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Tuberculosis Preventive Treatment Update — U.S. President's Emergency Plan for AIDS Relief, 36 Countries, 2016–2023

Aderonke S. Ajiboye, MPH[1,*]; Stephanie O'Connor, MPH[1,*]; Jonathan P. Smith, PhD[1]; Sevim Ahmedov, MD[2]; William L. Coggin, MSA[1]; Macarthur Charles, MD[1]; Smita Ghosh, DrPH[1]; Paul Pierre, MD[3]; Neha Shah, MD[4]; Richard A. Teran, PhD[1]; Patrick K. Moonan, DrPH[1]; Anand Date, MD[1]

Abstract

Tuberculosis (TB) is the leading cause of death among persons with HIV. In 2022, an estimated 167,000 TB-related deaths occurred globally among persons with HIV. TB preventive treatment (TPT) helps prevent TB disease and is recommended for persons at high risk for developing TB, including those with HIV. TPT, when taken with antiretroviral treatment (ART), can reduce TB-attributable deaths among persons with HIV. In 2018, the U.S. President's Emergency Plan for AIDS Relief (PEPFAR) program committed to offer one course of TPT to all eligible clients receiving ART. This analysis describes trends in TPT initiation and completion among PEPFAR-supported programs in 36 countries in Africa, Central and South America, and Asia during fiscal years (FYs) 2017–2023. Overall, TPT initiation rates peaked in FY19, a possible sign of programmatic saturation. TPT initiation among clients who had been on ART <6 months reached 59%, and overall completion rates up to 87% were reported. Approximately 13 million persons with HIV have completed TPT since FY17, but widespread adoption of shorter regimens, patient-centered approaches, and electronic medical record systems might be needed to ensure full TPT coverage. Through PEPFAR's partnership with national HIV programs, TPT has become the standard of care for persons with HIV.

Introduction

In 2022, an estimated 167,000 persons living with HIV experienced tuberculosis (TB)–related deaths globally, making TB the leading cause of death in this group (*1*). World Health Organization–recommended TB preventive treatment (TPT) regimens (*2*) reduce the risk for TB disease and TB-attributable deaths among persons with HIV.† TPT is recommended for persons living with HIV once active TB disease has been ruled out, even when latent TB infection status is unknown (*2*). TPT has historically consisted of once-daily isoniazid for 6 or 9 months; shorter 1- and 3-month rifapentine-based regimens are now available (*2*). At the 2018 United Nations General Assembly High-Level Meeting (UNHLM) on TB, member countries agreed to provide TPT to 6 million persons with HIV by 2022.§ In alignment with this announcement, the U.S. President's Emergency Plan for AIDS Relief (PEPFAR) committed to offer at least one course of TPT to all eligible clients receiving antiretroviral treatment (ART), including pregnant women.¶ This report summarizes PEPFAR's global progress on providing TPT to all ART clients in PEPFAR-supported programs, a cohort that includes approximately 19 million persons with HIV.

* These authors contributed equally to this report.

† https://www.cdc.gov/globalhivtb/who-we-are/success-stories/success-story-pages/scaling-tpt-ethiopia.html
§ https://www.who.int/publications/m/item/political-declaration-of-the-un-general-assembly-high-level-meeting-on-the-fight-against-tuberculosis
¶ https://na.usembassy.gov/wp-content/uploads/sites/132/PEPFAR-COP18-Guidance_FINAL-1.pdf

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Methods

Data were collected through PEPFAR monitoring, evaluation, and reporting indicators.** Data were collected at 6-month intervals and disaggregated by age group (<15 and ≥15 years), sex, and HIV treatment status (<6 months on ART [ART-naive] and ≥6 months on ART [ART-experienced]). Semiannualized TPT initiation and completion rates were calculated among persons on ART in 36 PEPFAR-supported programs that reported TPT data at any time during fiscal years (FYs) 17–23.†† Initiation rates were calculated through FY23 quarter (Q) 2, and completion rates were calculated through FY23 Q4. TPT initiation rates were calculated as the number of TPT initiations in a 6-month period divided by the number of ART clients on treatment at the end of that period. Analysis of TPT initiation rates among ART-naive clients included only those initiating TPT within 6 months of ART initiation. TPT completion rates were calculated as the number of TPT completions in a 6-month period divided by the number of TPT initiations in the previous reporting period. TPT initiation and completion rates were aggregated across all PEPFAR-supported programs. Mann-Whitney-U tests ($\alpha = 0.05$) were used to assess stratum-specific differences in TPT initiation and completion rates. Data were analyzed using R software (version 4.3.2; R Foundation). This activity was reviewed by CDC, deemed not research, and conducted consistent with applicable federal law and CDC policy.§§

Results

Tuberculosis Preventive Treatment Initiation

The number of PEPFAR-supported countries that reported TPT data more than doubled during the analytic period (17 in FY17 and 36 in FY21). Overall, 16,832,651¶¶ TPT initiations were reported during FY17–23. The number of persons who initiated TPT increased by an average of 26% between each semiannual period during FY17–19 (Table). In the following semiannual period (FY20 Q2), the number of persons who initiated TPT decreased by 12%. TPT initiations began increasing again after FY20 Q2 and reached an all-time high in FY21 Q4 (1,802,814). Since then, the number of persons initiating TPT per year has declined. The overall increase in TPT initiations until FY20 was also reflected in

** https://help.datim.org/hc/article_attachments/10003735798420

†† The U.S. government FY runs October–September. In alignment with the PEPFAR reporting calendar, Q2 for semiannual metrics represents October–March of the following calendar year, and Q4 covers April–September.

§§ 45 C.F.R. part 46.102(l)(2), 21 C.F.R. part 56; 42 U.S.C. Sect. 241(d); 5 U.S.C. Sect. 552a; 44 U.S.C. Sect. 3501 et seq.

¶¶ This value includes 555,936 TPT initiations that were reported in FY17 Q2 but occurred in FY16, in accordance with PEPFAR's standard indicator definition for TPT. To calculate TPT initiation rates, the number of TPT initiations must be aligned with the number of persons on ART in the previous reporting period. TPT initiations reported in FY17 Q2 were included in total counts, but initiation rates for that period were not calculated because the denominator (number of persons on ART) was outside the temporal scope of this report.

