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# Epidemiological and Clinical Features of a Large Blastomycosis Outbreak at a Paper Mill in Michigan

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***Background.*** Blastomycosis is an environmentally acquired fungal infection that can result in severe pulmonary illness and high hospitalization rates. In 2023, a blastomycosis outbreak was detected among workers at a paper mill in Delta County, Michigan.

***Methods.*** We included patients with clinical and laboratory evidence of blastomycosis who had spent ≥40 hours in Delta County since 1 September 2022 and had illness onset 1 December 2022–1 July 2023. We assessed epidemiological and clinical features of patients and evaluated factors associated with hospitalization. We performed whole-genome sequencing to characterize genetic relatedness of clinical isolates from 8 patients.

***Results.*** In total, 131 patients were identified; all had worked at or visited the mill. Sixteen patients (12%) were hospitalized; 1 died. Compared with nonhospitalized patients, more hospitalized patients had diabetes ($P = .03$) and urine antigen titers above the lower limit of quantification ($P < .001$). Hospitalized patients were also more likely to have had ≥1 healthcare visits before receiving a blastomycosis diagnostic test ($P = .02$) and to have been treated with antibiotics prior to antifungal prescription ($P = .001$). All sequenced isolates were identified as *Blastomyces gilchristii* and clustered into a distinct outbreak cluster.

***Conclusions.*** This was the largest documented blastomycosis outbreak in the United States. Epidemiologic evidence indicated exposures occurred at or near the mill, and genomic findings suggested a common exposure source. Patients with diabetes may have increased risk of hospitalization, and elevated urine antigen titers could indicate greater disease severity. Early suspicion of blastomycosis may prompt earlier diagnosis and treatment, potentially reducing unnecessary antibiotic prescriptions and improving patient outcomes.

**Keywords.** blastomycosis; disease outbreaks; *Blastomyces*; risk factors; epidemiological and clinical features of fungal infections.

Blastomycosis is a fungal disease caused by inhalation of *Blastomyces* conidia (spores). Pulmonary symptoms are the most common manifestation, although extrapulmonary disease occurs in approximately 20% of patients [1–3]. A majority of reported blastomycosis cases require hospitalization, and in-hospital death occurs in 8%–14% of hospitalized patients [4–6]. Immunosuppressive conditions and delayed treatment are associated with greater disease severity [7–9]. Clinical similarities with other respiratory infections often result in diagnostic delays [10].

*Blastomyces* grows in moist soil and decomposing organic material [11–13]. Most blastomycosis cases are sporadic [8], but outbreaks have been linked to activities such as hiking near waterways, construction, and excavation [8, 11, 12, 14]. Although exposure sources are often difficult to identify due to the long incubation period (3 weeks to 3 months) and limited environmental detection methods [11, 15, 16], outbreak investigations provide insights into the epidemiology and clinical characteristics of blastomycosis [8]. Canine cases may also serve as sentinels for possible human exposures [17, 18].

We characterized epidemiological and clinical features of patients with blastomycosis during a large blastomycosis outbreak, and assessed factors associated with hospitalization.

## METHODS

### Index Cases and Public Health Response

A cluster of 3 blastomycosis cases among employees at a paper mill in Delta County in the Upper Peninsula of Michigan (Supplementary Figure 1) was identified in late February 2023, with 4 additional cases reported shortly thereafter. On March 6, Public Health Delta & Menominee (PHDM) and the Michigan Department of Health and Human Services (MDHHS) sent a health alert to healthcare providers

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recommending clinical workup for patients with community-acquired pneumonia (CAP) and notified the Centers for Disease Control and Prevention (CDC). The PHDM, MDHHS, and CDC jointly conducted outbreak response and prevention activities. This analysis focused on initial epidemiological findings and clinical features of outbreak cases detected through routine surveillance. An investigation to actively identify additional cases and further assess potential exposure sources was also conducted, the analysis of which is ongoing.

#### Case Definition and Case Finding

For this analysis, we included blastomycosis cases in patients who resided or had spent 40 or more hours in Delta County since 1 September 2022 who met the 2020 Council of State and Territorial Epidemiologists (CSTE) clinical and laboratory criteria for confirmed or probable blastomycosis cases [19], and who had illness onset between 1 December 2022 and 1 July 2023. (The CSTE blastomycosis clinical criteria include cases with at least 2 blastomycosis symptoms [cough, fever or chills or night sweats, shortness of breath, poor appetite or weight loss, myalgia, arthralgia, and fatigue] or who have 1 of the following clinical findings: abnormal lung findings on chest imagine, single or multiple skin lesions, bone or joint abnormality, meningitis or encephalitis or focal brain lesion, or abscess or granuloma or lesion in other body system. Confirmatory laboratory evidence includes identification of *Blastomyces* by culture, histopathology, cytopathology, or molecular assays. Presumptive laboratory evidence includes positive *Blastomyces* antigen or antibody tests. Antigen test results below the lower limit of quantification were also included in our case definition.) Cases were identified through healthcare provider reports and electronic laboratory records reported through the Michigan Disease Surveillance System (MDSS) [20]. Blastomycosis is a reportable disease in Michigan.

