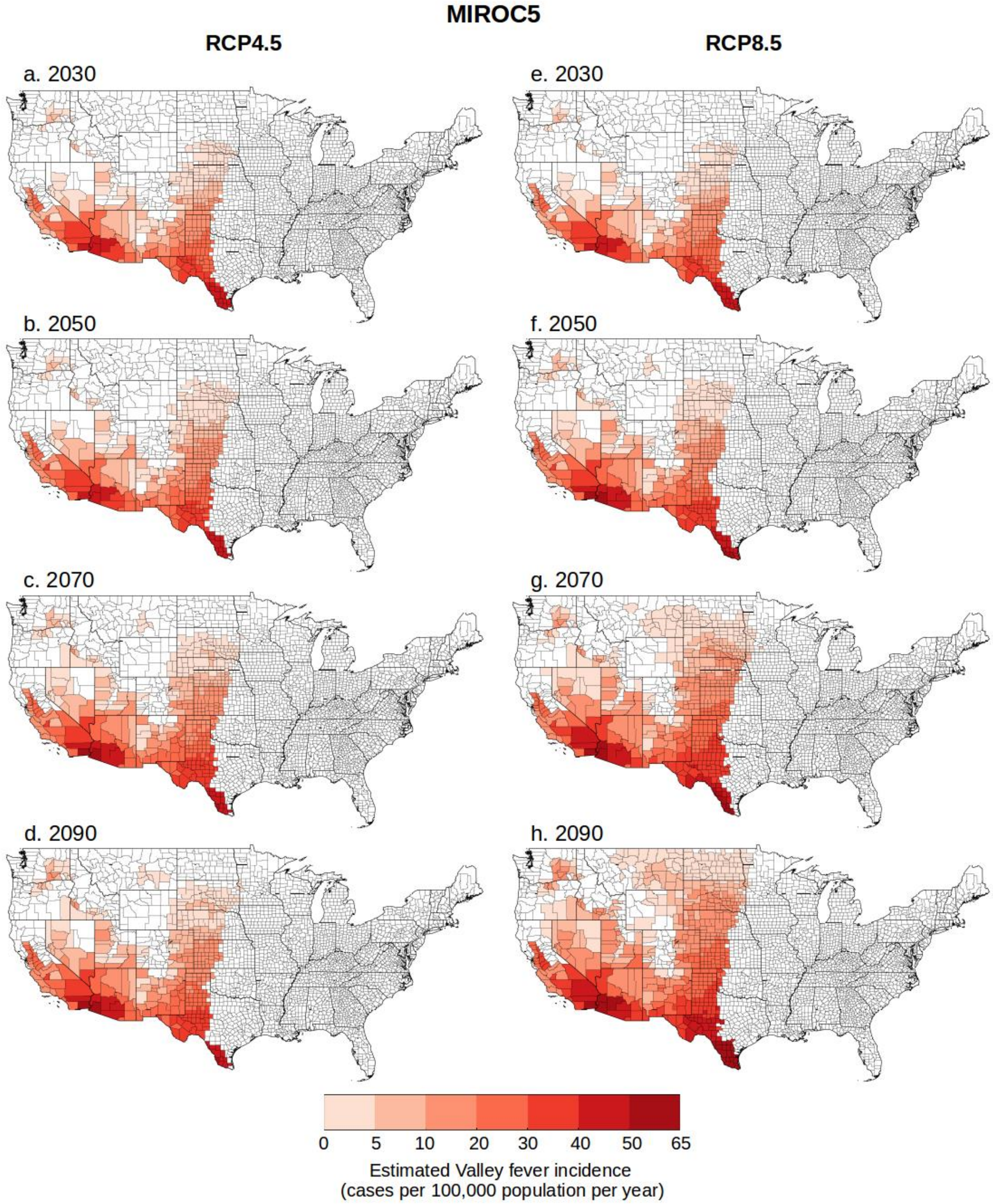


Figure S8. We used an OLS regression model to estimate future Valley fever incidence for the counties projected to be endemic using MIROC5 climate projections, shown for both the RCP4.5 climate scenario (a-d) and the RCP8.5 scenario (e-h) for years (a,e) 2030, (b,f) 2050, (c,g) 2070, and (d,h) 2090.

