

# **Epidemiology of Coccidioidomycosis in Arizona**

**Rebecca Sunenshine, MD  
CAPT, USPHS**

**Medical Director, Disease Control Division  
Maricopa County Department of Public  
Health**

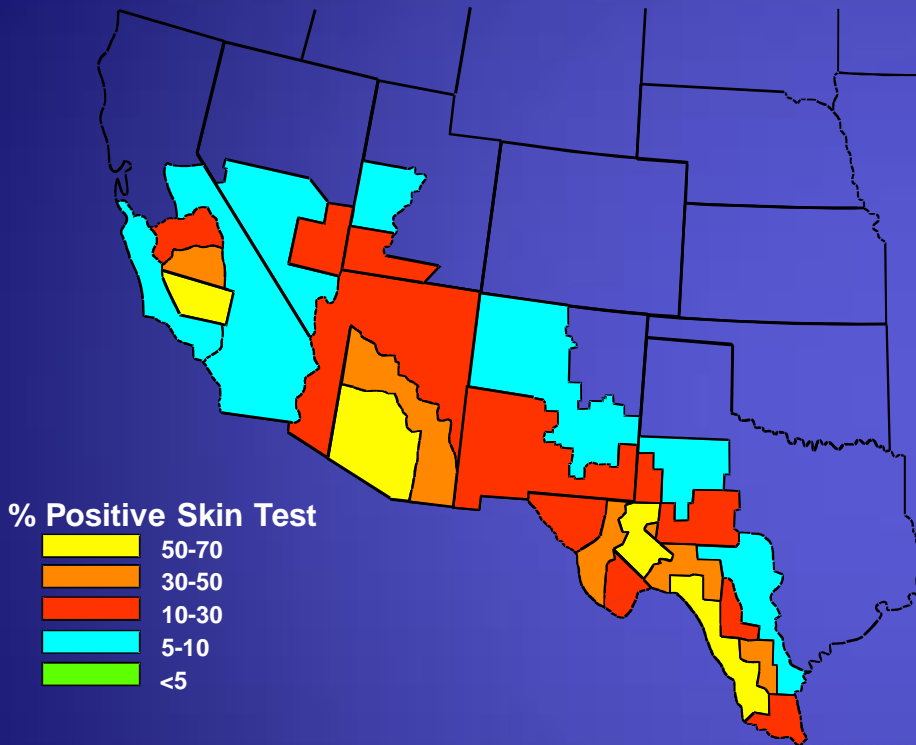
# Disclaimer

**The findings and conclusions in this presentation are those of the author(s) and do not necessarily represent the views of the Centers for Disease Control and Prevention or the Arizona Department of Health Services.**

# Objectives

- Understand the epidemiology of coccidioidomycosis in the US and Arizona
- Appreciate the impact of cocci on Arizona's citizens, healthcare system, and economy
- Know what Public Health is doing about cocci in Arizona

# Coccidioidomycosis Epidemiology



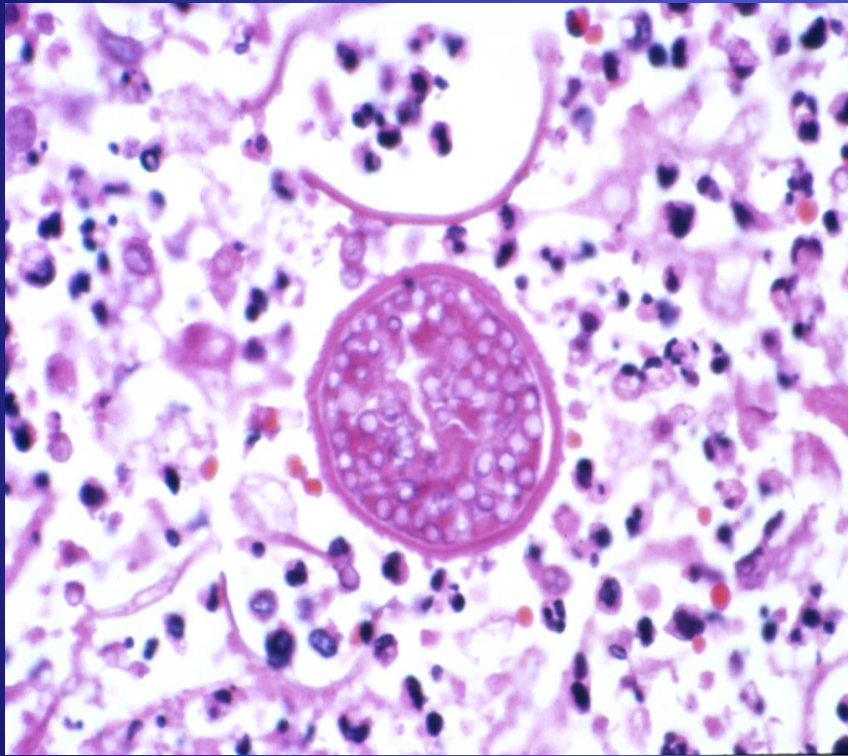
P. Q. Edwards and C. E. Palmer. Prevalence of sensitivity to coccidioidin, with special reference to specific and nonspecific reactions to coccidioidin and to histoplasmin. *Dis.Chest* 31:35-60, 1957

- Caused by a fungus found in “thermic” soil
  - *C. immitis* (California)
  - *C. posadasii* (Arizona)
- Endemic areas: Southwestern US, Mexico, parts of Central and South America
- 60% of US disease in AZ

# Cocci Identified in South Central Washington 2010-11

- Three lab confirmed cocci cases identified in south central Washington
  - No travel to cocci endemic areas within 22 months prior to illness
  - Novel RT PCR assay developed by CDC and T-Gen North detected cocci in 6/22 soil samples from areas where patients recreated
  - Environmental isolate genotypes matched clinical cocci isolate from one patient

# Coccidioidomycosis (Cocci)



Spherules (Hematoxylin-Eosin stain)

- No licensed vaccine available
- Reportable disease in Arizona and US



# Transmission

- Inhalation of airborne arthrospores from soil
  - Wind
  - Soil disturbance, construction
  - Outdoor activities, gardening, golf etc.
  - Filming TV series outdoors\*
- Incubation period: 1 – 4 weeks
- No person-to-person spread
- Usually found in soil 2-8 inches from the surface



# Risk Factors for Primary Cocci

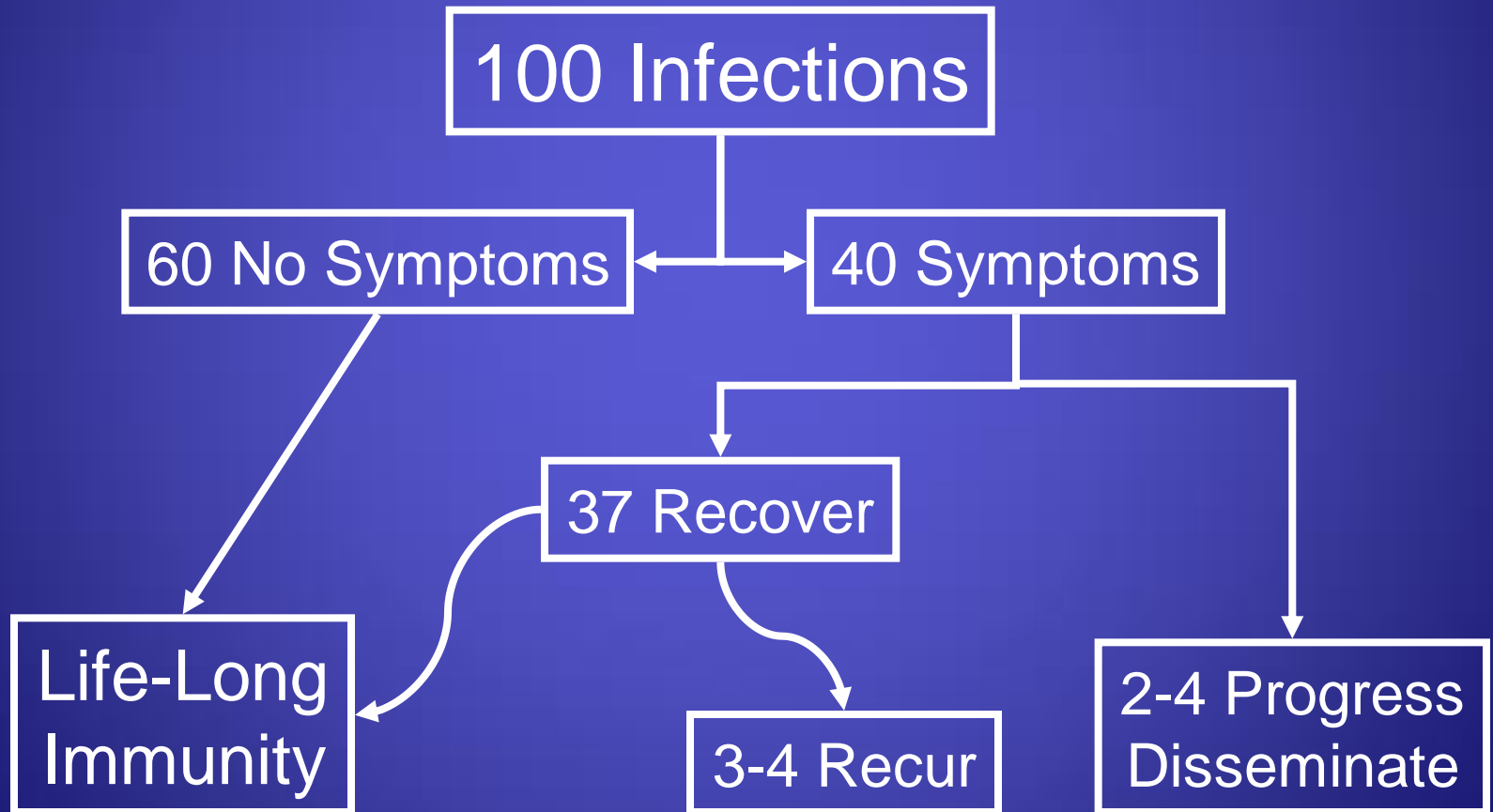
- Exposure to an endemic area
- Immune naïve
- Male Sex



