



Brief Report

Antibiotic and antifungal treatment among persons with confirmed coccidioidomycosis – Southern California, 2011

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Received 13 April 2019; Revised 24 May 2019; Accepted 17 June 2019; Editorial Decision 3 June 2019

Abstract

We investigated coccidioidomycosis testing and treatment patterns among persons in an integrated health-care delivery system to identify gaps in diagnosis and treatment. Coccidioidomycosis diagnosis delays were common. Among persons who tested positive, 70% were prescribed antibiotics before positive coccidioidomycosis tests. Antibiotic treatment decreased and antifungal treatment increased after positive testing.

Key words: coccidioidomycosis, antibiotics, antifungals, treatment, electronic health records.

Coccidioidomycosis (Valley fever) is caused by inhalation of aerosolized spores from the soil-dwelling fungus *Coccidioides*.¹ Coccidioidomycosis is endemic in the western United States.² Approximately 40% of coccidioidomycosis infections are symptomatic, and clinical presentations are typically indistinguishable from those of common bacterial and viral respiratory infections.² Thus, clinicians might not initially suspect coccidioidomycosis, which can lead to limited testing and delayed or missed diagnosis.³ Misdiagnosis of coccidioidomycosis as bacterial pneumonia can lead to unnecessary antibiotic use, which can contribute to antimicrobial resistance and other adverse consequences.⁴ Moreover, misdiagnosis can lead to treatment delays or non-treatment, which might be particularly harmful for persons with risk factors for severe disease.¹

We investigated coccidioidomycosis testing and antimicrobial treatment patterns at Kaiser Permanente Southern California (KPSC), a large, integrated healthcare delivery system, to identify opportunities to promote judicious antibiotics use.

KPSC serves >4.5 million members who are representative of southern California's population.⁵ We identified coccidioidomycosis cases from positive laboratory tests from January 1 to December 31, 2011, documented in KPSC electronic health records (EHRs). We excluded persons who had coccidioidomycosis *International Classification of Disease, Ninth Revision, Clinical Modification* diagnosis codes in the year before their first positive test. KPSC's testing algorithm typically involves screening with enzyme immunoassay, with subsequent automatic reflex testing for positives off-site by immunodiffusion, complement fixation, or both to confirm the diagnosis. Cases were also identified by culture or histological report identifying *Coccidioides* spp.

We queried EHRs to identify health care events, including coccidioidomycosis tests and antimicrobial prescriptions. We identified the specimen collection date of the first of any positive coccidioidomycosis test for each person (hereafter all dates for coccidioidomycosis tests refer to the specimen collection dates and not the result dates). We then identified systemic antifungal