Supplemental Information on Valley Fever Incidence from HCUP and CDC Wonder

Data Sources

We collected historical incidence data for coccidioidomycosis for three medical outcomes: emergency room visits, inpatient hospitalizations, and mortality. For emergency room visits and hospitalizations, we queried the Healthcare Cost and Utilization Project (HCUPnet) dataset. The CDC WONDER database provides detailed information on mortality.

Using HCUP, we collected hospitalization and emergency room data for coccidioidomycosis at the national and state level. We collected time series data between 1993 and 2015 using International Classification of Diseases, Ninth Revision codes (ICD-9). Within ICD-9, coccidioidomycosis is defined under code 114. Nationally, we collected time series data on emergency room (ER) visits from 2006 to 2014. These data include information on the total number of ER visits, the number of patients subsequently admitted to the hospital, and the number of patients discharged without hospitalization. Regarding emergency room visits, Arizona is the only state with unsuppressed data.

Exhibit 1. Annual ER Visits for Coccidioidomycosis

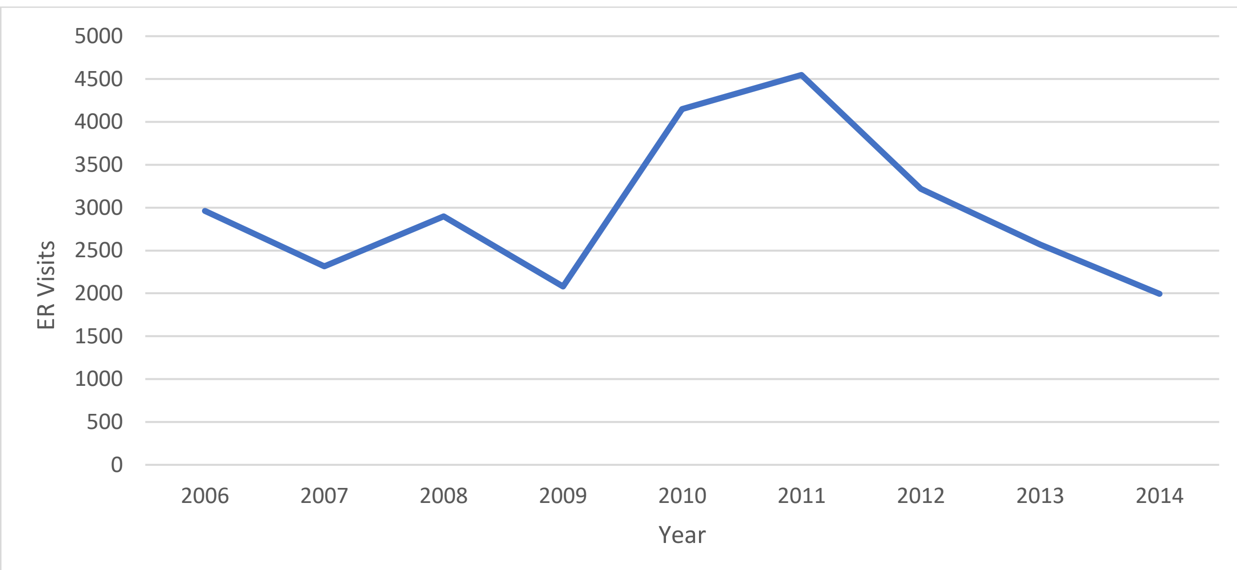


Exhibit 2. Annual Hospitalization rates from ER

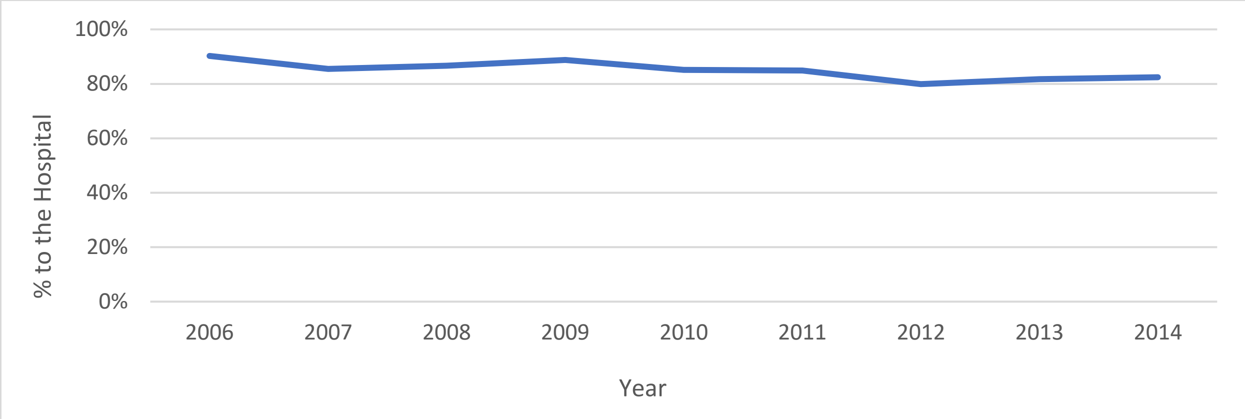
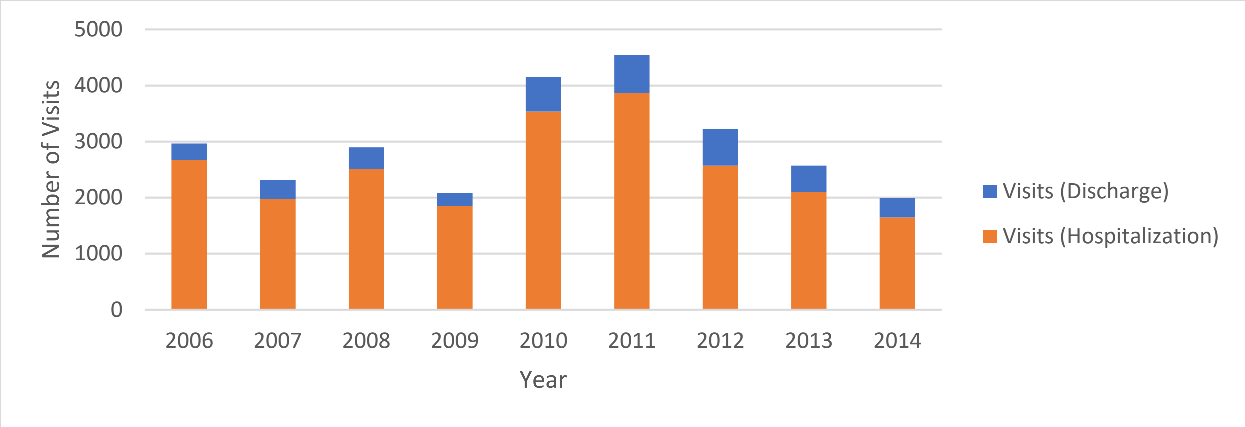


Exhibit 3. Breakdown of the Total Number of ER Visits



Between 2006 and 2014, ER visits due to coccidioidomycosis ranged between 1,994 and 4,548. In Exhibit 1, there is no clear trend in the data between these years; however, ER visits peaked between 2010 and 2012 suggesting a higher incidence of the disease in those years. Exhibits 2 and 3 suggest that most patients in an ER setting for coccidioidomycosis treatment are subsequently hospitalized. Between 2006 and 2014, the percentage of patients hospitalized after an initial ER visit ranged between 82% and 90%.

We also collected data for inpatient hospitalizations from 1993 and 2015. These data include information on the number of discharges, length of stay, hospital charges, and in-hospital deaths. We also estimated total admissions and total days in the hospital using these data.