# Risk Factors for Disseminated Cocci or Severe Disease

- Infants and elderly ( $\geq 65$ )
- Male sex
- Diabetes mellitus (severe pulmonary dz)
- Filipino, African American, Native American, Hispanic (?), Asian
- Pregnancy, third trimester and post-partum
- Immunosuppression including HIV

# Coccidioidomycosis Spectrum of Disease



# Disease Prevalence Estimates and Data

- National and Arizona\*
  - Estimated 150,000 cases in US annually
  - 90,000 (60%) in Arizona
  - 36,000 (40%) symptomatic AZ cases/year
- Maricopa County\*\*
  - NW Valley: 9 of 797 (1.1%) seropositive by ID
  - Remainder of MC: 6 of 797 (0.75%)
  - $15/1594 = 0.94\%$  prevalence in MC

\*Galgiani JN, Ampel NM, Blair JE, Catanzaro A, Johnson RH, Stevens DA, et al. Coccidioidomycosis. Clin Infect Dis. 2005;41:1217–23.

\*\*Unpublished data from CDC

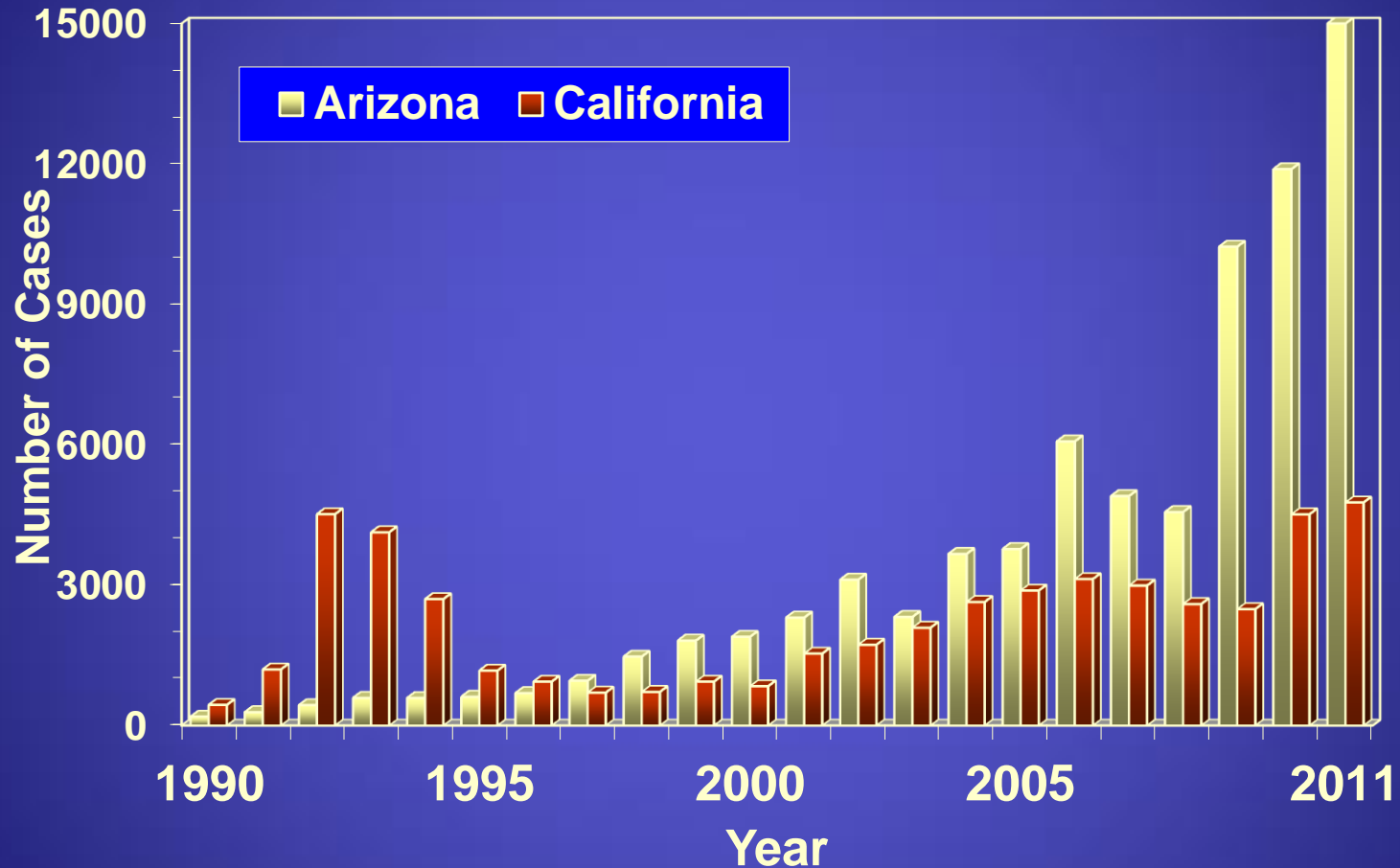
# CDC Seroprevalence Survey, NW Phoenix

- Objective: to investigate the high reported cocci rates in the NW Phoenix metro area
  - Compared to rest of Maricopa County
  - ID performed on 1594 remnant sera from  $\geq 65$  y.o. (797 in each area)
  - 9/797 (1.13% ) vs. 6/797 (0.75%) positive SC & MC respectively,  $p =$  not significant
  - Prevalence estimate 39,459 – 59,451 cases

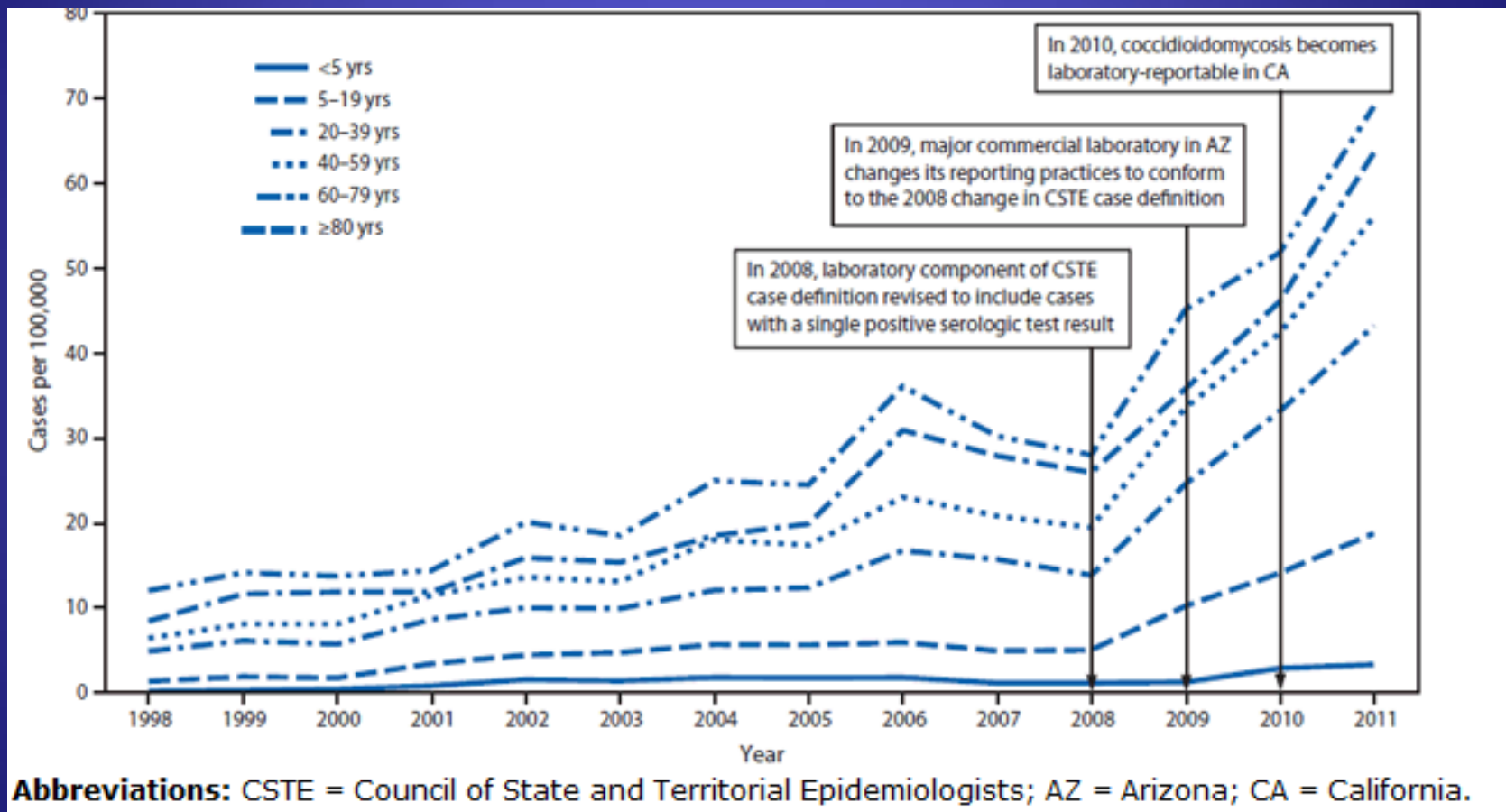
# Cocci Surveillance

- 40% are symptomatic
- $< 1/3$  are clinically evaluated
- Only 8-10% of total infections are serologically confirmed
- Only serologically confirmed are reported to public health

