We conducted a cohort study to identify characteristics associated with testing for, and testing positive for, coccidiodomycosis among patients with community-acquired pneumonia in southern California, USA. Limited and delayed testing probably leads to underdiagnosis among non-Hispanic black, Filipino, or Hispanic patients and among high-risk groups, including persons in whom antimicrobial drug therapy has failed.

The public health impact of coccidiodomycosis (Valley fever) in the United States is increasing. The causative fungus, *Coccidioides*, is endemic to the southwestern and western United States. In 2015, California reported 3,015 cases, ≈25% of all US cases (1,2). In areas of Arizona where coccidiodomycosis is highly endemic, the disease might be responsible for 15%–29% of community-acquired pneumonia (CAP) cases; however, in some studies, <15% of CAP patients are tested, suggesting that the disease is underrecognized, even in endemic areas (3–5). Testing practices for CAP patients in southern California have not been well documented. Therefore, we determined the proportion of CAP patients who were tested, the proportion who tested positive, and clinical factors associated with being tested and having confirmed coccidiodomycosis among patients enrolled in the Kaiser Permanente Southern California (KPSC) healthcare system in 2011.

The Study
KPSC is an integrated healthcare organization with ≈4.4 million members who are representative of the socioeconomic and racial/ethnic diversity of the area’s population (6). KPSC uses electronic health records (EHRs) to integrate medical information from all care and laboratory settings. We included all KPSC patients meeting membership criteria who had CAP diagnosed and received treatment for CAP as outpatients (online Technical Appendix Table 1, https://wwwnc.cdc.gov/EID/article/24/4/16-1658-Techapp1.pdf). Information about each patient’s medical history during 2001–2011 was based on International Classification of Disease, Ninth Revision (ICD-9), codes retrieved from EHRs.

We searched CAP patient EHRs to identify coccidiodomycosis laboratory testing from all care settings (online Technical Appendix Table 1). We sought documentation of a coccidiodomycosis-related ICD-9 code (114.X) in any encounter type from 1 week before to 1 year after the sample collection date for patients with confirmed coccidiodomycosis cases. We excluded patients having received an ICD-9 coccidiodomycosis diagnosis before 2011 and those who had a hospitalization during the 2 weeks before CAP diagnosis.

To identify factors for multivariable modeling, we used χ² and t-tests (statistical significance defined as p<0.2), clinical knowledge, and a backward selection algorithm testing for interaction terms. We conducted analyses in SAS version 9.3 (SAS Institute, Cary, NC, USA).

After exclusions, the final cohort consisted of 33,756 patients (online Technical Appendix Table 2). Among patients with CAP, 2,061 (6%) were tested for coccidiodomycosis within 1 year of CAP diagnosis. A median of 6 (mean 46) days and a median of 2 (mean 5) clinic encounters elapsed between the index CAP date (i.e., the date the CAP ICD-9 code was first used) and the first order for a coccidiodomycosis test. Among patients who initially tested negative, 5% had a repeat test within 30 days and 8% within 90 days.

In adjusted analyses, testing for coccidiodomycosis was less likely among female patients and among Hispanic patients who survived 1 year after the index CAP date (compared with surviving non-Hispanic whites) (online Technical Appendix Table 2). Pulmonary clinics were most likely to test for coccidiodomycosis. Increasing
numbers of healthcare encounters involving a CAP ICD-9 code, inpatient visits, chest radiograph orders, and antimicrobial drug prescriptions in the years after CAP diagnosis increased the odds of being tested for coccidioidomycosis. Patients whose race/ethnicity was Filipino, Hispanic, American Indian/Alaska Native multiple, other, or unknown who died (from any cause) had increased odds of being tested for coccidioidomycosis compared with surviving non-Hispanic whites.

Of the 2,061 CAP patients tested for coccidioidomycosis, 377 (18%) were positive by any test; of these, 45 (12%) had ≥1 previous negative test before testing positive, and 172 (46%) were confirmed by complement fixation or immunodiffusion. Among those who tested positive by both IgG and IgM enzyme immunoassay (EIA), 88% were confirmed by complement fixation or immunodiffusion; only 10% of IgG-positive results and 7% of IgM-positive results were confirmed (online Technical Appendix Table 3).

In adjusted analyses, female sex was associated with reduced odds of testing positive (adjusted odds ratio [aOR] 0.60 [95% CI 0.42–0.86]). Persons of Filipino ethnicity (aOR 3.56 [95% CI 1.57–8.08]), non-Hispanic black race (aOR 2.78 [95% CI 1.50–5.12]), and Hispanic ethnicity (aOR 1.83 [95% CI 1.23–2.73) were more likely to test positive than were non-Hispanic whites. Kern County residents were more likely to test positive than Los Angeles County residents (aOR 2.48 [95% CI 1.56–3.95]) (online Technical Appendix Table 4). Having antimicrobial drugs prescribed ≥2 times (in addition to the treatment-defining CAP diagnosis) from 1 week before the first CAP visit to the first coccidioidomycosis test (aOR 4.57 [95% CI 1.29–16.12]) and having chest radiographs within 1 year after CAP diagnosis (aOR 2.30 [95% CI 1.54–3.45]) were associated with increased odds of testing positive.

Conclusions
We assessed testing practices for coccidioidomycosis among patients with CAP in southern California and found that only 6% of CAP patients were tested, of whom 18% were coccidioidomycosis-positive by any test and 8% by confirmatory testing. Further, our data highlight delayed testing for some patients, low rates of retesting, and opportunities to reduce unnecessary antibiotic use.

In conclusion, limited testing for coccidioidomycosis likely precludes accurate assessment of the overall frequency of the disease among CAP patients. Physician and community education might improve overall detection and result in earlier detection, which could be beneficial in decreasing overuse of antimicrobial drugs, reducing time and resources spent seeking other diagnoses, and improving monitoring for coccidioidomycosis complications.
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S.Y.T. had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. F.X. and R.C. conducted and are responsible for data analyses. R.K.M. and K.B. contributed to the design and conduct of the study; collection, management, analysis, and interpretation of the data; and preparation, review, or approval of the manuscript.

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References

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