Exhibit 4. Hospitalization incidence (Deaths vs Discharge)[1]

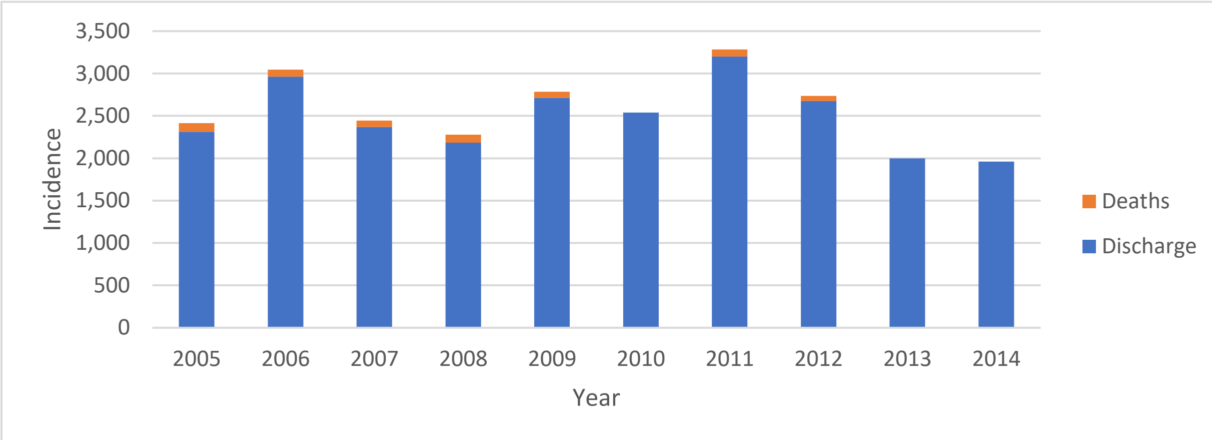


Exhibit 5. Hospital Charges (Nominal)

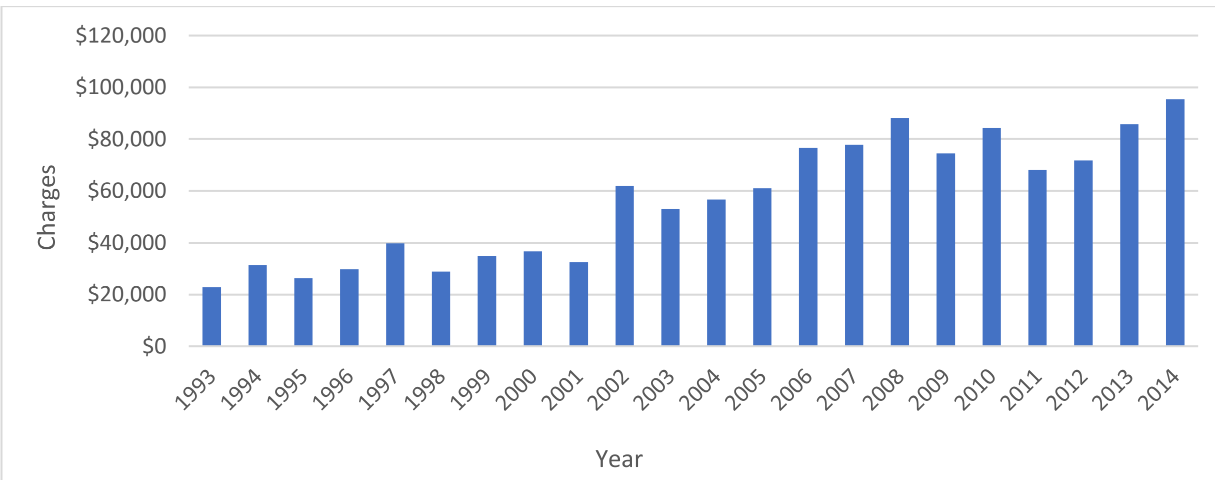
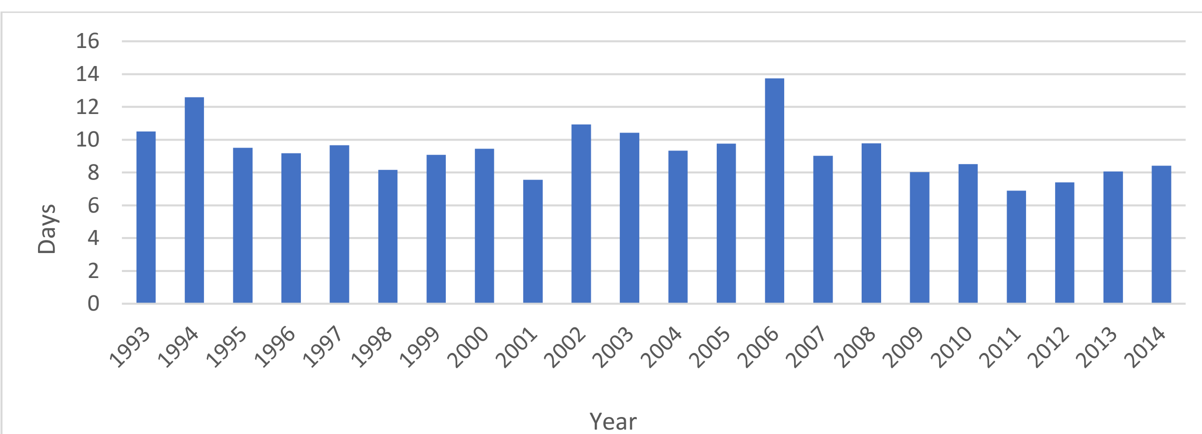