# Reported Valley Fever



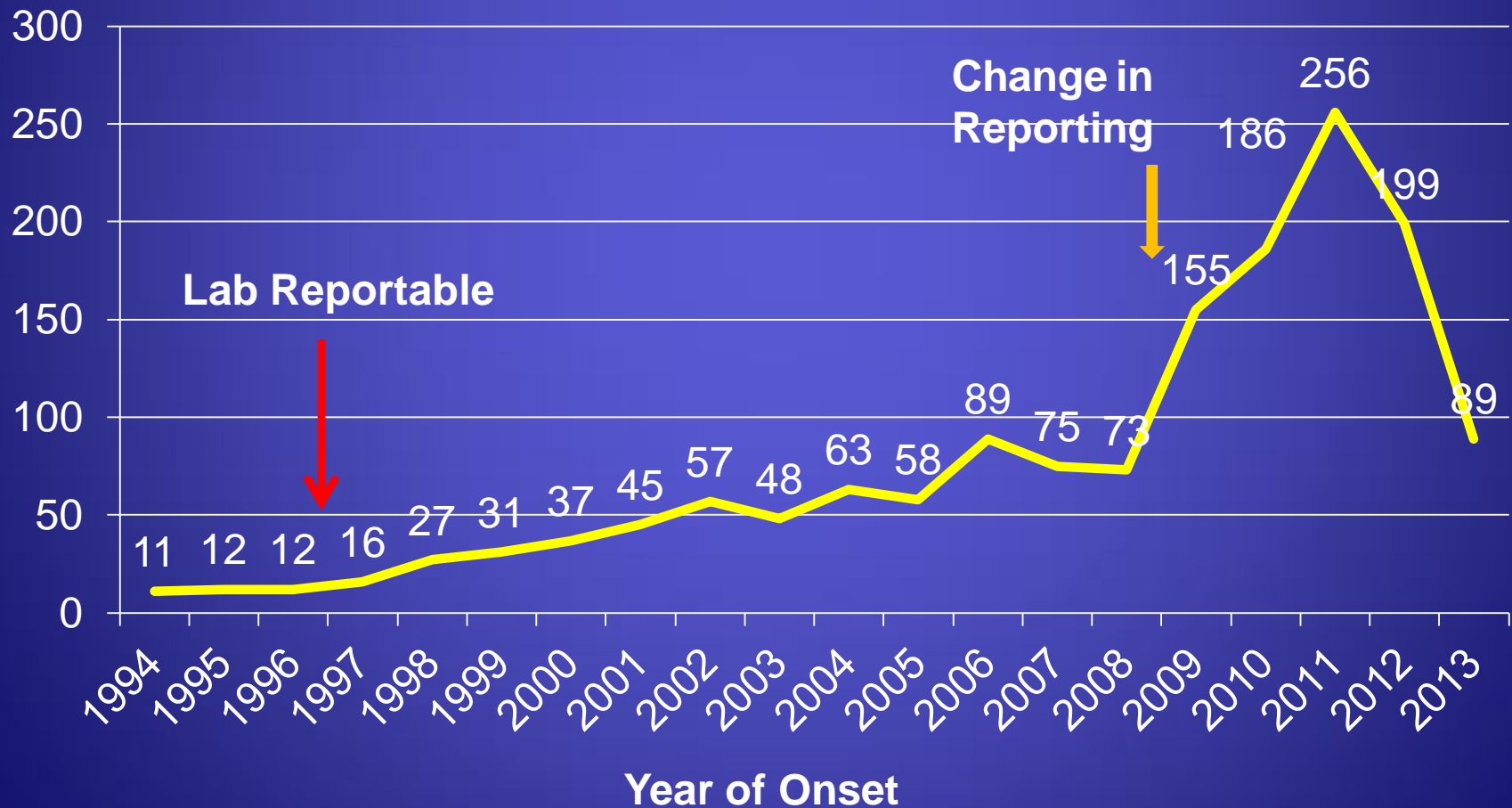
# Coccidioidomycosis incidence per 100,000 population, by age group — Arizona, California, Nevada, New Mexico, and Utah, 1998–2011



Cocci Rate increased from 5.3 to 42.6 per 100,000 from 1998-2011

MMWR March 29, 2013 / 62(12);217-221

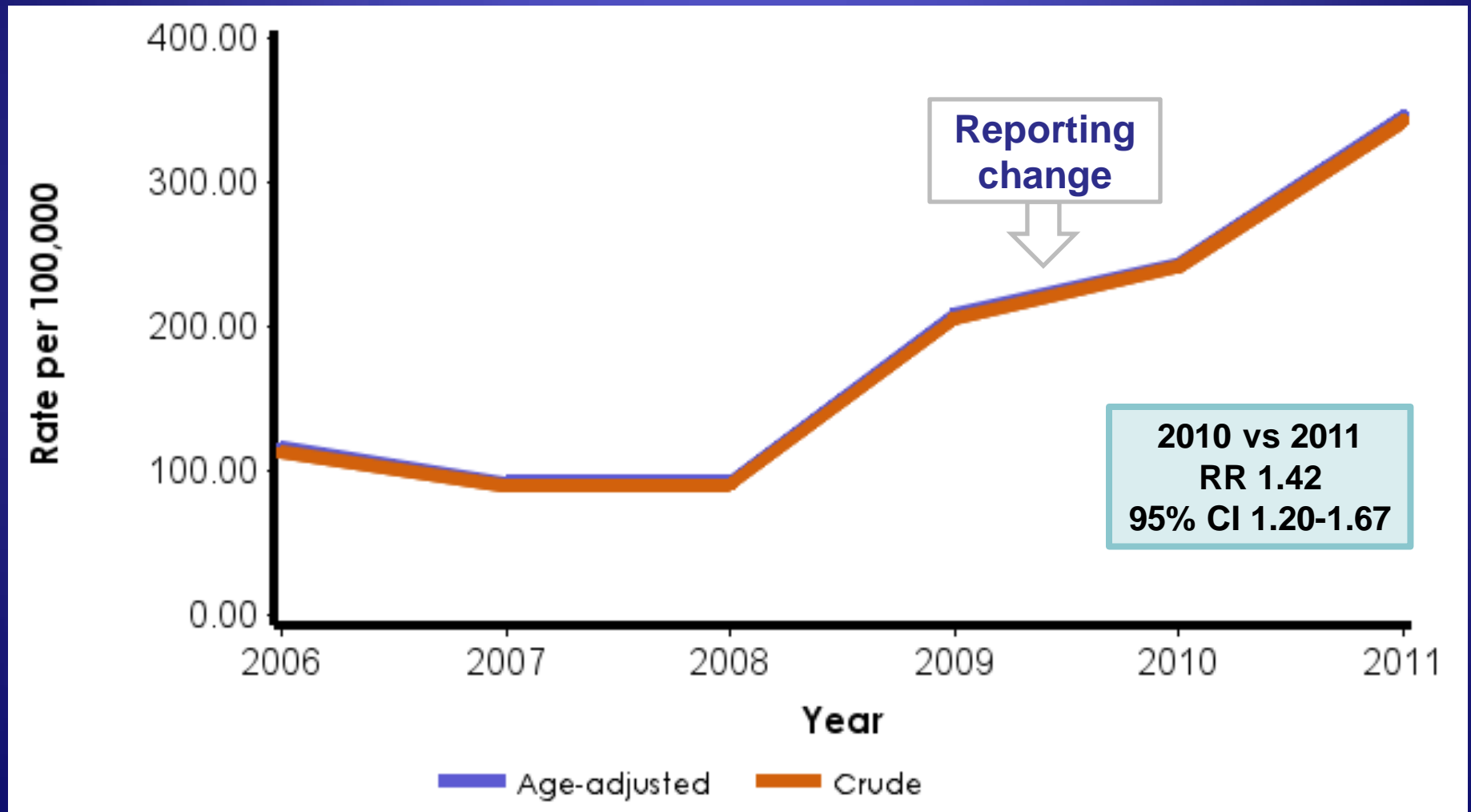
# Rates of Reported Valley Fever (VF) in Arizona, 1994-2013