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TABLE. Tuberculosis preventive treatment initiations* among persons with HIV — 36 U.S. President's Emergency Plan for AIDS Relief–supported countries, October 2016–March 2023

Semiannual period†	Date range	Persons on ART	Persons on ART initiating TPT, no. (%)	Persons newly on ART	Persons newly on ART initiating TPT, no. (%)
FY17 Q2	Oct 2016–Mar 2017	11,726,101	654,161 (6)	—	—
FY17 Q4	Apr–Sep 2017	13,245,470	562,345 (4)	—	—
FY18 Q2	Oct 2017–Mar 2018	13,235,513	750,282 (6)	—	—
FY18 Q4	Apr–Sep 2018	14,769,349	750,431 (5)	1,437,294	243,744 (17)
FY19 Q2	Oct 2018–Mar 2019	13,433,062	1,192,952 (9)	1,236,576	308,431 (25)
FY19 Q4	Apr–Sep 2019	15,686,915	1,784,375 (11)	1,426,483	449,964 (32)
FY20 Q2	Oct 2019–Mar 2020	15,480,007	1,577,641 (10)	1,287,300	529,323 (41)
FY20 Q4	Apr–Sep 2020	17,383,890	1,651,619 (10)	1,194,562	579,085 (48)
FY21 Q2	Oct 2020–Mar 2021	17,248,709	1,750,779 (10)	1,173,027	615,747 (52)
FY21 Q4	Apr–Sep 2021	17,931,849	1,802,814 (10)	1,107,204	643,338 (58)
FY22 Q2	Oct 2021–Mar 2022	18,573,343	1,473,871 (8)	1,041,786	609,569 (59)
FY22 Q4	Apr–Sep 2022	19,238,096	1,311,024 (7)	1,007,261	591,548 (59)
FY23 Q2	Oct 2022–Mar 2023	19,472,835	1,014,421 (5)	934,074	494,023 (53)

Abbreviations: ART = antiretroviral treatment; FY = fiscal year; PEPFAR = U.S. President's Emergency Plan for AIDS Relief; Q = quarter; TPT = tuberculosis preventive treatment.
* TPT initiation rates were calculated as the number of TPT initiations in a 6-month period divided by the number of ART clients on treatment at the end of that period. Analysis of TPT initiation rates among ART-naive (newly on ART) clients include only those initiating TPT within 6 months of ART initiation. TPT initiations are reported in the period after the 6-month period when they occur. TPT initiations reported in FY17 Q2 were included in total counts but initiation rates for that period were not calculated, because the denominator (number of persons on ART) was outside the temporal scope of this report.
† The U.S. government FY runs October–September. In alignment with the PEPFAR reporting calendar, Q2 for semiannual metrics represents October–March of the following calendar year, and Q4 covers April to September.

initiation rates. During FY17–18, the semiannualized TPT initiation rates among all persons receiving ART (ART-naive and -experienced) ranged between 4% and 6% (Table). The TPT initiation rate peaked in FY19 Q4 (11%) and has since declined to 5% as of FY23 Q2. By contrast, the TPT initiation rate among ART-naive clients rose through FY22 Q4, from 17% in FY18 Q4 to 59% in FY22 Q4, before dropping to 53% in the most recent period assessed.

Tuberculosis Preventive Treatment Completion

Overall, 13,323,186 persons with HIV have completed TPT in PEPFAR-supported programs that report TPT data. TPT completion rates steadily increased from 56% in FY18 Q2 to 87% in FY23 Q2, before dropping to 86% in FY23 Q4 (Figure 1).

Differences by Sex, Age, and HIV Treatment Status

No statistically significant differences existed in overall TPT initiation or completion rates between sex and age groups (Figure 2). Among ART-naive clients, initiation rates were lower among those aged <15 years than among those aged ≥15 years (32% and 51%, respectively; p = 0.04). TPT completion rates were lower among ART-naive clients compared with ART-experienced clients (79% and 86%, respectively; p<0.01).

Discussion

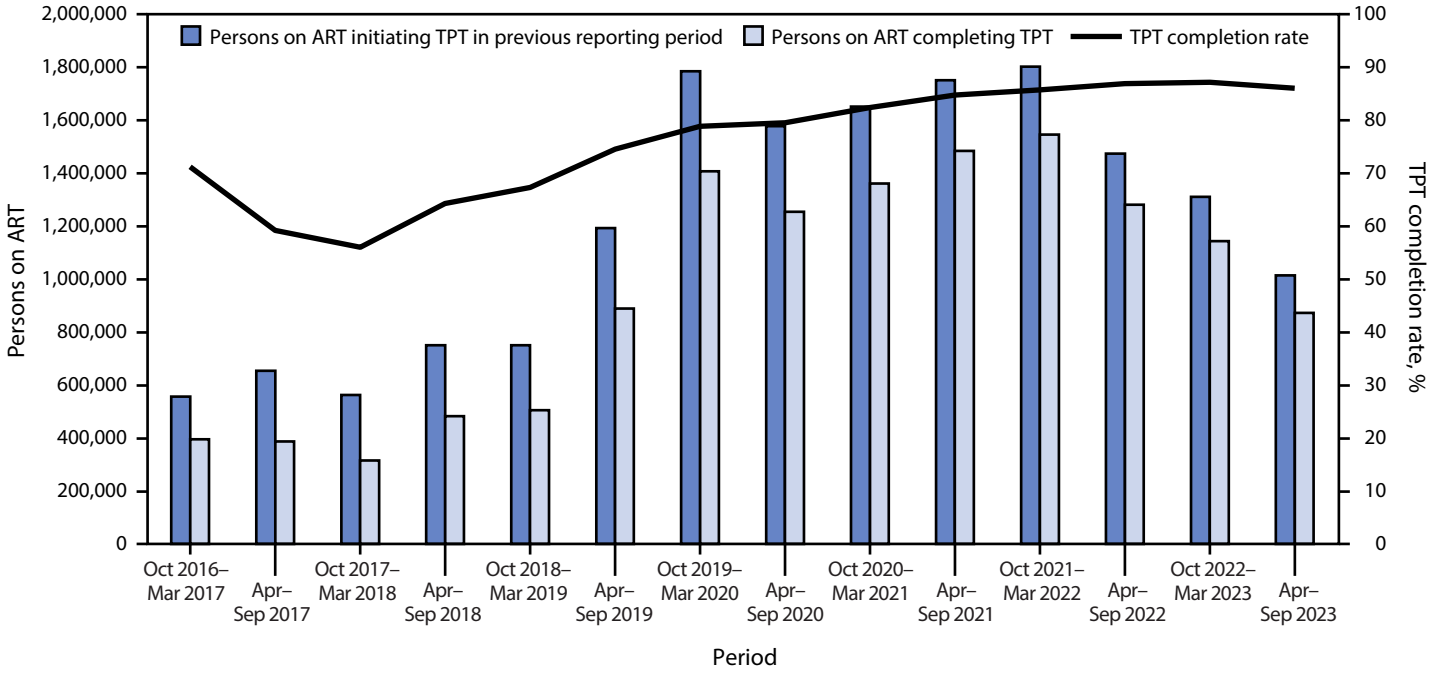
PEPFAR has supported the widespread integration of TPT as part of the HIV standard of care. As a result, approximately 13 million persons with HIV have completed TPT. These TPT completions meaningfully contributed to the 2018 UNHLM target for TPT among persons with HIV, the only UNHLM target achieved (*1*).