Exhibit 6. Length of Hospital Stay



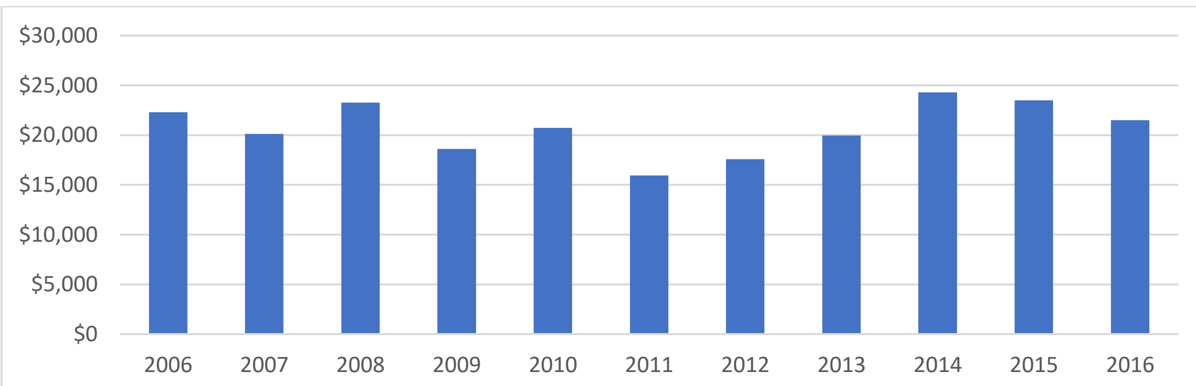
[1] No data was available after 2012 for mortality because the it was suppressed due to confidentiality restraints.

Exhibit 4 presents a stacked bar graph of total hospital admissions and whether these visits led to a discharge or a death. Unsurprisingly, hospital discharges far outweigh hospital deaths for coccidioidomycosis. Between 2005 and 2014, the number of hospital admissions range from 1,960 to 3,045. Like trends within ER data, we observe slight peaks in 2006 and in 2011 and 2012, suggesting that these time periods saw higher prevalence of coccidioidomycosis.

Exhibits 5 and 6 illustrate hospital charges (nominal) and length of stay, respectfully. Hospital charges increased overtime, from $22,847 in 1993 to $95,401 in 2014. Between 1993 and 2014 the average length of stay was about 9 days.

Along with charges, we also collected cost data for coccidioidomycosis. A complete time series for cost data was only available between 2006 and 2016. Exhibit 7 illustrates costs for inpatient treatment. For this period, cost remain relatively consistent.