#### Data Collection and Epidemiological and Clinical Characteristics

PHDM and MDHHS conducted telephone interviews with all patients to collect information on patient demographics, potential exposures, and underlying medical conditions. MDHHS and CDC staff also conducted medical chart reviews through MDSS to further assess reported symptoms and underlying medical conditions, clinical findings, care-seeking and testing delays, laboratory testing within 2 weeks of incident specimen collection date, and treatment information. To assess care-seeking delays, we calculated the days between symptom-onset date and first healthcare visit date for blastomycosis-like symptoms (the care-seeking interval). We assessed delays in provider recognition of blastomycosis by calculating the number of healthcare visits before receiving a blastomycosis diagnostic test, and the days between a patient's first healthcare visit and the first specimen collection date (the testing interval), regardless of result [21]. We calculated the weekly median and interquartile range (IQR) of the care-seeking interval to assess changes in care seeking over the course of the outbreak. Similarly, we calculated the weekly median and IQR of the testing interval to assess changes in provider recognition of blastomycosis. Finally, we calculated total time from symptom onset to prescription of antifungal treatment. We also contacted 4 Delta County veterinary practices to informally inquire whether veterinarians had noted recent increases in canine blastomycosis cases.

#### Data Analysis

We compared epidemiological and clinical characteristics of patients who had hospital admissions for blastomycosis (hospitalized patients) with those who were diagnosed and managed in the outpatient setting (nonhospitalized patients) using Pearson's chi-square tests and Fisher's exact tests for categorical variables and Wilcoxon rank-sum tests for numeric variables ($\alpha = .05$). We conducted analyses in R (version 4.2.3; R Project for Statistical Computing).

#### Genomic Analysis

Fungal specimens from patients with culture-confirmed blastomycosis ($n = 8$) were sent to the MDHHS Bureau of Laboratories for whole-genome sequencing (WGS) to identify *Blastomyces* species and characterize phylogenetic relatedness. We included 2 Michigan contextual isolates in phylogenetic analyses to help further interpret phylogenetic relatedness: 1 was collected in May 2023 from a non–epidemiologically linked patient who resided in an adjacent county. The second isolate was collected in July 2023 from a dog that had stayed within 1 mile of the paper mill. We also included 8 publicly available comparators (Supplementary Methods).

This activity was reviewed by CDC, deemed not research, and was conducted consistent with applicable federal law and CDC policy (eg, 45 C.F.R. part 46, 21 C.F.R. part 56; 42 U.S.C. §241(d); 5 U.S.C. §552a; 44 U.S.C. §3501 et seq).

## RESULTS

A total of 131 patients were identified during the outbreak with symptom-onset dates from December 2022 to May 2023 (Figure 1*A*). The median age was 41 years (IQR: 33–51 years) (Table 1). Most (89%) were male, and 81% were non-Hispanic White. All were employees, contractors, or visitors to the paper mill. The attack rate was 13% among employees at the mill (117 cases/889 total employees). Total numbers of contractors and visitors were not available to estimate attack rates for these groups. A minority (30%) reported potential recreational exposures, such as hunting or all-terrain vehicle usage, within 3 months before symptom onset, and 12% reported exposure to soil or wood outside of the workplace. No other community-associated cases in Delta County were reported during the