TPT initiation rates among ART-naive clients help monitor adoption of TPT into routine practice and are expected to be higher than initiation rates among ART-experienced clients, who might have already completed a course of TPT. Trends in overall initiations provide insight into TPT scale-up over time because climbing initiation rates would be expected when programs are rolling out TPT to the existing patient population. Declining overall TPT initiation rates over time might suggest programmatic saturation, in which all eligible ART clients have already received TPT. Importantly, PEPFAR program data cannot be used to directly measure saturation because these data are not person-level, and TPT completion was not collected before FY17.

Although overall TPT initiation rates trended downward, the percentage of ART-naive clients who received TPT increased. These trends might be indicative of a prioritization of TPT provision for those newly initiated on ART. At the country level, TPT coverage might vary by clinical guidance, eligibility, or supply chain mechanisms. Initiation rates were similar by age and sex, suggesting these factors did not play a major role in TPT initiation overall. However, lower initiation rates were noted among younger ART-naive clients compared with those aged ≥15 years.

Findings from this analysis were consistent with other reports that found lower TPT completion rates among ART-naive clients (*3*). Lower TPT completion rates have been found to be associated with perceived stigma (*4*), which might be higher among those recently diagnosed with HIV (*5*). High levels of

FIGURE 1. Tuberculosis preventive treatment completions* among persons on antiretroviral treatment — 36 U.S. President's Emergency Plan for AIDS Relief–supported countries, October 2016–September 2023



Abbreviations: ART = antiretroviral treatment; TPT = tuberculosis preventive treatment.
* TPT completion rates were calculated as the number of TPT completions in a 6-month period divided by the number of TPT initiations in the previous reporting period.

stigma related specifically to TPT have also been documented (*6*), and other barriers to TPT completion such as pill burden (*7*), lack of health education, and distance to health facilities (*8*) can affect ART-naive clients differently.

Limitations

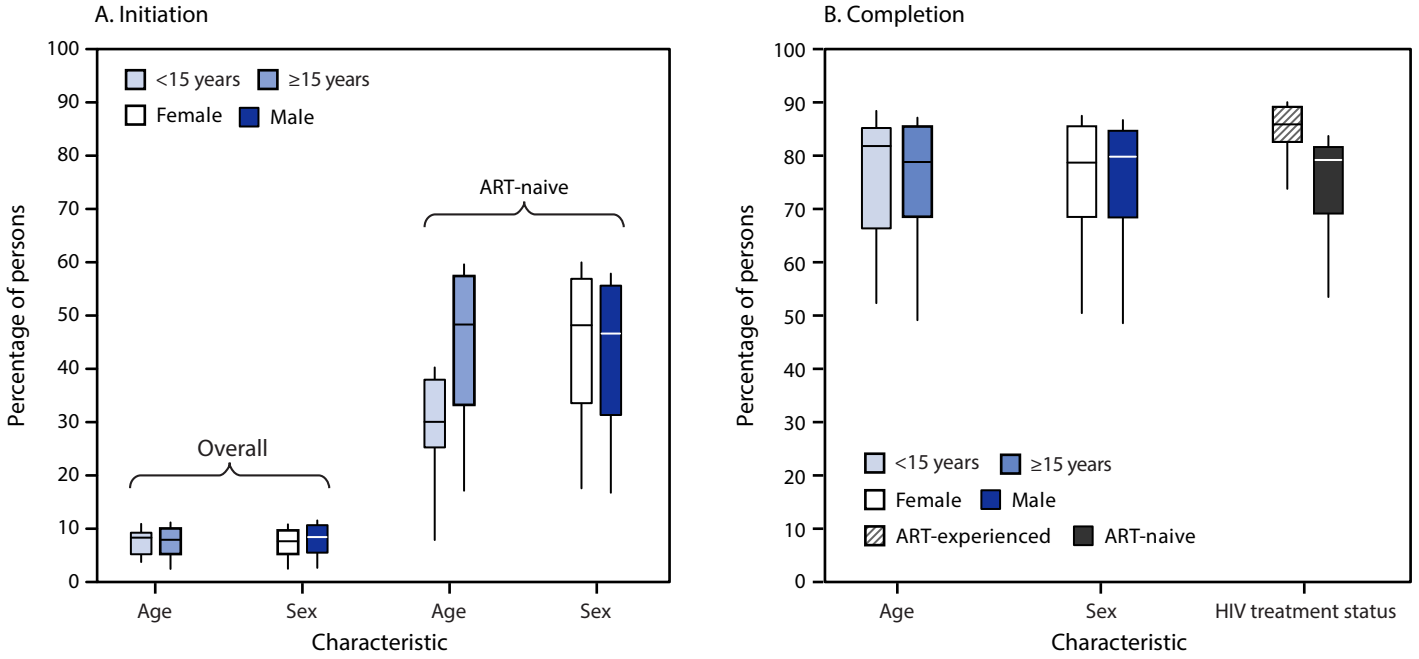
The findings in this report are subject to at least four limitations. First, PEPFAR-wide results represent a diverse range of settings and populations, and the number of countries reporting TPT data varied over time.*** As a result, aggregated values might not reflect trends in individual countries or subnational units, and trends over time are not representative of a true cohort. Second, because TPT completion is often measured on the basis of pill dispensation and self-report rather than direct observation or biomarker monitoring, completion rates might be overestimated. Third, the data used for this analysis were collected in a programmatic setting for monitoring purposes. Data quality might fall short of the accuracy and precision of data collected for clinical studies or in other research settings. Finally, no person-level data were available, and data were reported in broad age bands (<15 and ≥15 years), precluding more specific analyses.

*** Because of ongoing data quality assessments, data from one country that has historically reported a large number of TPT completions were not included in the most recent period assessed (FY23 Q4).

Implications for Public Health Practice

The steady increase in TPT completion rates suggests substantial improvements in HIV and TB service delivery, monitoring, and reporting practices. However, opportunities remain to ensure full TPT coverage and maximize the impact of TPT in reducing TB morbidity and mortality. An ongoing need exists to ensure all ART-naive clients receive the requisite support to access and complete a full course of TPT. Patient-level electronic medical record systems could be developed and expanded to better identify underserved geographic areas and subpopulations and to monitor outcomes over time. Offering patient-centered approaches to treatment delivery can help make health care access a positive and convenient experience for clients by aligning service delivery with their preferences and needs (*9*). Increasing access to short-course regimens for all could improve completion rates (*2*), and ensuring availability of pediatric TPT formulations might increase coverage among persons with HIV aged <15 years. Promoting the use of digital adherence tools, such as mobile telephone applications and electronic sensor-enabled pill boxes (*10*), could help support clients throughout the course of treatment. Finally, further population-level analyses could help determine whether TPT implementation has been associated with reductions in TB incidence and TB-attributable deaths in settings where broad TPT coverage was achieved. Importantly, lessons learned from

FIGURE 2. Differences* in tuberculosis preventive treatment initiation (A)† and completion (B)§ rates among persons on antiretroviral treatment, by age, sex, and HIV treatment status¶ — 36 U.S. President's Emergency Plan for AIDS Relief–supported countries, October 2016–September 2023**



Abbreviations: ART = antiretroviral treatment; TPT = tuberculosis preventive treatment.