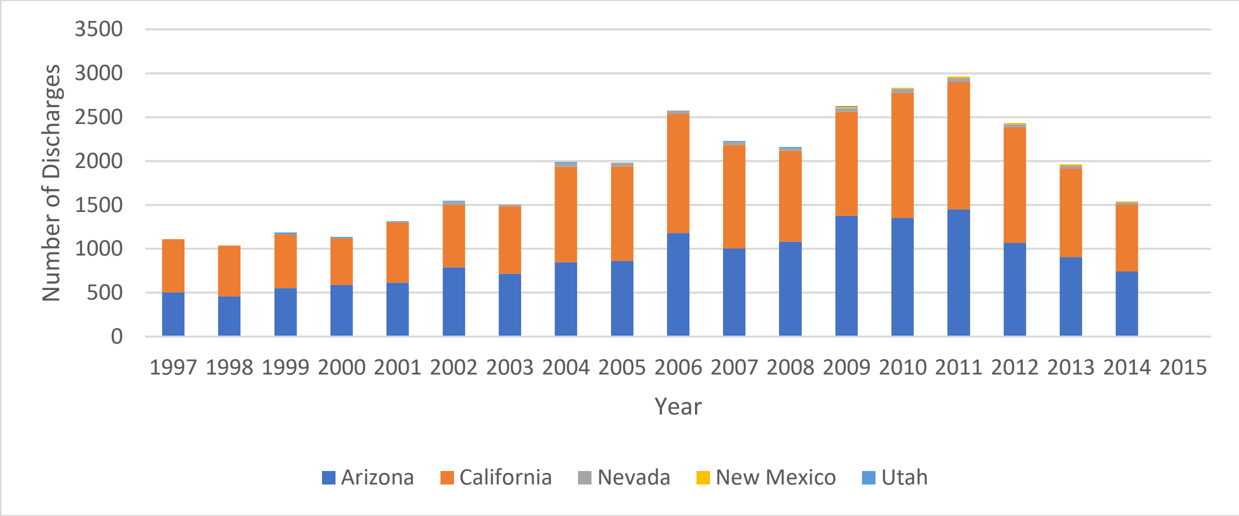
Exhibit 7. Hospital Costs (nominal)



State-level

To evaluate whether coccidioidomycosis hospitalizations were geographically clustered, we evaluated state-level data for Arizona, California, Nevada, New Mexico, and Utah. Between 1997 and 2014, California and Arizona have a complete timeseries. In contrast, for Nevada, New Mexico, and Utah, the timeseries data is incomplete, with the data either suppressed or missing. We presented this data using three key variables: number of discharges, length of stay, and charges. Exhibit 8 shows the breakdown of discharges between states. Across all five states, discharges peak in 2006 and between 2009 and 2012. The majority of these discharges are in California and Arizona.