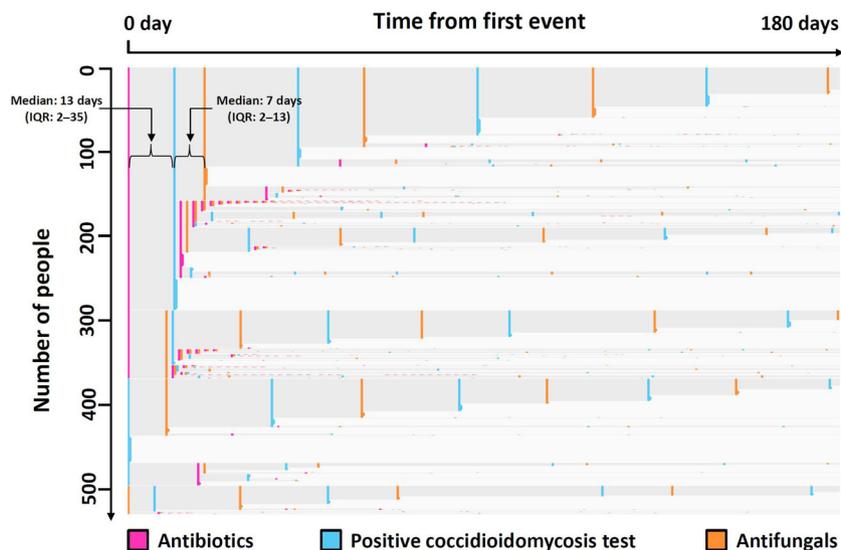


Figure 1. EventFlow plot of treatment and coccidioidomycosis event sequences. Events are represented by vertical bars and persons (on the y-axis) are aggregated by the order of their events. All events are aligned by the time from first event, which is represented on the x-axis. Bar height represents the proportion of patients with a given sequence, and bar color represents event type. Three events are shown: antibiotic treatment, positive coccidioidomycosis test, and antifungal treatment. Distance between bars represents the median time in days between any two events. All persons experienced ≥ 1 event type. Subsequent events of the same type were combined into the first event of that type. Time from first event is truncated to 180 days for clarity. The most common first event was antibiotic treatment, and the most common event sequence was antibiotic treatment followed by positive coccidioidomycosis test, and then antifungal treatment. Labels indicated with braces show median times with interquartile ranges between key events for persons who experienced the most common event sequence (i.e., antibiotic prescription, followed by positive coccidioidomycosis test, followed by antifungal prescription). For events that occurred on the same day, antibiotic treatments were considered to have occurred before other events, and antifungal treatments to have occurred before specimen collection of positive tests.

prescriptions filled ± 1 year and systemic antibiotic (specifically antibacterial) prescriptions filled ± 3 months after that test date (Table S1). We restricted the time interval for antibiotics to better identify antibiotics likely prescribed for coccidioidomycosis-related symptoms.

We used EventFlow, a data visualization tool developed by University of Maryland,⁶ to explore, organize, and identify patterns in the longitudinal events (i.e., date of positive coccidioidomycosis test, antifungal prescriptions, and antibiotic prescriptions). We also conducted EventFlow analyses by age group, sex, race/ethnicity, and county of residence. SAS[®] version 9.3 (SAS Institute, Cary, NC, USA) was used to obtain medians and interquartile ranges for the number of events and time to events. This study was approved by the KPSC institutional review board. CDC reviewed this study for human subjects' protections and deemed it to be nonresearch.

We identified 530 persons with coccidioidomycosis (median age: 43 years, range: 3–90). Of these, 334 (63.0%) were male, 209 (39.4%) were Hispanic (regardless of race), 204 (38.5%) were white, 43 (8.1%) were black, 23 (4.3%) were Filipino, 23 (4.3%) were other Asian/Pacific Islander, and 28 (5.3%) were of other race/ethnicity (Table S2). Most were residents of Kern County ($n = 277$, 52.3%) and Los Angeles County ($n = 116$, 21.9%).

Overall, 70% of persons received antibiotics in the 3 months before their first positive coccidioidomycosis test, and 36%

received them in the 3 months after their first positive coccidioidomycosis test. In contrast, 14% of persons received antifungals in the year before the first positive coccidioidomycosis test, and 79% received them after. In addition, half of all persons with confirmed coccidioidomycosis received ≥ 1 antibiotic prescription before their first positive test. The top five antibiotics were azithromycin, ceftriaxone, doxycycline, ciprofloxacin, and vancomycin.

The most common first event was antibiotic prescription ($n = 369$, 69.6%), followed by first positive coccidioidomycosis test ($n = 127$, 24.0%), and lastly, antifungal prescription ($n = 34$, 6.4%) (Fig. 1). Filipinos had the highest proportion of antibiotics as the first event ($n = 21$, 91.3%), compared with other race/ethnicity groups ($< 82.6\%$) (Table S2). Persons who had antibiotics first received a median of three antibiotic prescriptions (interquartile range [IQR]: 2–7) at any time during the study period, and a median of 12 days (IQR: 2–33) elapsed between date of first antibiotics and date of first coccidioidomycosis positive test.

The most common event sequence (limited to the first three events) was antibiotic prescription, followed by positive coccidioidomycosis test, followed by antifungal prescription (Fig. 1). Median time between first positive coccidioidomycosis test and antifungals was 7 days (IQR: 2–13).

The following statistics are limited to the 158 (29.8%) persons experiencing the most common sequence. Median time