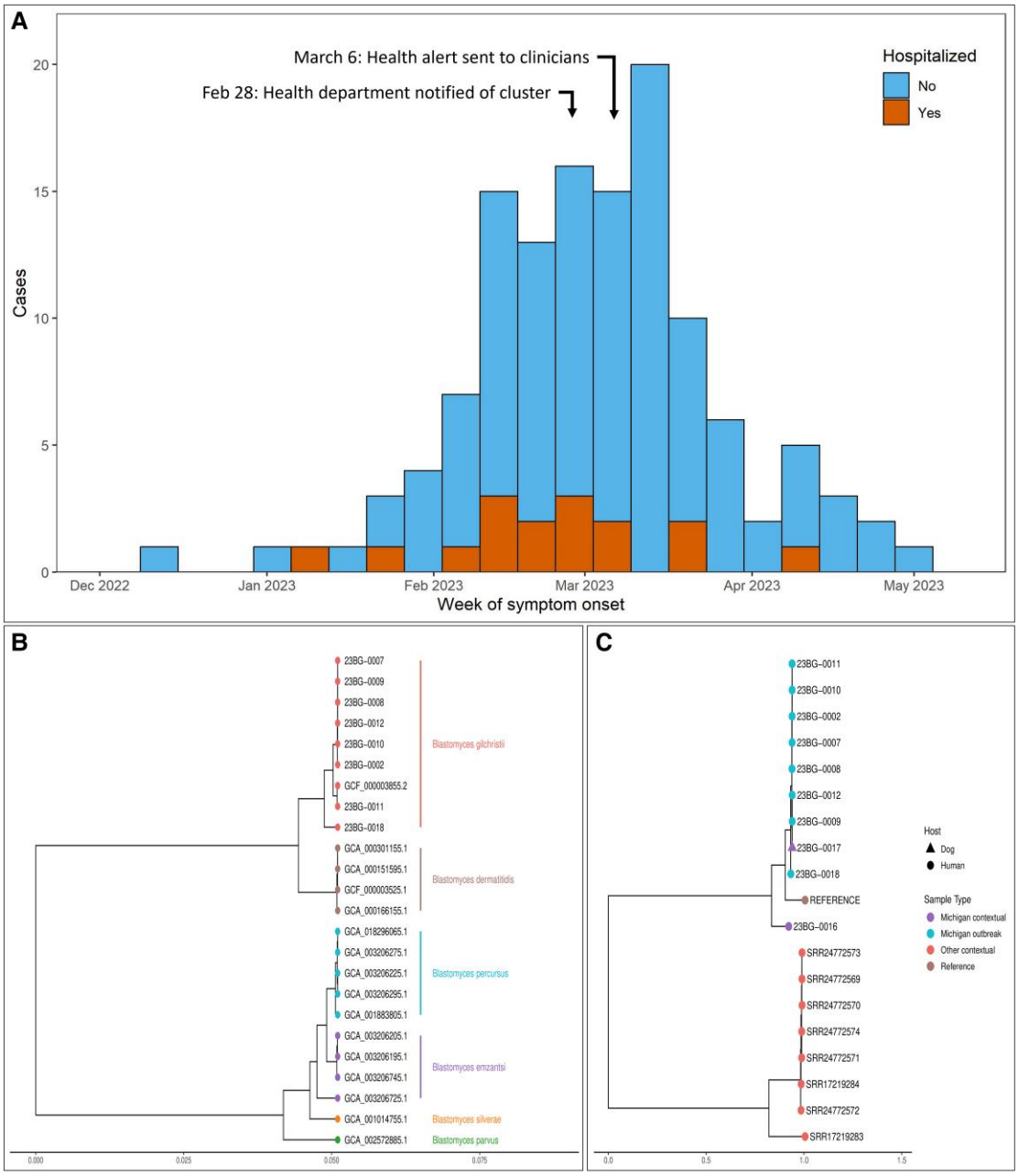


**Figure 1.** Number of blastomycosis cases by week of symptom-onset date and hospitalization status (*A*), phylogenetic tree based on Mash distances showing outbreak-associated isolates clustering with *Blastomyces gilchristii* (*B*), and maximum-likelihood phylogenetic tree of the 8 outbreak isolates and 2 Michigan contextual isolates compared with 8 publicly available contextual comparators (*C*).

outbreak period, and local veterinarians reported not observing any increases in canine cases.

All 8 outbreak isolates were identified as *Blastomyces gilchristii* (Figure 1*B*) and clustered into a single cluster (bootstrap value = 100%) (Figure 1*C*). The isolate from the dog that stayed at a house near the mill also clustered with the outbreak isolates, whereas the human contextual isolate from an adjacent county was not closely related (Figure 1*C*). The 8 outbreak isolates and the canine isolate were all within 100 single nucleotide polymorphisms (SNPs) from each other, whereas they were more than 3500 SNPs away from the other contextual isolate and more than 10 000 SNPs away from the public comparators.

Cough was the most commonly reported symptom (95%), followed by fatigue (81%), dyspnea (80%), myalgia (71%), night sweats (66%), and chest pain (64%) (Table 2). Patients reported both anginal and pleuritic chest pain, and the site of the reported chest pain generally correlated with imaging findings (Supplementary Table 1). Skin lesions were reported in 5