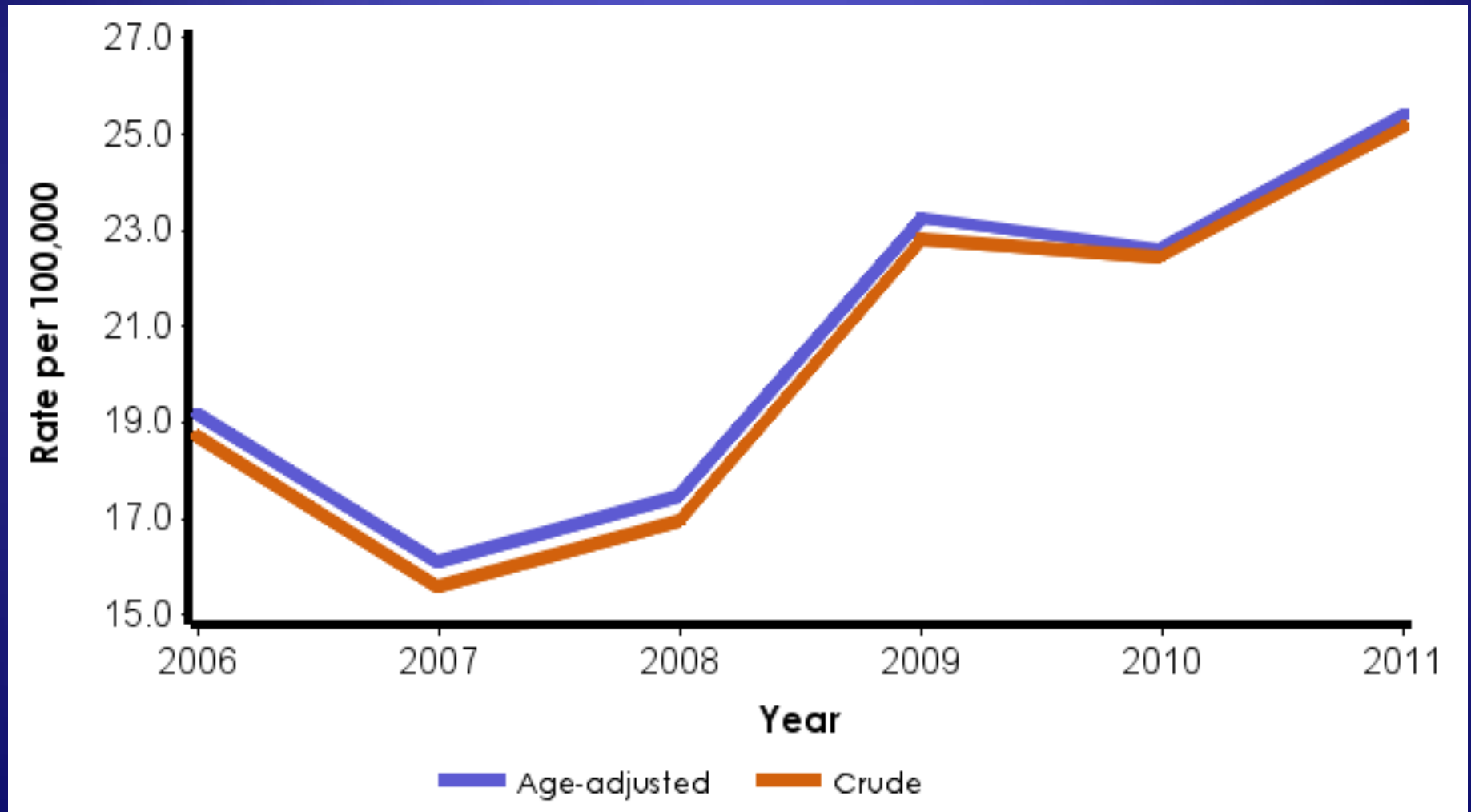
4849 Cases reported to date in 2014



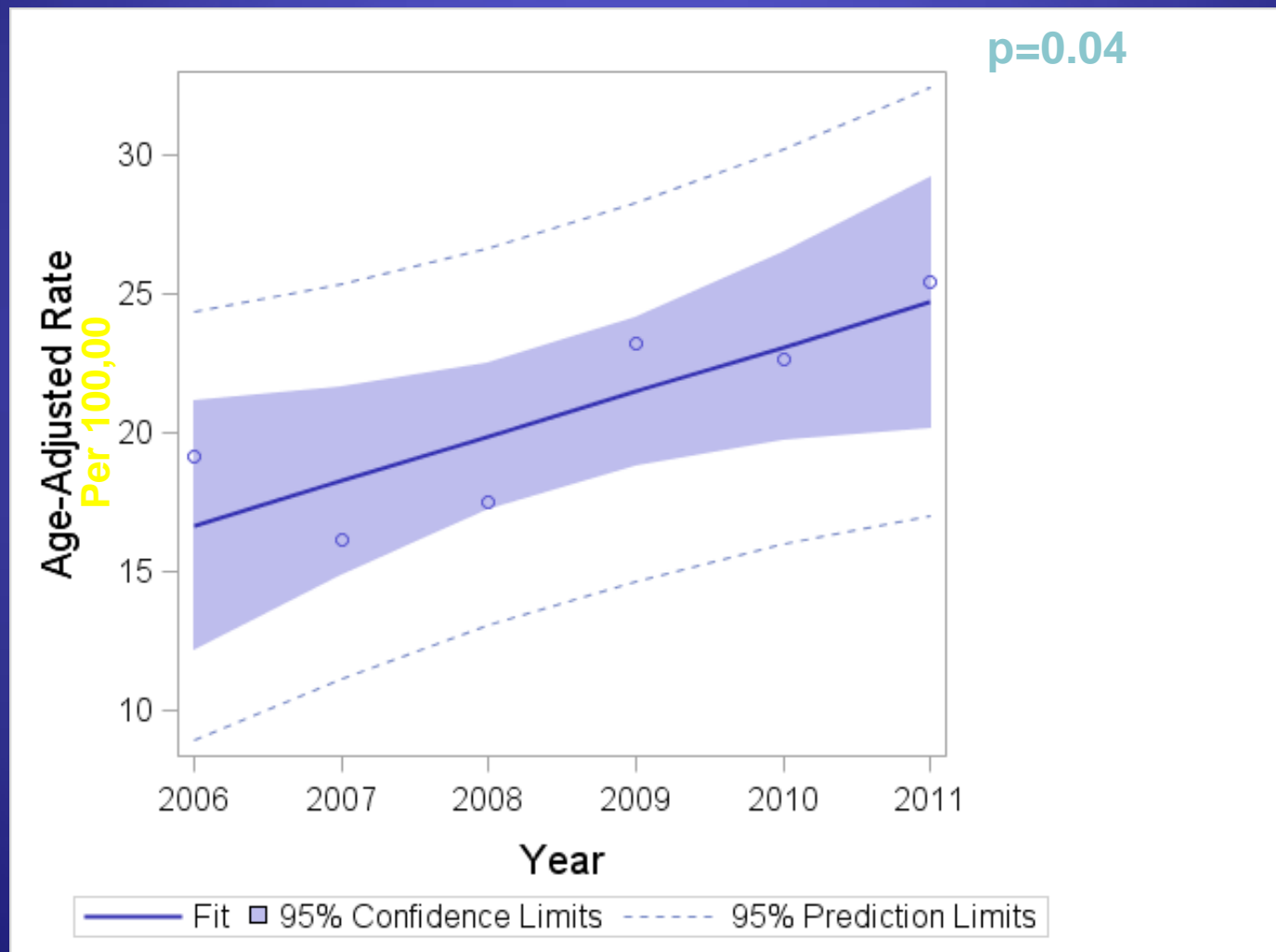
# Rates of reported cases of coccidioidomycosis in Maricopa County, 2006-2011



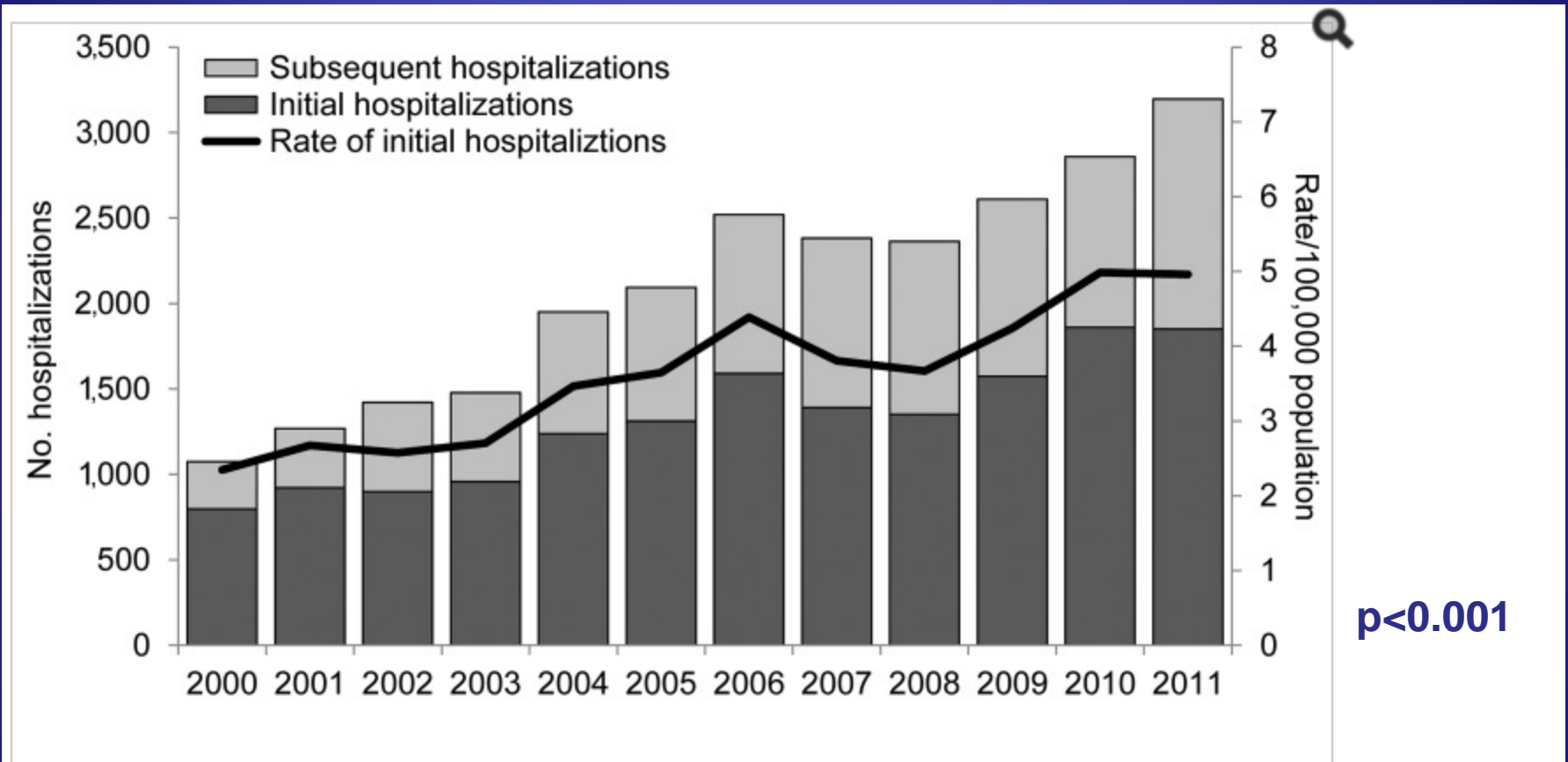
# Rates of hospitalizations from coccidioidomycosis in Maricopa County, 2006-2011