* Mann-Whitney-U test (α = 0.05) assessed stratum-specific differences in TPT initiation and completion rates.

† TPT initiation rates were calculated as the number of TPT initiations in a 6-month period divided by the number of ART clients on treatment at the end of that period. Analysis of TPT initiation rates among ART-naive clients include only those initiating TPT within 6 months of ART initiation. P-values for differences by characteristic were age (overall): p = 0.72; sex (overall): p = 0.48; age (ART-naive): p = 0.04; and sex (ART-naive): p = 0.53.

§ TPT completion rates were calculated as the number of TPT completions in a 6-month period divided by the number of TPT initiations in the previous reporting period. P-values for differences by characteristic were age: p = 0.98; sex: p = 0.98; and HIV treatment status: p<0.01.

¶ Persons who initiated TPT within 6 months of ART initiation were included in the analysis of TPT initiation rates among ART-naive clients; those on ART for ≥6 months when initiating TPT were ART-experienced.

** Whiskers display the full range of values for each metric. Boxes display IQRs, with median values indicated by a horizontal line within the box.

Summary

What is already known about this topic?

Tuberculosis (TB) is the leading cause of death among persons with HIV. TB preventive treatment (TPT), combined with antiretroviral treatment (ART), reduces TB-attributable deaths among persons with HIV. In 2018, the U.S. President's Emergency Plan for AIDS Relief (PEPFAR) committed to offer TPT to eligible ART clients.

What is added by this report?

During October 2016–October 2023, approximately 13 million ART clients completed TPT in 36 countries. PEPFAR-supported programs achieved TPT completion rates up to 87%; initiation rates among clients who had been on ART <6 months (ART-naive) reached 59%.

What are the implications for public health practice?

Continued efforts are needed to maximize TPT coverage, especially for ART-naive clients. Short-course regimens, patient-centered care, and modernized medical record systems might help accomplish this goal.

TPT implementation in PEPFAR-supported programs might prove useful for TPT provision among other populations at risk, including household contacts of persons with TB.

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Corresponding author: Stephanie O'Connor, ovi6@cdc.gov.

[1]Division of Global HIV and Tuberculosis, Global Health Center, CDC; [2]Tuberculosis Division, U.S. Agency for International Development, Washington, DC; [3]Bureau of Global Health Security and Diplomacy, U.S. Department of State, Washington, DC; [4]U.S. Military HIV Research Program, Walter Reed Army Institute of Research, Silver Spring, Maryland.

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References

1. World Health Organization. Global tuberculosis report 2023. Geneva, Switzerland: World Health Organization; 2023. https://www.who.int/teams/global-tuberculosis-programme/tb-reports/global-tuberculosis-report-2023
2. World Health Organization. WHO consolidated guidelines on tuberculosis: module 1: prevention. Geneva, Switzerland: World Health Organization; 2020. https://iris.who.int/bitstream/handle/10665/331170/9789240001503-eng.pdf?sequence=1
3. Musaazi J, Sekaggya-Wiltshire C, Okoboi S, et al. Increased uptake of tuberculosis preventive therapy (TPT) among people living with HIV following the 100-days accelerated campaign: a retrospective review of routinely collected data at six urban public health facilities in Uganda. PLoS One 2023;18:e0268935. PMID:36821550 https://doi.org/10.1371/journal.pone.0268935
4. Ayele HT, van Mourik MSM, Bonten MJM. Predictors of adherence to isoniazid preventive therapy in people living with HIV in Ethiopia. Int J Tuberc Lung Dis 2016;20:1342–7. PMID:27725045 https://doi.org/10.5588/ijtld.15.0805
5. Subedi B, Timilsina BD, Tamrakar N. Perceived stigma among people living with HIV/AIDS in Pokhara, Nepal. HIV AIDS (Auckl) 2019;11:93–103. PMID:31118826 https://doi.org/10.2147/HIV.S181231
6. Palacios CF, Hough MA, Shrestha R, et al. Perceived stigma related to TB preventive therapy. Int J Tuberc Lung Dis 2023;27:209–14. PMID:36855038 https://doi.org/10.5588/ijtld.22.0570
7. Sterling TR, Njie G, Zenner D, et al. Guidelines for the treatment of latent tuberculosis infection: recommendations from the National Tuberculosis Controllers Association and CDC, 2020. MMWR Recomm Rep 2020;69(No. RR-1):1–11. PMID:32053584 https://doi.org/10.15585/mmwr.rr6901a1
8. Amanya I, Muhoozi M, Aruhomukama D, Ssebagereka A, Mugambe R. Isoniazid preventive therapy completion and factors associated with non-completion among patients on antiretroviral therapy at Kisenyi Health Centre IV, Kampala, Uganda. PLoS One 2023;18:e0277739. PMID:37607176 https://doi.org/10.1371/journal.pone.0277739
9. Tram KH, Mwangwa F, Chamie G, et al.; SEARCH collaboration. Predictors of isoniazid preventive therapy completion among HIV-infected patients receiving differentiated and non-differentiated HIV care in rural Uganda. AIDS Care 2020;32:119–27. PMID:31181961 https://doi.org/10.1080/09540121.2019.1619661
10. Wong YJ, Ng KY, Lee SWH. Digital health use in latent tuberculosis infection care: a systematic review. Int J Med Inform 2022;159:104687. PMID:35007924 https://doi.org/10.1016/j.ijmedinf.2022.104687

Surveillance for Coccidioidomycosis, Histoplasmosis, and Blastomycosis During the COVID-19 Pandemic — United States, 2019–2021

Samantha L. Williams, MPH[1]; Dallas J. Smith, PharmD[1]; Kaitlin Benedict, MPH[1]; Jamie R. Ahlers, MPH[2]; Connie Austin, DVM, PhD[3]; Rachael Birn, MPH[4,5]; Angel M. Carter[6]; Natalie N. Christophe, MPH[7]; Katie Cibulskas, MGIS[8]; Paul R. Cieslak, MD[9]; Suzanne N. Gibbons-Burgener, DVM, PhD[10]; Michael Gosciminski, MPH[11]; Malia J. Ireland, DVM[12]; Katelyn V. Lazenby, MPH[13]; Tom Loftus, MPH[14]; Kristy Lunquest, ScM[15]; Abby A. Mathewson, DVM[16]; Alyssa D. Nguyen[17]; Hanna N. Oltean, PhD[18]; BreAnne Osborn, MPH[19]; Erin M. Petro, DVM[20]; Danny J. Power, MPH, MPA[21]; Rebecca R. Reik, MPH[22]; Levi Schlosser, MPH[23]; Judi Sedivy, MPH[24]; Chad B. Smelser, MD[25]; Tom Chiller, MD[1]; Mitsuru Toda, PhD[1]