**Table 1. Demographic Characteristics and Potential Exposures Among Patients During a Large Blastomycosis Outbreak at a Paper Mill in Michigan**

| Characteristic | Overall (n = 131) | Hospitalized: Yes (n = 16) | Hospitalized: No (n = 115) | P[a] |
|---|---|---|---|---|
| Age, y | 41 (33, 51) | 46 (33, 52) | 41 (33, 51) | .63 |
| Age group | | | | .62 |
| 29 y and younger | 20 (15%) | 1 (6%) | 19 (17%) | |
| 30–39 y | 35 (27%) | 5 (31%) | 30 (26%) | |
| 40–49 y | 37 (28%) | 4 (25%) | 33 (29%) | |
| 50–59 y | 31 (24%) | 4 (25%) | 27 (23%) | |
| 60+ y | 8 (6%) | 2 (13%) | 6 (5%) | |
| Sex | | | | .22 |
| Male | 117 (89%) | 16 (100%) | 101 (88%) | |
| Female | 14 (11%) | 0 (0%) | 14 (12%) | |
| Race/ethnicity | | | | .43 |
| White, NH | 106 (81%) | 13 (81%) | 93 (81%) | |
| Unknown | 22 (17%) | 2 (13%) | 20 (17%) | |
| Other | 3 (2%) | 1 (6%) | 2 (2%) | |
| Association with paper mill | | | | .73 |
| Employee | 117 (89%) | 14 (88%) | 103 (90%) | |
| Contractor | 12 (9%) | 2 (13%) | 10 (8%) | |
| Visitor | 2 (2%) | 0 (0%) | 2 (2%) | |
| Potential recreational exposure[b] | 39 (30%) | 4 (25%) | 35 (30%) | .78 |
| Hunting | 20 (15%) | 3 (19%) | 17 (15%) | .71 |
| All-terrain vehicle (ATV) usage | 18 (14%) | 3 (19%) | 15 (13%) | .46 |
| Hiking | 12 (9%) | 0 (0%) | 12 (10%) | .36 |
| Potential exposure to soil or wood outside of work[b] | 16 (12%) | 0 (0%) | 16 (14%) | .22 |
| Wood/brush cutting | 11 (8%) | 0 (0%) | 11 (10%) | .36 |
| Handling wet soil | 9 (7%) | 0 (0%) | 9 (8%) | .60 |
| Excavation/digging | 6 (5%) | 0 (0%) | 6 (5%) | >.99 |

Values are median (interquartile range) or n (%).

Abbreviation: NH, non-Hispanic.

[a]*P* values derived by using Wilcoxon rank-sum test, Fisher's exact test, or Pearson's chi-square test.

[b]Potential exposures outside of work reported by patients in 90 days before symptom onset.

**Table 2. Signs and Symptoms, Underlying Conditions, and Social History of Patients During a Large Blastomycosis Outbreak at a Paper Mill in Michigan**

| Characteristic | Overall (n = 131) | Hospitalized: Yes (n = 16) | Hospitalized: No (n = 115) | P[a] |
|---|---|---|---|---|
| Signs and symptoms | | | | |
| Cough | 124 (95%) | 16 (100%) | 108 (94%) | .60 |
| Fatigue | 106 (81%) | 15 (94%) | 91 (79%) | .31 |
| Dyspnea | 105 (80%) | 16 (100%) | 89 (77%) | .04 |
| Myalgia | 93 (71%) | 11 (69%) | 82 (71%) | .78 |
| Night sweats | 86 (66%) | 13 (81%) | 73 (63%) | .16 |
| Chest pain | 84 (64%) | 10 (63%) | 74 (64%) | .89 |
| Fever | 63 (48%) | 14 (88%) | 49 (43%) | <.001 |
| Weight loss | 27 (21%) | 10 (63%) | 17 (15%) | <.001 |
| Headache | 22 (17%) | 3 (19%) | 19 (17%) | .73 |
| Hemoptysis | 10 (8%) | 3 (19%) | 7 (6%) | .11 |
| Skin lesions | 5 (4%) | 0 (0%) | 5 (4%) | >.99 |
| Neurological symptoms | 0 (0%) | 0 (0%) | 0 (0%) | |
| Underlying conditions and medications[b] | | | | |
| Obesity[c] | 54 (59%) | 10 (71%) | 44 (56%) | .29 |
| Diabetes mellitus[d] | 11 (8%) | 4 (25%) | 7 (6%) | .03 |
| Kidney disease | 2 (2%) | 1 (6%) | 1 (1%) | .23 |
| Immune-suppressive medications | 2 (2%) | 0 (0%) | 2 (2%) | >.99 |
| COPD | 1 (1%) | 0 (0%) | 1 (1%) | >.99 |
| Malignancy[e] | 1 (1%) | 0 (0%) | 1 (1%) | >.99 |
| Transplantation | 0 (0%) | 0 (0%) | 0 (0%) | |
| HIV | 0 (0%) | 0 (0%) | 0 (0%) | |
| Social history | | | | |
| Tobacco use, current | 8 (6%) | 1 (6%) | 7 (6%) | >.99 |
| Tobacco use, previous | 41 (31%) | 6 (38%) | 35 (30%) | .57 |
| Alcohol use disorder | 0 (0%) | 0 (0%) | 0 (0%) | |

Values are shown as n (%).