# Trend analysis of age-adjusted rates for hospitalizations

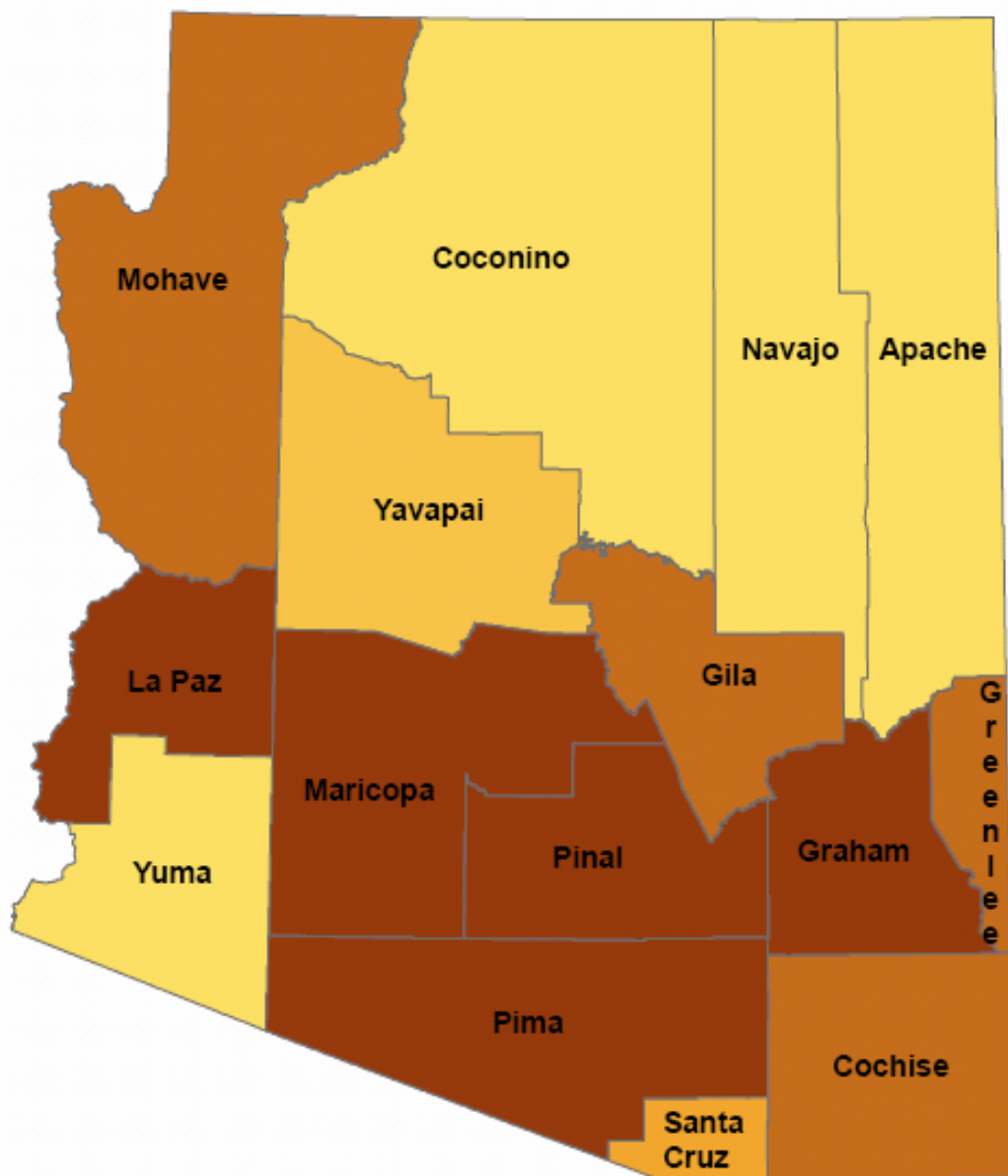


# Coccidioidomycosis-associated Hospitalizations, California, USA, 2000–2011

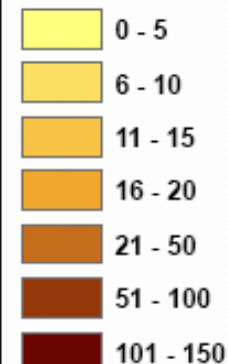


Numbers and annual rates of initial and subsequent coccidioidomycosis-associated hospitalizations (N = 25,217) by year of admission, California, 2000–2011.

# Arizona 2007 Reported Valley Fever Cases by County



## Cases per 100,000 County Residents



## Arizona 2007 Reported Valley Fever Cases

County	Cases per 100,000 Residents	Total Cases
Pima	90	904
Maricopa	89	3,459
Pinal	87	256
La Paz	69	15
Graham	66	24
Gila	27	15
Mohave	25	50
Greenlee	24	2
Cochise	23	32
Santa Cruz	15	7
Yavapai	12	26
Coconino	10	13
Navajo	10	11
Apache	7	5
Yuma	6	13

# US Coccidioidomycosis Mortality

- Based on cause of-death data from US death certificates from the National Center for Health Statistics for 1990–2008
- Included if cocci was listed as an underlying or contributing cause of death

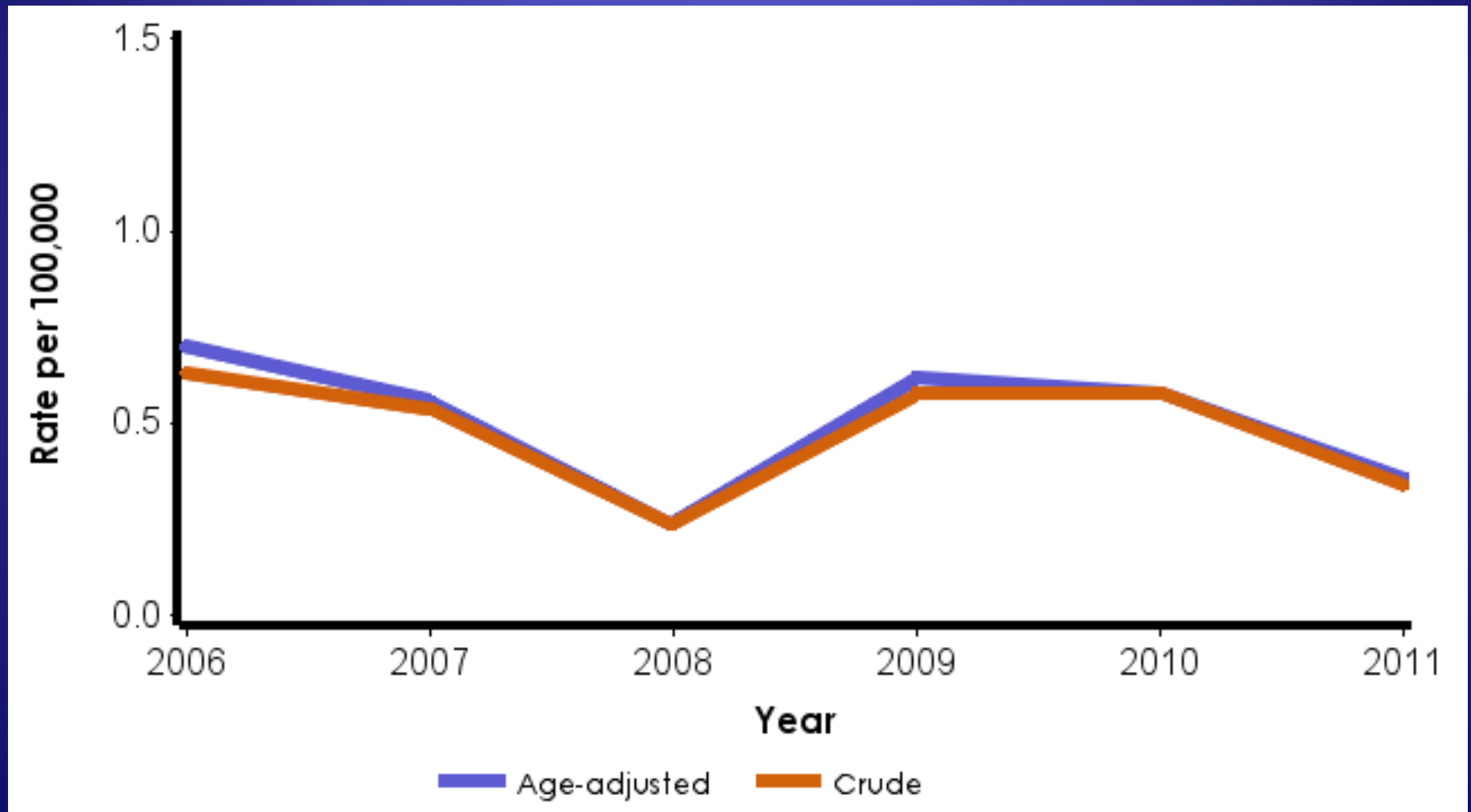
Huang JY, Bristow B, Shafir S, Sorvillo F. Emerg Infect Dis. 2012 Nov;18(11):1723-8.