Abstract

Coccidioidomycosis, histoplasmosis, and blastomycosis are lower respiratory tract fungal infections whose signs and symptoms can resemble those of other respiratory illnesses, including pneumonia caused by bacterial or viral etiologies; this overlap in clinical presentation might lead to missed or delayed diagnoses. The causative fungi live in the environment, often in soil or plant matter. To describe the epidemiologic characteristics of cases of coccidioidomycosis, histoplasmosis, and blastomycosis during the COVID-19 pandemic, CDC analyzed case surveillance data for 2019–2021. During this period, a total of 59,655 coccidioidomycosis cases, 3,595 histoplasmosis cases, and 719 blastomycosis cases were reported to CDC. In 2020, fewer cases of each disease occurred in spring compared with other seasons, and most cases occurred in fall; national seasonality is not typically observed, and cases were seasonally distributed more evenly in 2019 and 2021. Fewer cases coinciding with the start of the COVID-19 pandemic, along with an unusually high blastomycosis case fatality rate in 2021 (17% compared with more typical rates of 8%–10%), suggest that the pandemic might have affected patients' health care–seeking behavior, public health reporting practices, or clinical management of these diseases. Increased awareness and education are needed to encourage health care providers to consider fungal diseases and to identify pneumonia of fungal etiology. Standardized diagnostic guidance and informational resources for fungal testing could be incorporated into broader respiratory disease awareness and preparedness efforts to improve early diagnosis of coccidioidomycosis, histoplasmosis, and blastomycosis.

Introduction

Coccidioidomycosis, histoplasmosis, and blastomycosis are fungal infections that cause illness with primarily respiratory presentation ranging from mild symptoms to severe pulmonary or disseminated disease. The causative fungi live in soil and plant matter, and transmission usually occurs through inhalation of aerosolized spores. These diseases are typically limited to specific geographic ranges, but these ranges might be expanding because of climate change (*1*). Coccidioidomycosis primarily occurs in the southwestern United States, whereas histoplasmosis and blastomycosis are more commonly acquired in central and eastern states (*2*).

Diagnosis of these infections is challenging. Clinical signs and symptoms commonly resemble those of other respiratory infections, including COVID-19 and bacterial or viral community-acquired pneumonia, and laboratory tests might be difficult to access and interpret. Consequently, patients commonly can experience missed or delayed diagnosis and treatment, which can lead to persistent symptoms, severe disease, and adverse health outcomes (*3*).

Coccidioidomycosis, histoplasmosis, and blastomycosis are reportable in certain states (*4*). Each state designates reportable diseases, mandating health care providers and laboratories to notify public health departments of diagnosed cases or positive laboratory test results. Cases are classified according to the Council of State and Territorial Epidemiologists' case definitions.* For nationally notifiable diseases such as coccidioidomycosis, states and the District of Columbia voluntarily submit case data to CDC through the National Notifiable Diseases Surveillance System (NNDSS).

The 2019 U.S. surveillance data for these fungal infections indicated that males and certain racial and ethnic populations were disproportionately affected. No pronounced national seasonality was observed. Histoplasmosis and blastomycosis were associated with high hospitalization and case fatality rates (*5*).

During the COVID-19 pandemic, many persons avoided or delayed seeking medical care because of concerns regarding disease transmission and busy medical facilities (*6*). Although few cases of coinfection with COVID-19 and coccidioidomycosis, histoplasmosis, or blastomycosis have been reported, how the COVID-19 pandemic might have otherwise affected acquisition, diagnosis, patient outcomes, and reporting of these diseases is not known (*7*,*8*). This report summarizes 2019–2021 U.S. surveillance data for coccidioidomycosis, histoplasmosis, and blastomycosis and examines epidemiologic changes that occurred during the COVID-19 pandemic compared with prepandemic data.

* https://ndc.services.cdc.gov/case-definitions/coccidioidomycosis-2011/; https://ndc.services.cdc.gov/case-definitions/histoplasmosis-2017/; https://ndc.services.cdc.gov/case-definitions/blastomycosis-2020/

Methods

Data Sources

Case-level coccidioidomycosis data were submitted to NNDSS by 26 states and the District of Columbia.† Aggregate case data, including hospitalizations and deaths, were submitted for histoplasmosis by 13 states§ and for blastomycosis by five states¶ (*4*). Death data were based on vital records; coccidioidomycosis-associated hospitalizations and deaths are not captured through NNDSS.

Analysis

Confirmed coccidioidomycosis cases and confirmed and probable histoplasmosis and blastomycosis cases were included. Descriptive analyses of case counts, sex, age, race and ethnicity, and event month (the earliest known month associated with the illness, which could correspond to symptom onset, diagnosis, or laboratory testing) were performed. To better illustrate the potential impact of the COVID-19 pandemic, 2019 case counts, seasonality, hospitalizations, and deaths are presented in the results section to compare 2020–2021 cases with prepandemic data; demographic results include 2020–2021 data only to reflect the most up-to-date numbers. State-specific incidence (cases per 100,000 population) by sex, age, and race and ethnicity were calculated using 2020 and 2021 U.S. Census Bureau data. Univariate incidence rate ratios were calculated using robust Poisson models to compare different demographic groups with the referent population. Analyses were completed in RStudio (version 4.0.3; RStudio). This activity was reviewed by CDC, deemed not research, and was conducted consistent with applicable federal law and CDC policy.**

Results

During 2019–2021, a total of 59,655 coccidioidomycosis cases (2019 = 20,061; 2020 = 19,284; 2021 = 20,320), 3,595 histoplasmosis cases (2019 = 1,124; 2020 = 1,012; 2021 = 1,459), and 719 blastomycosis cases (2019 = 240; 2020 = 238; 2021 = 241) were reported (Table 1). During 2020, fewer cases of each disease occurred in the spring than in other seasons (Supplementary Figure 1; https://stacks.cdc.gov/view/cdc/148381), whereas cases were seasonally distributed more evenly throughout 2019 and 2021 (Figure). In 2020, a higher percentage of total coccidioidomycosis and histoplasmosis cases occurred in winter and fall compared with other seasons, and the highest percentage of blastomycosis cases occurred during summer and fall.

During 2020–2021, the majority of cases of all three diseases occurred in males (coccidioidomycosis = 53%; histoplasmosis = 59%; blastomycosis = 64%), and the highest percentages occurred among persons aged 40–64 years (coccidioidomycosis = 16,153 [41%]; histoplasmosis = 1,001 [41%]; blastomycosis = 215 [45%]) (Table 1); incidences of all diseases were slightly higher among persons aged 65–79 years (coccidioidomycosis = 27.3 per 100,000; histoplasmosis = 2.5; blastomycosis = 1.3) (Table 2).