Exhibit 8. Hospital Discharges by State

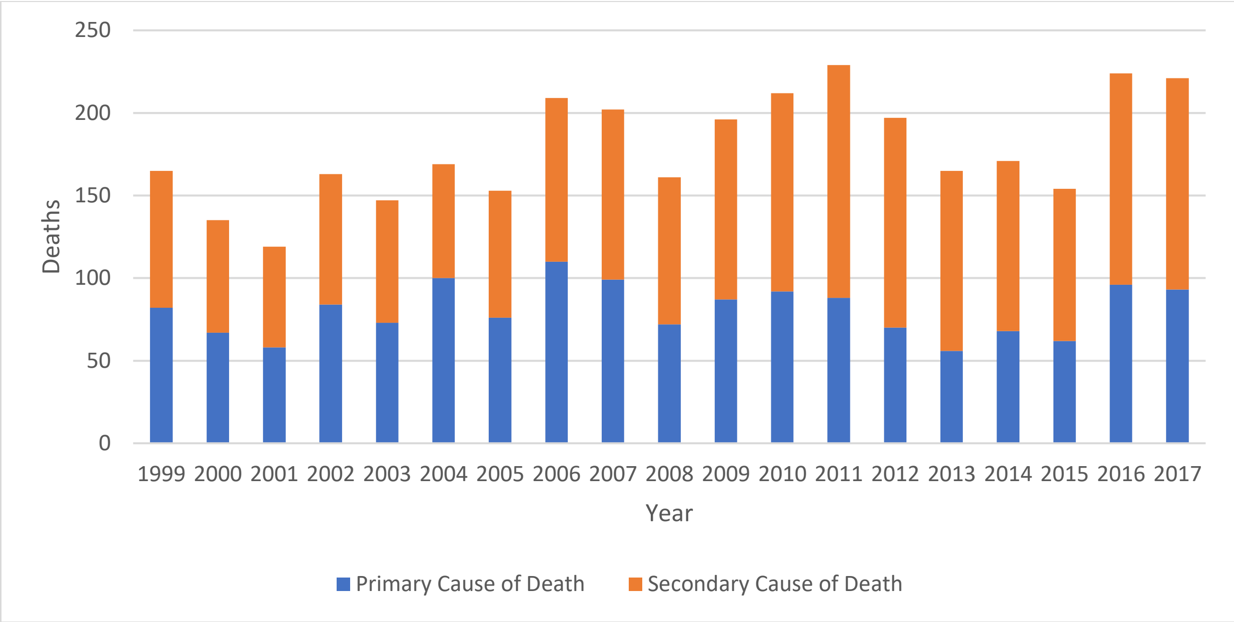


Summary Statistics- Mortality

We collected two datasets pertaining to mortality. The first (Underlying Cause of Death, UCD) includes deaths primarily caused by coccidioidomycosis. The second dataset (Multiple Cause of Death, MCD) summarizes all deaths that involve coccidioidomycosis. To query these datasets, we utilized the International Classification of Diseases, Tenth Revision codes (ICD-10). Within ICD-10, coccidioidomycosis is defined under code B-38.

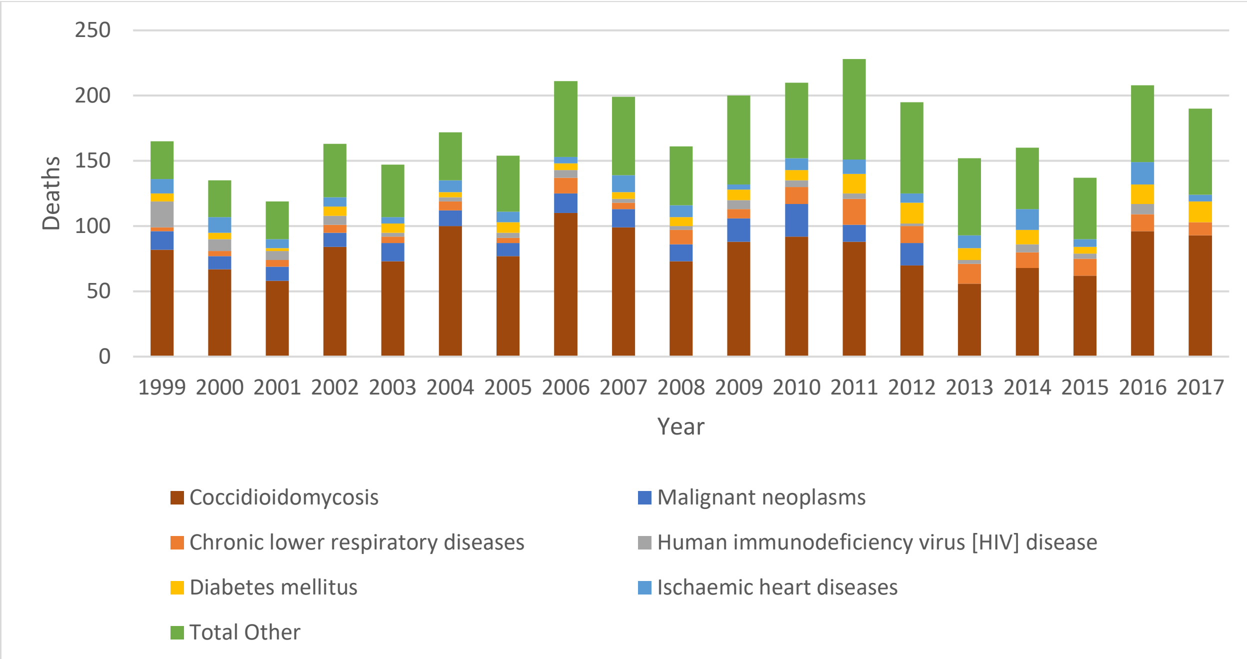
Exhibit 9 compares these datasets. Deaths are segregated between the primary and secondary cause of death. Primary cause of death includes all deaths primarily caused by coccidioidomycosis. We used UCD data to represent primary cause of death. Secondary cause of death represents deaths that involve coccidioidomycosis, but where coccidioidomycosis is not necessarily the primary cause of death. To find secondary cause of death, we subtracted deaths found in the MCD dataset by deaths in the UCD dataset.