# US Cocci Mortality 1990-2008

- 3,089 coccidioidomycosis- associated deaths among US residents
- 55,264 years of potential life lost
- Crude mortality rate: 0.58 per 1 million person-years (95% CI 0.56–0.61)
- Adjusted mortality rate: 0.59 per 1 million person-years (95% CI 0.57–0.61)

Huang JY, Bristow B, Shafir S, Sorvillo F. Emerg Infect Dis. 2012 Nov;18(11):1723-8.

# Rates of deaths from coccidioidomycosis in Maricopa County, 2006-2011





# Risk Factors for Death

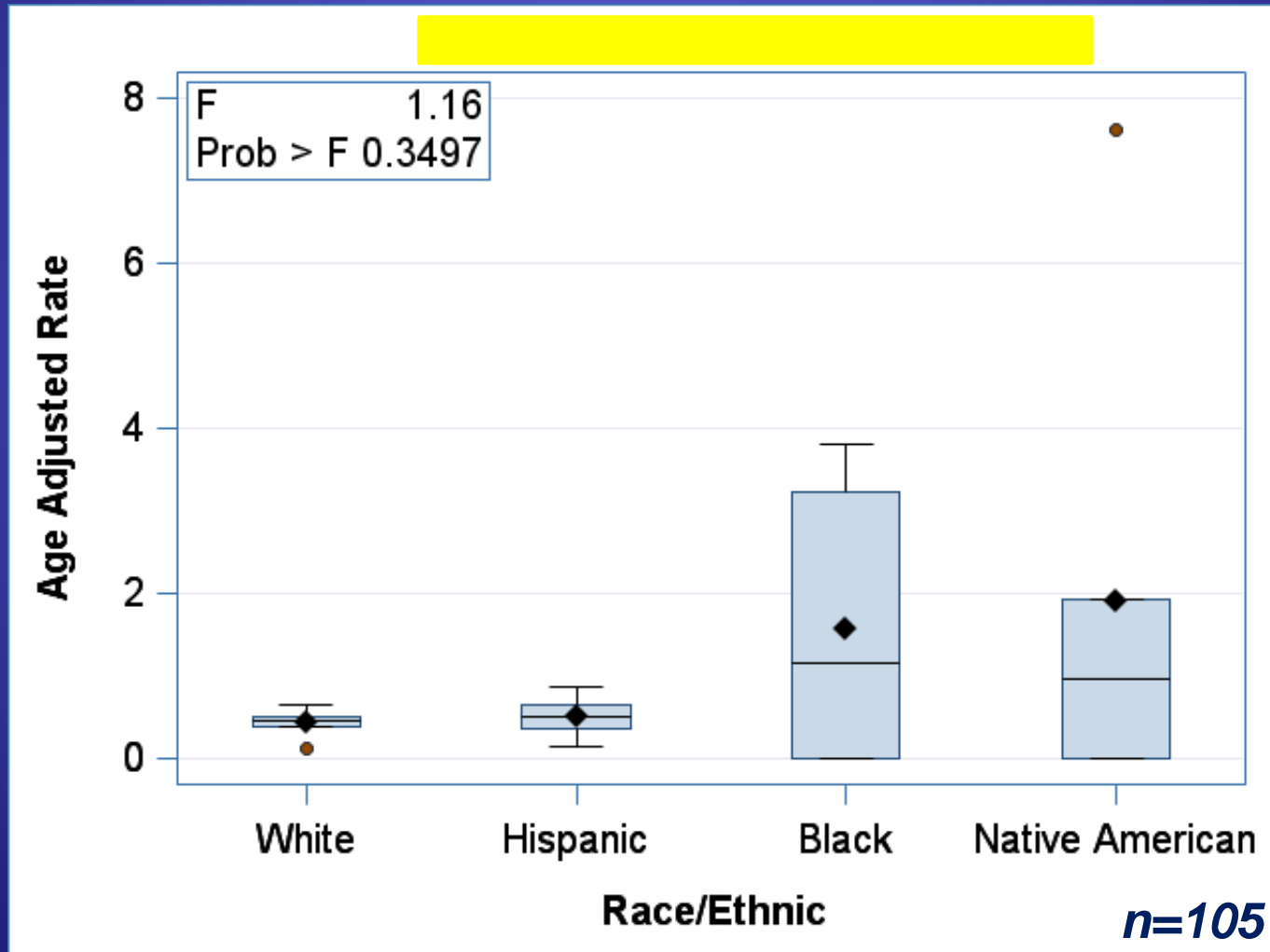
- Male RR 2.04 (95% CI 2.84–3.26)
- >65 years of age
- Non-White race or ethnicity

Huang JY, Bristow B, Shafir S, Sorvillo F. Emerg Infect Dis. 2012 Nov;18(11):1723-8.

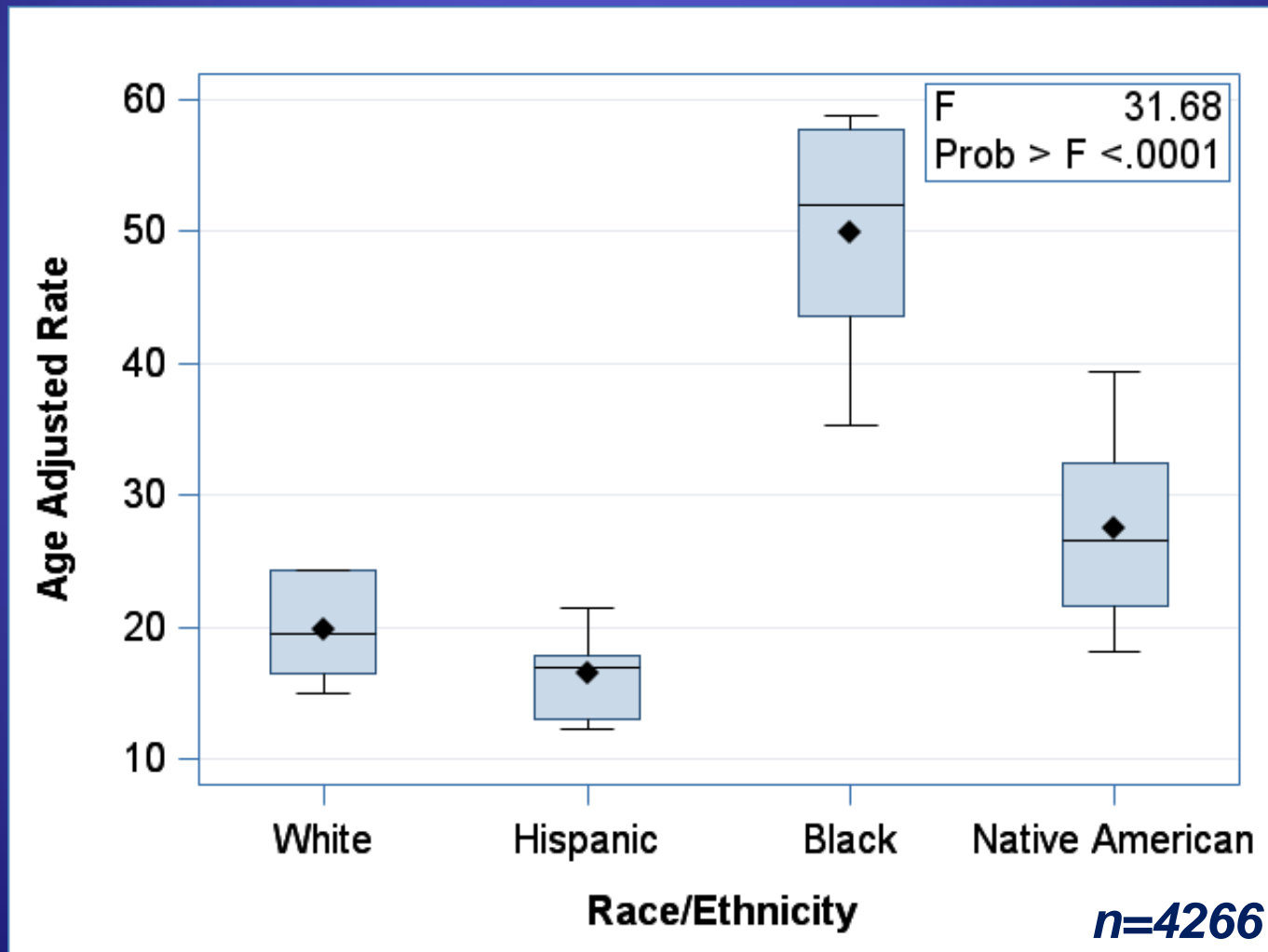
# US Adjusted Risk of Death Associated with Cocci by Race/Ethnicity, 1990-2008