Abbreviations: BMI, body mass index; COPD, chronic obstructive pulmonary disease; HIV, human immunodeficiency virus.

[a]*P* values derived by using Fisher's exact test or Pearson's chi-square test.

[b]Present in the 90 d before symptom onset.

[c]Obesity was defined as BMI ≥ 30 kg/m$^2$. Obesity prevalence was only calculated for 91 patients for whom BMI values were available.

[d]Diabetes type was available for 8 of 11 patients, all of whom had type 2 diabetes mellitus.

[e]Prostate cancer was reported in 1 patient.

patients (4%), and none reported neurological symptoms or other signs of disseminated disease. Sixteen patients (12%) were hospitalized during the outbreak. Hospitalized patients were more likely than nonhospitalized patients to have dyspnea (100% vs 77%; $P = .04$), fever (88% vs 43%; $P < .001$), and weight loss (63% vs 15%; $P < .001$). Diabetes was more common among hospitalized patients (25%) compared with nonhospitalized patients (6%) ($P = .04$), as was obesity, although the difference was not statistically significant (71% vs 56%; $P = .28$). Compared with nonhospitalized patients, hospitalized patients more frequently had abnormal chest radiograph findings (100% vs 73%; $P = .06$) and pneumonia diagnoses (94% vs 34%; $P < .001$) (Supplementary Table 2). Patients who met the CSTE criteria for confirmed cases based on confirmatory laboratory evidence (n = 28) were more likely to have been hospitalized ($P = .006$) and have weight loss and hemoptysis ($P < .05$) compared with those with laboratory evidence that met the CSTE definition for probable cases (n = 103) (Supplementary Table 3). Other characteristics, such as underlying conditions, demographics, and potential nonoccupational exposures, were not significantly different between the 2 groups.

Median in-hospital admission time was 7 days (IQR: 4–12 days) (Supplementary Table 4). Four (25%) hospitalized patients received supplemental oxygen, 2 patients (13%) received intensive care unit (ICU) care, and 1 patient (6%) received invasive mechanical ventilation and died. The median care-seeking interval was 8 days (IQR: 4–11 days) among hospitalized patients compared with 10 days (IQR: 3–24 days) among nonhospitalized patients ($P = .32$) (Figure 2*A*, Supplementary Table 5).

Hospitalized patients had a longer testing interval (median = 2 days; IQR: 0–7 days) compared with nonhospitalized patients (median = 0 days; IQR: 0–0 days) ($P = .002$) (Figure 2*C*) and were more likely to have had 1 or more healthcare visits before first receiving a blastomycosis diagnostic test (44% vs 17%; $P = .02$). Weekly median intervals for care seeking and testing both declined substantially over the course of the outbreak (Figure 2*B* and 2*D*, Supplementary Table 5).

*Blastomyces* urine antigen tests were the most frequently used diagnostic tests: 86% of patients received at least 1 urine antigen test, and 97% of patients who received at least 1 urine antigen test had a positive result (Table 3). Average turnaround times from specimen collection to result date varied between medians of 0 and 1 day (IQR: 0–1 day) for histopathology and cytology, 5 days (IQR: 4–6 days) for antigen tests, and 13 days (IQR: 3–18 days) for culture. Culture, cytology, serology, and histopathology were more often used in hospitalized patients compared with nonhospitalized patients (Supplementary Table 6). Hospitalized patients were also more likely to have urine antigen results within quantifiable limits or above the upper limit of quantification (100%) compared with nonhospitalized patients (47%) ($P < .001$); this association remained when restricting to tests collected before antifungal prescription (100% vs 38%; $P < .001$) (Supplementary Table 7). Concern for potential workplace exposure (eg, the patient citing concern about a blastomycosis outbreak at their workplace, or that numerous colleagues had tested positive for blastomycosis) was documented in medical charts from 86% of 158 healthcare visits with available exposure and testing information. Patients were more likely to receive blastomycosis diagnostic tests during visits when concern for potential workplace exposure was documented (76%), compared with visits when it was not (5%) ($P < .001$) (Supplementary Table 8).