Data on race and ethnicity during 2020–2021 were available for 48% of coccidioidomycosis, 80% of histoplasmosis, and 90% of blastomycosis cases. Compared with incidence in non-Hispanic White (White) persons (0.7 per 100,000), blastomycosis incidence was approximately eight times higher among non-Hispanic American Indian or Alaska Native (AI/AN) persons (5.5) and twice as high among non-Hispanic Asian and Native Hawaiian or other Pacific Islander (A/NHOPI) populations (1.4). Compared with incidence among White persons (5.1) coccidioidomycosis incidence was more than four times as high among AI/AN persons (22.0) and twice as high among Hispanic or Latino (Hispanic) persons (11.1). Histoplasmosis incidence among AI/AN persons (2.2) was 1.6 times as high as that among White persons (1.4) (Supplementary Figure 2; https://stacks.cdc.gov/view/cdc/148382) (Supplementary Table; https://stacks.cdc.gov/view/cdc/148380).

Among cases for which hospitalization data were available during 2019–2021 (67% of histoplasmosis and 92% of blastomycosis cases), 1,150 (48%) patients with histoplasmosis and 428 (64%) with blastomycosis were hospitalized. Among those with available mortality data (53% of histoplasmosis cases and 92% of blastomycosis cases), 108 (6%) histoplasmosis patients and 80 (14%) blastomycosis patients died (Table 1). Although the histoplasmosis case fatality rate (CFR) remained stable from 2020 to 2021, the blastomycosis CFR nearly doubled from 9% in 2019 and 2020 to 17% in 2021.

Discussion

Coccidioidomycosis, histoplasmosis, and blastomycosis caused substantial illness nationwide during 2019–2021. The predominance among males, older adults, and AI/AN persons aligns with previous data and historical trends (*5*). Yearly case count fluctuations during 2019–2021, changes in seasonality, and increase in the blastomycosis CFR in 2021 were atypical and are potentially related to the COVID-19 pandemic, which might have affected acquisition, diagnosis, management, and reporting

† Coccidioidomycosis cases reported for Alabama, Arizona, Arkansas, California, Delaware, District of Columbia, Indiana, Kansas, Louisiana, Maryland, Michigan, Minnesota, Missouri, Montana, Nebraska, Nevada, New Hampshire, New Mexico, North Dakota, Ohio, Oregon, Rhode Island, South Dakota, Utah, Washington, Wisconsin, and Wyoming.

§ Histoplasmosis cases reported for Arkansas, Delaware, Illinois, Indiana, Kansas, Kentucky, Louisiana, Michigan, Minnesota, Nebraska, Pennsylvania, Rhode Island, and Wisconsin.

¶ Blastomycosis cases reported for Arkansas, Louisiana, Michigan, Minnesota, and Wisconsin.

** 45 C.F.R. part 46.102(l)(2), 21 C.F.R. part 56; 42 U.S.C. Sect. 241(d); 5 U.S.C. Sect. 552a; 44 U.S.C. Sect. 3501 et seq.

TABLE 1. Number and percentage of coccidioidomycosis, histoplasmosis, and blastomycosis cases, by selected patient characteristics and clinical outcomes — United States, 2019–2021

Characteristic	No. (%)								
	Coccidioidomycosis*			Histoplasmosis†			Blastomycosis§		
	2019	2020	2021	2019	2020	2021	2019	2020	2021
Sex									
Female	9,638 (48)	9,108 (47)	9,330 (46)	488 (44)	410 (41)	606 (42)	71 (30)	87 (37)	86 (36)
Male	10,392 (52)	10,132 (53)	10,966 (54)	631 (56)	601 (59)	851 (58)	168 (70)	151 (63)	155 (64)
Age group, yrs									
<5	67 (<1)	77 (<1)	43 (<1)	6 (1)	13 (1)	9 (1)	2 (<1)	1 (<1)	0 (—)
5–19	1,252 (6)	1,056 (5)	981 (5)	102 (9)	116 (12)	168 (12)	22 (9)	25 (11)	17 (7)
20–39	4,695 (23)	4,466 (23)	4,346 (21)	287 (26)	233 (23)	384 (26)	75 (31)	56 (24)	49 (20)
40–64	8,184 (41)	7,832 (41)	8,321 (41)	482 (43)	423 (42)	578 (40)	93 (39)	106 (45)	109 (45)
65–79	4,520 (23)	4,573 (24)	5,055 (25)	202 (18)	203 (20)	274 (19)	42 (18)	43 (18)	58 (24)
≥80	1,323 (7)	1,256 (7)	1,533 (8)	35 (3)	24 (2)	41 (3)	6 (3)	7 (3)	8 (3)
Race and ethnicity									
AI/AN, NH	241 (3)	242 (3)	263 (2)	4 (<1)	<7 (1)	4 (<1)	10 (5)	10 (5)	8 (4)
Asian and NH/OPI, NH	450 (6)	346 (4)	578 (5)	25 (3)	15 (2)	22 (2)	15 (7)	19 (9)	7 (3)
Black or African American, NH	528 (7)	539 (7)	798 (7)	79 (9)	88 (11)	121 (10)	24 (12)	27 (12)	20 (9)
White, NH	3,252 (41)	3,870 (48)	5,141 (47)	656 (76)	6,01 (75)	9,08 (78)	144 (69)	142 (65)	163 (77)
Hispanic or Latino (all races)	2,559 (33)	2,665 (33)	3,424 (32)	63 (7)	55 (7)	68 (6)	14 (7)	21 (10)	14 (7)
Other¶	816 (10)	357 (4)	632 (6)	32 (4)	35 (4)	42 (4)	1 (<1)	1 (<1)	2 (<1)
Season**									
Winter	4,797 (24)	5,623 (29)	5,849 (29)	210 (24)	307 (31)	347 (24)	35 (22)	51 (22)	66 (28)
Spring	4,631 (23)	3,468 (18)	4,957 (24)	223 (25)	204 (20)	390 (27)	38 (23)	47 (20)	58 (24)
Summer	4,860 (24)	4,396 (23)	4,787 (24)	201 (23)	205 (20)	340 (24)	46 (29)	60 (25)	58 (24)
Fall	5,601 (28)	5,797 (30)	4,727 (23)	253 (29)	290 (29)	347 (24)	42 (26)	78 (33)	58 (24)
Hospitalized									
Yes	—	—	—	249 (54)	386 (46)	515 (46)	147 (65)	138 (66)	143 (63)
No	—	—	—	211 (46)	451 (54)	602 (54)	81 (35)	70 (34)	85 (37)
Outcome									
Died	—	—	—	20 (5)	37 (6)	51 (6)	20 (9)	20 (9)	40 (17)
Survived	—	—	—	395 (95)	621 (94)	799 (94)	204 (91)	191 (91)	190 (83)
Total	**20,061**	**19,284**	**20,320**	**1,124**	**1,012**	**1,459**	**240**	**238**	**241**

Abbreviations: AI/AN = American Indian or Alaska Native; NH = non-Hispanic; NH/OPI = Native Hawaiian or other Pacific Islander.