Race/Ethnicity	Age-Adjusted Rate Ratio
White	Referent
Native American	6.34 (6.04–6.65)
Hispanic	4.38 (4.17–4.60)
Asian	2.82 (2.69–2.97)
Black	1.70 (1.61–1.80)

# Comparison of Average Age-Adjusted Death Rates from Cocci by Race/Ethnicity, Maricopa County 2006-11



# Comparison of Average Age-Adjusted Hospitalization Rates of Cocci by Race/Ethnicity, Maricopa County 2006-2011



# Valley Fever Surveillance (ES) - Arizona, 2007: Objectives

- To evaluate Arizona's coccidioidomycosis surveillance system
- To identify issues contributing to delayed diagnosis and under-reporting
- To measure the impact of cocci on Arizonans

# ES Methods

- 4832 cocci cases reported to ADHS in 2007
- Telephoned every 10<sup>th</sup> cocci case
- Interviews conducted using standardized questionnaire
- After at least 3 attempts, subsequent case contacted

# Valley Fever in Arizona, 2007

- Sex
  - 54% male (81 cases/100,000)
  - 46% female (68 cases/100,000)
- Race
  - 6% American Indian (28 cases/100,000)
  - 3% Asian (31 cases/100,000)
  - 8% African-American (37 cases/100,000)
- Average age: 51 years
  - Range: 38 days to 99 years
  - Rates among 65+ were more than twice the general population (163 cases/100,000 vs. 75 cases/100,000)

# Background: Cocci Case Definition

- Council for State and Territorial Epidemiologists (CSTE)
  - Updated in 1996
    - Clinical case definition
    - Lab criteria\*: cocci IgG – rising titer
  - Updated in 2007
    - Clinical case definition
    - Lab criteria\*: cocci IgG or IgM – single serology
- Arizona Department of Health Services (ADHS)
  - Since 1997
    - No clinical symptoms required
    - Lab criteria\*: cocci IgG or IgM– single serology

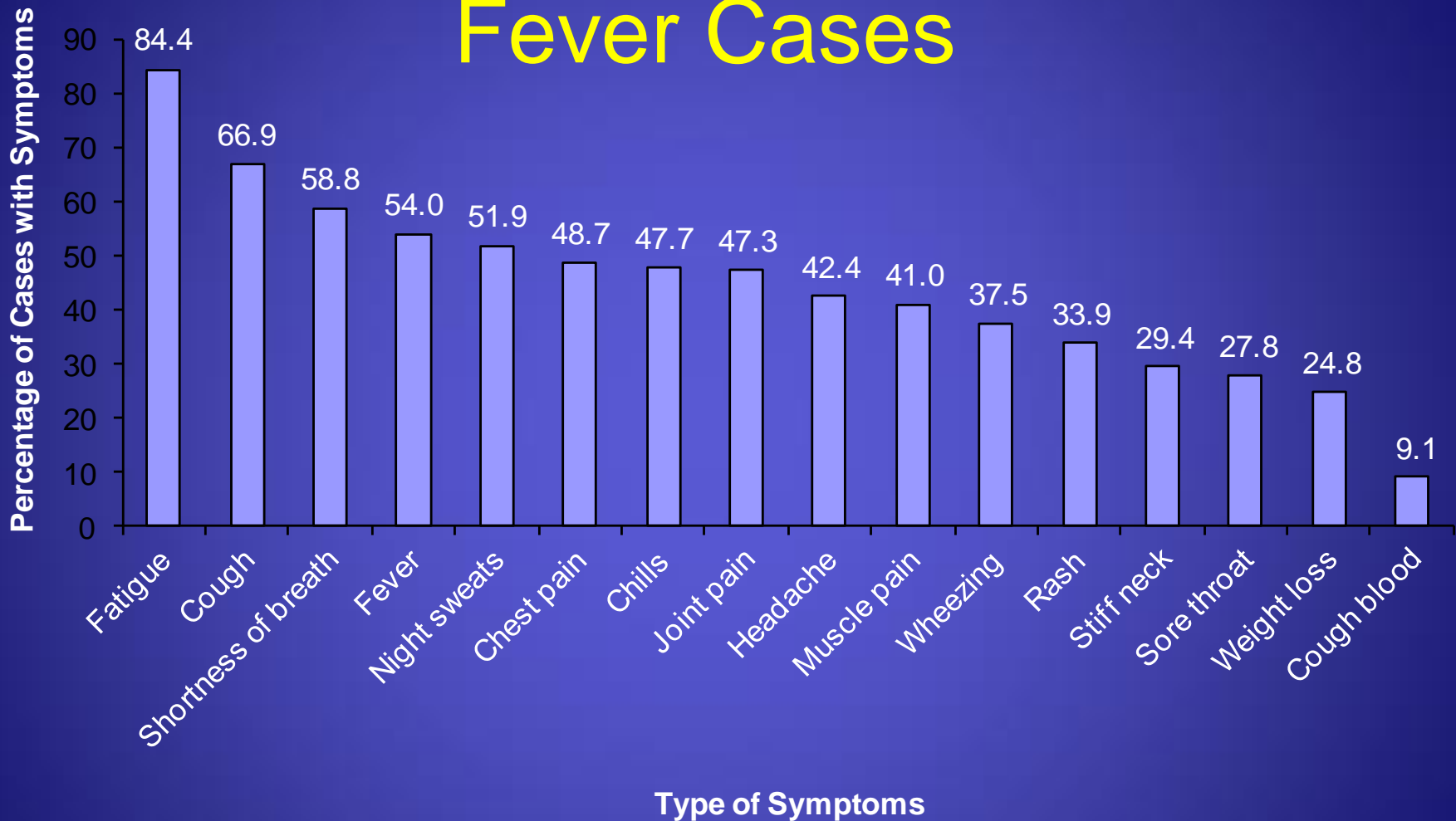
\*Lab criteria for diagnosis includes either detection of IgM/IgG or cultural, histopathologic, or molecular evidence of *Cocci* species



# Results – Evaluation of Arizona's Case Definition

- 493 cases interviewed
- 95% of Arizona cases ALSO meet the CSTE clinical case definition
  - Only 3% of cases reported no symptoms

# Common Symptoms of Valley Fever Cases



# Results – Impact on Healthcare System

- Almost half went to the ER for VF
- Over 40% were hospitalized overnight for the disease
- 1/4 saw their doctor at least 10 times during the course of their illness

# Cocci in Emergency Departments

- From cocci enhanced surveillance:
  - 23% of people with valley fever first sought care for their symptoms at an emergency department
  - 46% of the patients required care from an emergency room at some point during their illness
- From the Hospital Discharge Database:
  - 70% of inpatient visits started in the ED

# Results – Impact on People

- Cases were sick for an average of 6 months (median 109 days)
- 75% of cases missed work due to cocci
  - Average: 1 month (median 14 days)
- 75% unable to do usual daily activities
  - Average: > 3 months (median 47 days)

# Impact on Economy

- 2007 Hospital Discharge Database
  - 1,735 cocci-related hospital visits
  - Accounting for \$86 million in hospital charges
  - Average: \$50,000 hospital visit

# Results – Delays in Diagnosis

- Cases waited average of 44 days before seeking care for their valley fever
- Average time between seeking healthcare and getting diagnosed: 5 months
  - Those who knew about VF prior to seeking healthcare were more likely to be diagnosed and treated earlier than those who were not familiar with the disease (79 days vs. 282 days; p-value: 0.04)
- A mean of 3 provider visits occurred before cocci diagnostic testing ordered

# Behavioral Risk Factor Surveillance System (BRFSS)

- Conducts an annual population survey about health behaviors and opinions
- Designed to represent the entire population of Arizona



# BRFSS – Results

- 1/5 Arizonans have never heard of VF
- 60% believe VF is significant health problem
- More than 1/3 of general public do not know how VF is transmitted



# BRFSS – Results

- Length of time lived in Arizona
  - BRFSS average: 26 years
    - 25% lived in Arizona for less than 10 years
  - ES average: 16 years
    - 40% lived in Arizona for less than 10 years