Among 95 patients for whom antifungal treatment information was available, 98% received itraconazole and 8% received amphotericin B (Supplementary Table 9). Hospitalized patients

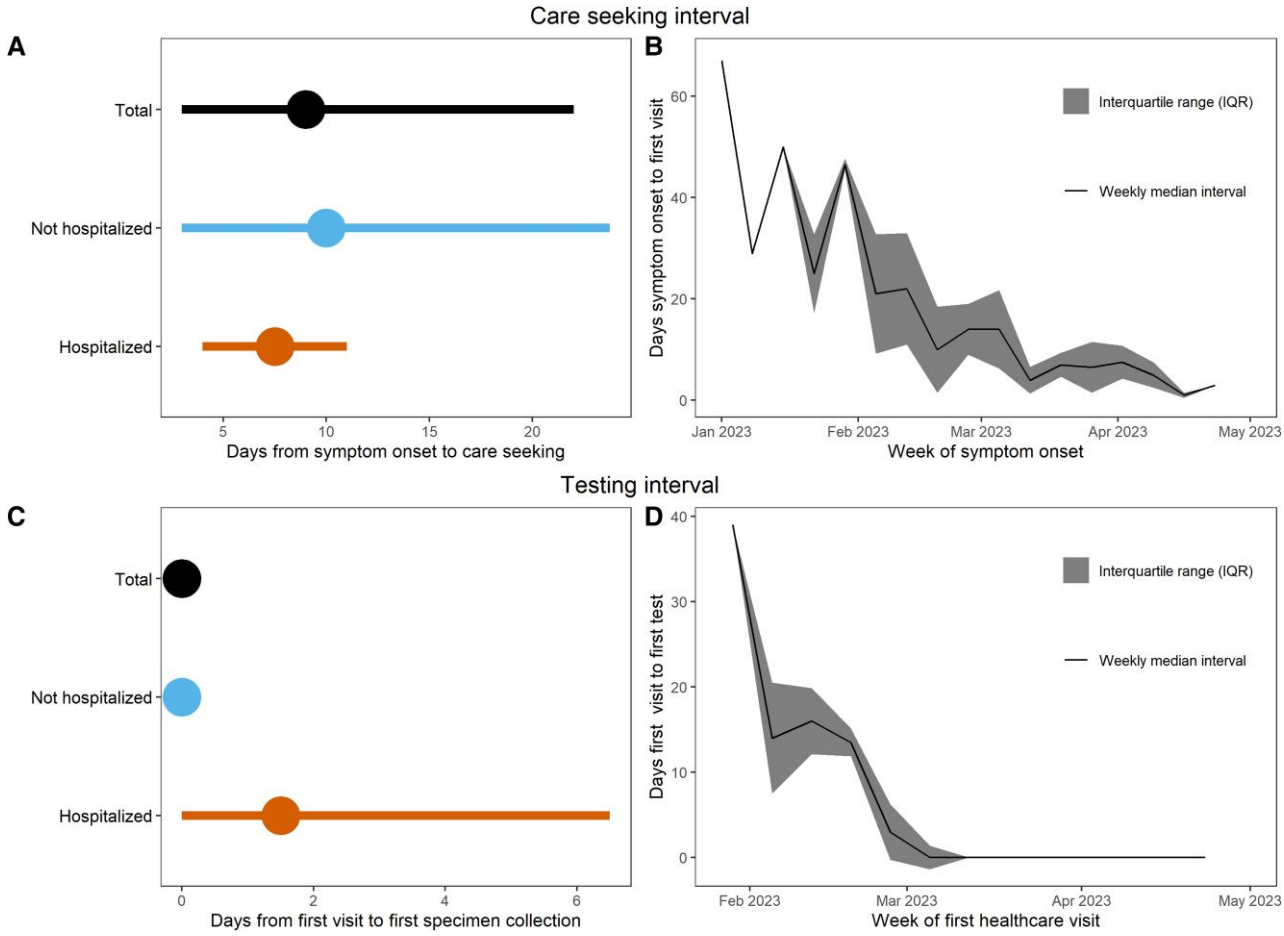


**Figure 2.** Median and interquartile range (IQR) days between symptom onset and first healthcare visit (care seeking interval, *A* and *B*) and first healthcare visit to first specimen collection, (testing interval, *C* and *D*). Panels *A* and *C* show the median IQR for care-seeking and testing intervals overall and by hospitalization status. Panels *B* and *D* show weekly medians in lines and IQRs in ribbons for the same intervals for all patients; insufficient data in some weeks prohibited the calculation of weekly intervals by hospitalization status. IQRs were not calculated for weeks with 1 patient observation; the plots therefore do not include gray ribbons for those weeks (eg, the weeks of Jan 1 and Jan 8 in panel *B*).