* Sex was missing for 95 cases, age was missing for 85 cases, and race and ethnicity were missing for 32,964 cases.

† Sex was missing for 10 cases, age was missing for 15 cases, race and ethnicity were missing for 762 cases, season was missing for 278 cases, hospitalization was missing for 1,181 cases, and death was missing for 1,672 cases.

§ Sex was missing for one case, race and ethnicity were missing for 80 cases, season was missing for 82 cases, hospitalization was missing for 55 cases, and death was missing for 54 cases.

¶ Calculated on basis of two or more reported race categories.

** Seasons defined as winter (December–February), spring (March–May), summer (June–August), and fall (September–November).

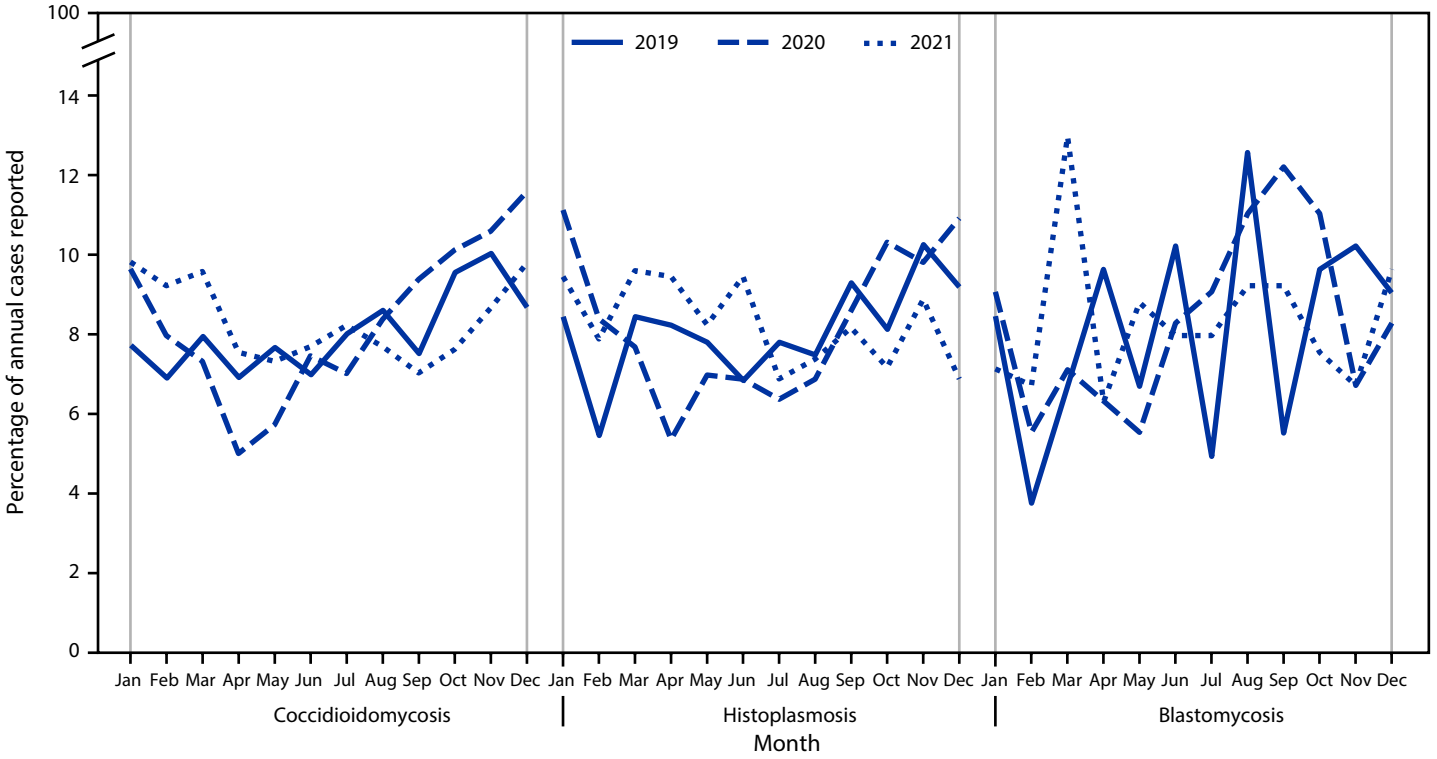
of these three fungal diseases. Seasonality is not typically observed nationally for these diseases, and the low percentage of cases observed during spring 2020 compared with spring 2019 and spring 2021 might be related to reduced health care–seeking behavior associated with concerns about potential COVID-19 transmission in health care settings. This delay or avoidance of medical care, which was prevalent in the early months of the pandemic (*6*), likely exacerbated misdiagnosis and diagnostic delays. Fewer reported coccidioidomycosis and histoplasmosis cases in 2020 compared with both 2019 and 2021 might also reflect changes in health care–seeking behavior, preventative measures for respiratory diseases such as mask-wearing, reduced travel to areas endemic for these fungal diseases, lower clinical suspicion of fungal infections given the focus on COVID-19, or underreporting by overwhelmed public health agencies (*5*). Until 2020, coccidioidomycosis cases had been consistently increasing each year since 2014.†† Compared with 2019, histoplasmosis case counts declined by 10% in 2020, but subsequently increased 44% in 2021 compared with 2020 (*5*). COVID-19 transmission concerns that prompted persons to spend more time outdoors in 2020 and 2021 than in 2019§§ might have increased exposure to pathogenic fungi. Further research is needed to understand the marked rise in reported histoplasmosis cases from 2020 to 2021.

Although in-hospital blastomycosis mortality has increased in recent years (*9*), the 2021 blastomycosis CFR (17%) was

†† https://www.cdc.gov/fungal/diseases/coccidioidomycosis/statistics.html

§§ https://outdoorindustry.org/wp-content/uploads/2015/03/2021-Outdoor-Participation-Trends-Report.pdf

FIGURE. Percentage of reported annual coccidioidomycosis, histoplasmosis, and blastomycosis cases,* by month of report — United States, 2019–2021



* Denominator is the total number of cases reported in each year (2019, 2020, and 2021) with a known earliest recorded event month for each fungal disease.

unusually high, particularly given the stable hospitalization rates during the reporting period, which was consistent with prepandemic rates; blastomycosis CFR generally ranges from 8%–10% (*5*,*9*). Diagnosis of blastomycosis is challenging because symptoms are nonspecific and the availability of laboratory tests is limited; diagnostic delays exacerbated by the pandemic might have impeded prompt management of blastomycosis or associated comorbidities, which could have led to more severe or disseminated disease during the pandemic. Some health departments noted that COVID-19 prompted better access to death reports and additional scrutiny of contributing causes of death, which might have influenced the observed CFR (*10*).