# Coccidioidomycosis and Community Acquired Pneumonia (CAP)

# **Coccidioidomycosis as a Common Cause of Community-acquired Pneumonia**

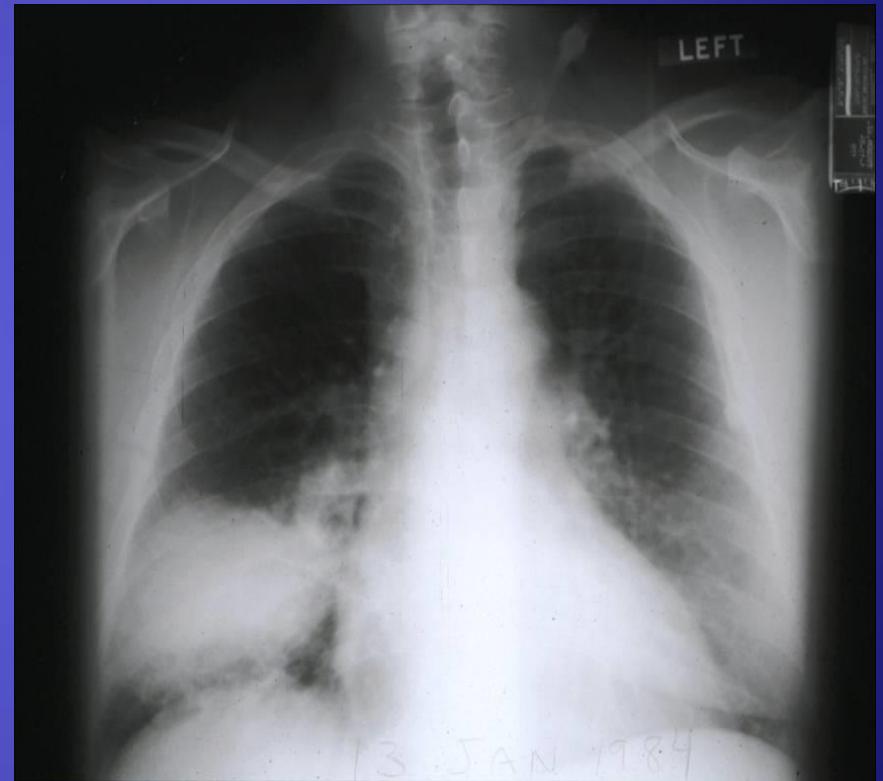
Lisa Valdivia,\*† David Nix,\*‡ Mark Wright,\* Elizabeth Lindberg,\* Timothy Fagan,§  
Donald Lieberman,§ T'Prien Stoffer,\* Neil M. Ampel,\*† and John N. Galgiani\*†

Emerging Infectious Diseases Vol 12 No 6, June 2006

- 56 patients with pneumonia recruited from 2 primary care sites and 1 urgent care clinic in Tucson
- 19 had positive antibody tests for valley fever (29%)
- 81% got antibiotics; 31% got > 1 course

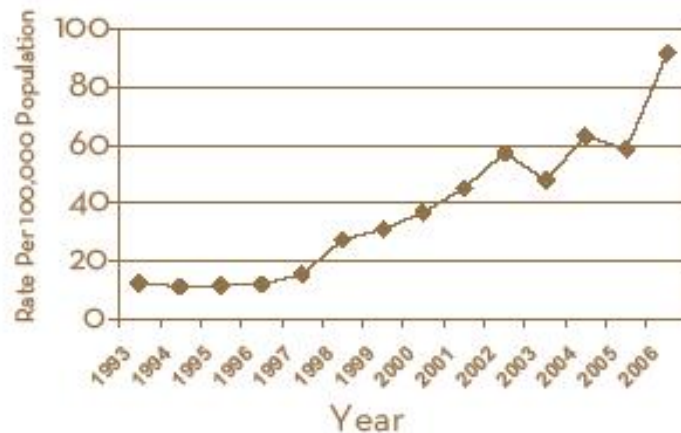
# Physician Education

- ADHS recommends patients with community-acquired pneumonia (CAP) are tested for cocci since May 2006
- Brochure and poster sent to 8,000 primary care providers across AZ
- Distributing another poster targeting EDs with CAP recommendation



## VALLEY FEVER CASES ARE INCREASING

Coccidioidomycosis rate per 100,000 population by year, Arizona -1993-2006



## WHAT CAN YOU DO?

- Order Cocci serology on CAP cases
- Manage Valley fever cases
  - Inform patient of diagnosis
  - Report the case to public health
  - Consider treatment with anti-fungal drugs if the patient is at risk for severe disease

For more information on treatment guidelines, visit [www.idsociety.org/pg](http://www.idsociety.org/pg)

## VALLEY FEVER MIMICS COMMUNITY ACQUIRED PNEUMONIA (CAP)

29% of Ambulatory CAP cases in Tucson, Arizona had diagnosis of Valley Fever.

Valdivia L, Nix D, Wright M, et al.

Coccidioidomycosis as a Common Cause of Community Acquired Pneumonia. *Emerging Infectious Diseases* 2006; 12: 958-62

### Resources

Arizona Department of Health Services  
Office of Infectious Disease Services  
150 N. 18th Ave, Suite 140  
Phoenix, Arizona 85007  
(602) 364-4562  
[www.valleyfeverarizona.org](http://www.valleyfeverarizona.org)

Valley Fever Center for Excellence  
Mail Stop 1111NF  
3601 S. 6th Avenue  
Tucson, Arizona 85723  
Hotline: (520) 629-4777  
<http://www.vfce.arizona.edu/>

# BIDS ED Study

- To evaluate the number of patients presenting with community-acquired pneumonia (CAP) in Tucson ERs tested for valley fever
- To determine the unmeasured burden of valley fever among these patients diagnosed with CAP
- Medical record review indicated:
  - Only 17% of CAP patients seen in the ER were tested, despite ADHS recommendations to test these patients for valley fever
  - 6% were positive

# Coccidioidal Pneumonia, AZ 2000-04

Kim, Blair, and Carey et al.

- Prospective study of 59 CAP patients
- 35 (59%) received paired serologic tests
- 6 (17%) had cocci pneumonia
- Cocci more likely to produce rash
- No help: med hx, occ or rec hx, time in endemic area, labs, CXR



# Three Studies, Three Answers

- Depending on
  - CAP definition
  - How cocci diagnosed
  - How much follow required
- 6% vs. 17% vs. 29% of CAP patients have cocci in endemic areas of AZ

# Knowledge, Attitudes and Practices Healthcare Provider Survey

- No data available on AZ healthcare providers regarding knowledge, attitudes and practices (KAP)
- Delays in cocci diagnosis due to patient and healthcare provider practices
- Objective: To assess health care providers' knowledge, attitudes and practices regarding diagnosis and treatment of cocci in AZ

# Study Design

- Study design:
  - Cross-sectional survey
  - Self-administered
  - Initial mailing in Oct 2007
  - Repeat mailing in Dec 2007

## Description of recipients (N= 7,608)

- Licensed primary care physicians (n= 5,554)
- Licensed nurse practitioners (n= 2,054)

# Questionnaire

- Demographics: clinical degree, specialty field, practice history
- Knowledge: burden of disease, vaccine availability, disease reporting
- Attitudes: confidence in ability to dx and treat
- Practices: counseling, dx, treatment, referral
- 9 treatment case scenarios, 5 straightforward
- Dichotomous and Likert-scale responses

# Response Results

First survey mailed to 9,248 AZ providers in Oct 2007

1,640 unable to contact

- 6 deaths
- 78 duplicates
- 228 retired
- 1,328 invalid addresses



Second survey mailed to 6,853 AZ providers in Dec 2007

5,785 non-respondents

1,068 respondents

1,823 (24%) total respondents

# Summary of Results

- 1/3 of providers were not aware that cocci is a reportable disease in Arizona
- 1/3 of providers were not sure if a cocci vaccine is available
- 2/3 confident in ability to diagnose cocci
- About half confident in ability to treat

# Summary of Results

- First cocci knowledge, attitudes and practices study conducted in the US
- 37.1% answered 2/2 knowledge questions correctly
- 42.2% answered  $\geq 70\%$  cocci treatment questions correctly based on current guidelines
- $< 20\%$  provide VF educational materials to pts
- Providers who received VF CME in last 12 months
  - Twice as likely to test CAP patients for cocci
  - Twice as likely to score  $\geq 70\%$

# Public Education

- Brochure with cocci info for the general public
- Video:  
“Valley Fever:  
The Impact on Arizonans”

Cough? Fever?  
Exhausted?

## Valley Fever?

Coccidioidomycosis



Photo courtesy of Rob Schumacher, The Arizona Republic, June 7, 2006



# COUGH? FEVER? EXHAUSTED?

*Photo courtesy of The Arizona Republic, June 7, 2006*



## ASK YOUR DOCTOR TO TEST YOU FOR VALLEY FEVER



Arizona Department of Health Services Office of Infectious Disease Services 150 N. 18th Ave, Suite 140 Phoenix, Arizona 85007 (602) 364-4562 [www.valleyfeverarizona.org](http://www.valleyfeverarizona.org)

# Future Studies

- Natural history study being conducted by CDC with AZ and CA to better describe
  - Coccidioidomycosis epidemiology
  - Who is tested, diagnosed, and treated
- NIH clinical trial to determine who to treat for primary pulmonary cocci
- Cocci skin test (Spherusol) approved by FDA – What is the true prevalence?

# Summary

- Reported cocci cases have been increasing in in the US and Arizona for the last decade with increasing hospitalization rates
- There are significant delays in diagnosing cocci due to provider AND patient practices
- Cocci has a tremendous impact on Arizonans
  - Healthcare system
  - Economic
  - Quality of life

# Take Home Points

- Coccidioidomycosis is a reportable disease in Arizona
- Think of cocci early and often in patients with prolonged (>2 weeks) of respiratory sxS and/or community acquired pneumonia
- If the first serology is negative, repeat it

# Website

The 2007 Valley Fever Annual Report and other materials are available at:

[www.valleyfeverarizona.org](http://www.valleyfeverarizona.org)

# Acknowledgments

- Clarisse Tsang
- Sara Imholte
- Shoana Anderson
- Ken Komatsu
- Cara Christ
- Laura Erhart
- Sanny Chen
- Ben Park
- Tom Chiller
- Peter Kelly
- Patty Gast
- John Galgiani
- Neil Ampel
- Orion McCotter
- Barbara Casimir
- Tina Wesoloskie
- Thom Wilson
- Andrew Comrie
- Valley Fever Center for Excellence
- Local Health Departments
- AZ hospitals and laboratories

# Questions?



# Phoenix, July 5<sup>th</sup>, 2011



Leadership for a Healthy Arizona

Department of  
Health Services