**Table 3. Diagnostic Testing for Patients During a Large Blastomycosis Outbreak at a Paper Mill in Michigan**

| Characteristic | Received at Least 1 Test,[a] n (%) | At Least 1 Positive Test,[b] n (%) | Average Test Turnaround Time, Median (IQR), d |
|---|---|---|---|
| Antigen testing | 116 (89%) | 115 (99%) | 5 (4, 6) |
| Urine antigen | 113 (86%) | 110 (97%) | 5 (4, 6) |
| Serum antigen | 71 (54%) | 44 (62%) | 4 (4, 6) |
| Culture | 32 (24%) | 15 (47%) | 13 (3, 18) |
| Sputum | 18 (14%) | 9 (50%) | 15 (3, 30) |
| Bronchial specimen | 10 (8%) | 6 (60%) | 13 (2, 14) |
| Specimen type not available | 4 (3%) | 0 (0%) | 8 (4, 11) |
| Cytology | 30 (23%) | 19 (63%) | 1 (0, 1) |
| Sputum | 14 (11%) | 10 (71%) | 1 (1, 1) |
| Bronchial specimen | 10 (8%) | 6 (60%) | 0 (0, 0) |
| Specimen type not available | 6 (5%) | 3 (50%) | 2 (1, 2) |
| Serology | 13 (10%) | 9 (69%) | 4 (3, 7) |
| Histopathology—bronchial or lung specimen | 6 (5%) | 4 (67%) | 0 (0, 1) |

Abbreviation: IQR, interquartile range.

[a]Tests that were done before or within 2 weeks after the patient's date of incident specimen were included.

[b]If patients had multiple of the same type of laboratory tests, positive results indicate that at least 1 test was positive.

were more likely to receive antibiotics for presumed bacterial CAP before antifungal prescription (86% vs 39%; $P = .001$). Approximately 71% of hospitalized patients and 39% of nonhospitalized patients received antifungal prescriptions before the result date of their first positive diagnostic test ($P = .08$). The median time between symptom onset and antifungal prescription was 16 days (IQR: 10–20 days) for hospitalized patients and 17 days (IQR: 8–27 days) for nonhospitalized patients ($P = .39$) (Supplementary Table 5). The median time between incident specimen collection to antifungal treatment prescription was 4 days (IQR: 0–6 days) for patients whose incident test was an antigen test compared with 1 day for patients who had other incident test types (IQR: 0–2 days; $P = .05$) (Supplementary Table 10).

The last outbreak-associated case was reported in May 2023, and the MDHHS declared the outbreak over in July 2023.

## DISCUSSION

This outbreak was the largest documented blastomycosis outbreak in the United States [12]. Blastomycosis is endemic in Michigan, with approximately 1 reported case per year in Delta County [22]. However, all outbreak cases were among workers or visitors to the mill, suggesting that exposures occurred at or near the mill. The absence of other community cases or observed increases in local canine cases provided additional evidence against broader community exposures. The phylogenetic clustering of the outbreak isolates and genetic relatedness to the local canine isolate pointed towards the possibility of a local environmental source of *Blastomyces* near the mill (eg, soil or decaying vegetation near local waterways) [13, 23].

These findings contributed to subsequent investigation and response activities, including a health hazard evaluation (HHE) led by CDC's National Institute for Occupational Safety and Health (NIOSH) to more fully characterize potential exposures and environmental sources at the mill [24]. Response efforts at the mill included recommendations to encourage voluntary NIOSH-approved N95 respirator use; inspect and maintain heating, ventilation, and air conditioning systems; and limit soil-disturbing activities beyond regular mill operations. Education efforts for mill workers also focused on blastomycosis signs and symptoms and the importance of early care seeking. Previous blastomycosis cases have been linked to occupational activities such as construction [14], and outbreaks of histoplasmosis, a related mycosis, have been reported in a paper mill and other industrial settings [25, 26]. However, this was the first documented blastomycosis outbreak at an industrial setting.

Nearly all (95%) patients reported cough and 80% reported dyspnea, which is substantially higher than previous reports [2, 27]. Chest pain was reported by 64% of patients, highlighting its potential importance in blastomycosis symptomology despite its absence from the CSTE case definition criteria [19]. Skin lesions were rare (4%), whereas previous studies reported skin lesions in more than 20% of patients [1, 28, 29]. All isolates were identified as *B gilchristii*, and prior reports have shown that pulmonary-only disease is more common with *B gilchristii* infections compared with *Blastomyces dermatitidis* [7, 30, 31]. Alternatively, relatively short periods between symptom onset to initiation of treatment for many patients might help explain lower rates of disseminated disease in this outbreak [16].

This outbreak occurred in a relatively young, healthy cohort of workers with few immunosuppressive conditions. However, hospitalized patients had higher rates of diabetes, which reflects previous findings [21, 32]. Clinicians should be aware of the potential for severe disease in diabetic patients in addition to classic immunosuppressing conditions such as cancer or transplantation [33]. Although obesity was not significantly associated with hospitalization, higher rates among hospitalized patients (71% vs 56%) were consistent with previous evidence highlighting obesity as a risk factor for severe blastomycosis [32].