Exhibit 9 Coccidioidomycosis Deaths (Primary versus secondary cause of death)



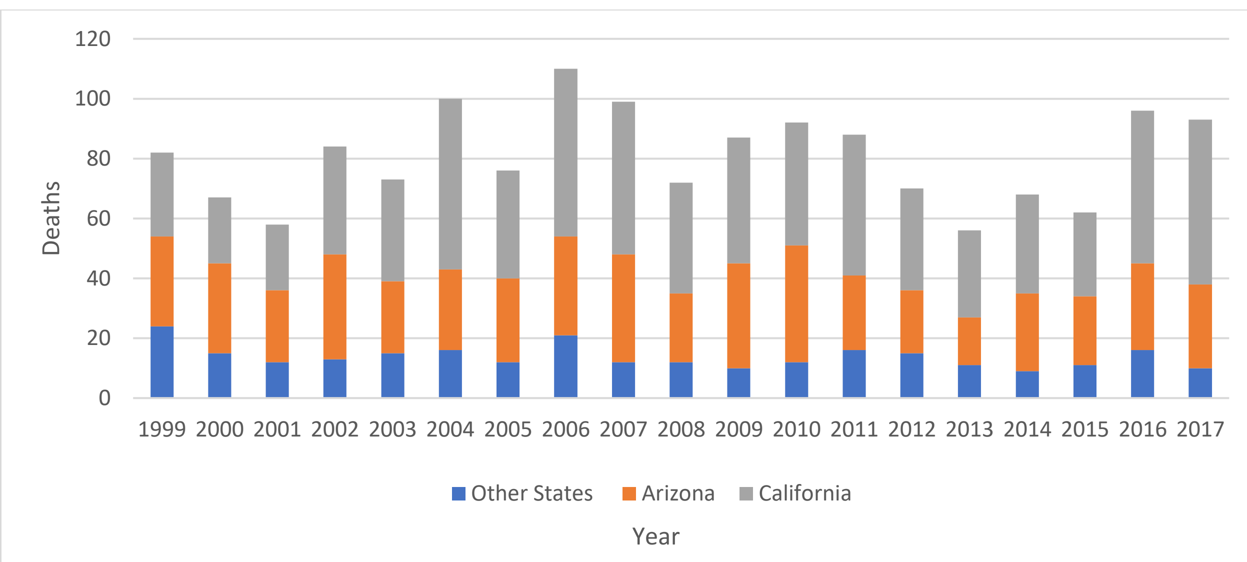
In Exhibit 10, we again present primary and secondary cause of death, but segregate secondary cause of death by its comorbidity. We relabeled primary cause of death as coccidioidomycosis. Common comorbidities of coccidioidomycosis are malignant neoplasms, chronic lower respiratory diseases, HIV, diabetes, and heart disease. All other comorbidities were grouped together and listed as “Total Other”.

Exhibit 10. Comorbidity[2]



For cases in which the primary cause of death is coccidioidomycosis, we stratified incidence by state. As displayed in Exhibit 11, most deaths occur in California and Arizona. Additionally, Exhibit 12 presents coccidioidomycosis-related deaths by age group. The majority of deaths occur in the oldest age brackets, between 45 and 84 years old.

Exhibit 11. Mortality by State



[2] To find Coccidioidomycosis, we used a broader ICD-10 code for Mycosis. As a result, three non-Coccidioidomycosis deaths are included in the Coccidioidomycosis category.

Exhibit 12. Underlying Deaths by age