Diagnostic testing delays and treatment for presumed bacterial infections were more common among hospitalized than nonhospitalized patients, which reflects previous reports that missed and delayed diagnoses are associated with increased disease severity [7, 21, 34, 35]. Additionally, unnecessary antibiotic prescriptions can lead to delayed initiation of appropriate antifungals and potentially contribute to antibiotic resistance [10, 36]. Early suspicion and testing for blastomycosis are important to improve outcomes, particularly in patients with links

to known outbreaks or those with CAP who have failed at least 1 course of antibiotics and who have been in areas where blastomycosis is endemic or emerging [37]. Empiric antifungal treatment is likely warranted in circumstances where blastomycosis is strongly suspected and patients have links to known outbreaks or exposures [38].

Care-seeking and testing intervals shortened considerably over the course of the outbreak (see Figure 2), which suggests increasing patient and provider awareness. This could be related to communications from the health department to local providers, communications from mill management and union leaders to mill workers, high media coverage of the outbreak, or accumulated local provider experiences. Concern for potential workplace exposure was documented during 86% of medical visits, demonstrating high awareness of the outbreak among the mill workers. In contrast, only 4% of respondents to a national survey reported having ever heard of blastomycosis [39]. Although not formally assessed, high awareness and early care seeking by patients and early recognition and treatment by providers might have helped reduce hospitalization rates during this outbreak. These results highlight the potential benefits of increasing public awareness of blastomycosis in endemic settings and improving early clinical suspicion and testing for patients with relevant exposures [37].

*Blastomyces* urine antigen testing was widely used during this outbreak. Given the high sensitivity documented in previous studies [40, 41], urine antigen testing should be considered for diagnosis, including in outbreak settings and in patients with mild-to-moderate disease [3, 37, 42]. Of note, however, test turnaround times and delays between incident specimen collection and treatment were longer for urine antigen tests compared with other test types such as cytology. Cytology had short turnaround times (0–1 day) and could support rapid presumptive diagnoses and earlier treatment initiation, particularly among hospitalized patients or other patients stable enough to tolerate collection of respiratory specimens [38]. However, additional testing (eg, urine antigen tests) may be required due to low sensitivity [37]. Urine antigen titers were also higher in hospitalized patients, even after restricting to tests done before antifungal prescription. This is consistent with previous evidence that urine antigen titers may reflect disease severity [41, 43]. More research is needed to understand whether this could guide clinical care.

This report had several limitations. Although we requested medical records for all blastomycosis-associated visits, visits without a positive specimen are not typically reported through MDSS and we relied on documented patient histories to assess whether patients previously sought care. We may therefore have underestimated the number of healthcare visits or antibiotic prescriptions before patients received a positive diagnostic test, and treatment information was not always available. We may have underestimated the prevalence of underlying conditions and signs and symptoms, as we did not have access to complete medical histories. All patients had epidemiologic links to the mill and all isolates belonged to the same outbreak cluster of *B gilchristii*. Nevertheless, because we did not have WGS results for all patients, we could not confirm that all infections were due to *B gilchristii*. Finally, this report did not capture information about mild or asymptomatic cases that did not require medical care, although this is a focus of the ongoing HHE investigation. Additionally, the case criterion requiring patients to have spent 40 or more hours in Delta County was initially established to exclude cases who may have been exposed elsewhere, but it is possible for patients to develop blastomycosis after shorter exposures. However, no cases were excluded based on these criteria.

This was the largest documented blastomycosis outbreak in the United States, with 12% of patients requiring hospitalization and 1 death. Diagnostic delays were associated with hospitalization, although care-seeking and testing delays decreased over time, likely reflecting increased patient and provider awareness. Early suspicion of blastomycosis may prompt earlier diagnosis and treatment, potentially reducing unnecessary antibiotic prescriptions and improving outcomes.

## Supplementary Data

Supplementary materials are available at *Clinical Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

## Notes

***Author Contributions.*** M. T., T. C., M. G. S., and J. M. conceptualized the study. M. S., R. L. Y., S. P., R. R., M. G. S., and J. M. supported initial patient interviews and data collection activities. I. H., S. P., R. R., J. A. W. G., and M. T. conducted chart abstractions. I. H., S. P., R. R., and M. T. analyzed all epidemiologic data. A. M. J., M. Y. N., H. M. B., R. K., A. H., A. P. L., L. A. P., and L. G. conducted laboratory and genomic analyses. I. H. drafted the initial manuscript. All authors provided critical feedback and revisions, and all authors approved the final draft of the manuscript for submission.

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