The racial and ethnic disparities observed in 2020–2021 generally align with those reported in 2019, with higher incidence of all three diseases among AI/AN persons as well as higher incidence of coccidioidomycosis among Hispanic persons and higher incidence of blastomycosis among A/NHOPI persons compared with incidence in White populations (*5*). Similar to coccidioidomycosis and blastomycosis, histoplasmosis incidence was also higher among AI/AN than White persons, which differed from 2019, when incidence was similar across racial and ethnic groups (*5*). How these racial and ethnic disparities might be affected by geographic, biologic, or sociodemographic differences is not clear. More complete and detailed race and ethnicity data are needed to better understand how these factors influence disease and to guide actionable public health responses.

Limitations

The findings in this report are subject to at least three limitations. First, because of longstanding diagnostic challenges, case counts underestimate the actual number of coccidioidomycosis, histoplasmosis, and blastomycosis cases, and data are limited to the subset of states where each disease is reportable (*4*). Second, data related to potential exposures, underlying conditions, laboratory testing, clinical course, and treatment were not available, hindering the ability to distinguish the potential effects of the COVID-19 pandemic from other influences, including weather patterns, awareness, or testing and reporting practices. Data were incomplete for race and ethnicity, event month, hospitalization, and death, and the lack of event date standardization could lead to misclassification of monthly case counts. Finally, only aggregate-level data were available for histoplasmosis and blastomycosis, which precluded bivariate analyses.

TABLE 2. Incidence* of coccidioidomycosis, histoplasmosis, and blastomycosis, by selected patient characteristics — United States, 2019–2021

Characteristic	Incidence* (95% CI)								
	Coccidioidomycosis†			Histoplasmosis§			Blastomycosis¶		
	2019	2020	2021	2019	2020	2021	2019	2020	2021
Sex									
Female	14.1 (14.1–14.7)	12.4 (12.2–12.7)	12.6 (12.4–12.9)	1.3 (1.2–1.4)	1.1 (1.0–1.2)	1.6 (1.5–1.8)	0.5 (0.4–0.6)	0.3 (0.2–0.4)	0.6 (0.5–0.7)
Male	15.8 (15.5–16.2)	14.1 (13.8–14.4)	15.0 (14.7–15.3)	1.8 (1.6–1.9)	1.7 (1.6–1.8)	2.3 (2.2–2.5)	1.2 (1.0–1.4)	1.3 (1.2–1.5)	1.1 (0.9–1.2)
Age group, yrs									
<5	0.8 (0.7–1.1)	0.9 (0.7–1.2)	0.5 (0.4–0.7)	0.1 (0.1–0.3)	0.3 (0.2–0.5)	0.2 (0.1–0.4)	0.1 (0–0.5)	0.1 (0–0.4)	0 (—)
5–19	4.9 (4.7–5.2)	4.0 (3.7–4.2)	3.6 (3.4–3.9)	0.7 (0.6–0.9)	0.8 (0.7–1.0)	1.2 (1.0–1.4)	0.4 (0.3–0.6)	0.5 (0.3–0.7)	0.3 (0.2–0.5)
20–39	12.9 (12.6–13.3)	11.9 (11.5–12.2)	11.6 (11.2–11.9)	1.5 (1.3–1.7)	1.2 (1.1–1.4)	2.0 (1.8–2.2)	1.0 (0.8–1.2)	0.7 (0.6–1.0)	0.6 (0.5–0.9)
40–64	19.8 (19.3–20.2)	18.0 (17.6–18.4)	18.9 (18.5–19.4)	2.0 (1.9–2.2)	1.8 (1.7–2.0)	2.5 (2.3–2.7)	1.0 (0.8–1.2)	1.1 (0.9–1.4)	1.2 (1.0–1.4)
65–79	27.3 (26.6–28.1)	27.5 (26.7–28.3)	27.6 (26.8–28.4)	2.1 (1.9–2.5)	2.2 (2.0–2.6)	2.7 (2.4–3.1)	1.1 (0.8–1.5)	1.2 (0.9–1.6)	1.4 (1.1–1.9)
≥80	26.2 (24.8–27.7)	23.8 (22.5–25.1)	30.0 (28.6–31.6)	1.1 (0.8–1.6)	0.8 (0.5–1.2)	1.5 (1.1–2.0)	0.5 (0.2–1.1)	0.6 (0.3–1.3)	0.7 (0.4–1.4)
Race and ethnicity									
AI/AN, NH	17.4 (15.3–19.7)	18.4 (16.2–20.8)	25.6 (22.7–28.9)	1.2 (0.5–3.2)	2.4 (1.1–5.0)	2.0 (0.8–5.4)	4.5 (2.4–8.4)	5.0 (2.7–9.3)	6.1 (3.0–12.1)
Asian and NH/OPI, NH	4.6 (4.2–5.0)	3.4 (3.1–3.8)	5.8 (5.4–6.3)	1.0 (0.7–1.5)	0.6 (0.3–0.9)	0.9 (0.6–1.3)	1.6 (1.1–2.4)	2.0 (1.3–3.1)	0.8 (0.4–1.6)
Black or African American, NH	4.0 (3.7–4.4)	3.9 (3.6–4.3)	5.9 (5.5–6.4)	0.9 (0.7–1.1)	1.0 (0.8–1.2)	1.4 (1.2–1.7)	0.6 (0.4–1.0)	0.7 (0.5–1.0)	0.5 (0.3–0.8)
White, NH	4.1 (4.0–4.2)	4.4 (4.3–4.6)	5.9 (5.7–6.0)	1.3 (1.2–1.4)	1.2 (1.1–1.3)	1.7 (1.6–1.9)	0.7 (0.4–1.2)	0.7 (0.6–0.8)	0.8 (0.7–0.9)
Hispanic or Latino (all races)	11.2 (10.8–11.6)	9.8 (9.5–10.2)	12.5 (12.1–12.9)	1.2 (0.9–1.5)	0.8 (0.6–1.0)	1.0 (0.8–1.3)	0.9 (0.8–1.1)	1.1 (0.7–1.7)	0.8 (0.5–1.3)
Other**	4.6 (4.0–5.3)	5.2 (4.7–5.8)	8.6 (8.0–9.3)	1.9 (1.3–2.6)	1.1 (0.8–1.6)	1.3 (0.9–1.7)	0.2 (0–1.4)	0.1 (0–0.6)	0.1 (0–0.6)
Total	**15.1 (14.9–15.3)**	**13.1 (12.9–13.2)**	**13.8 (13.6–14.0)**	**1.6 (1.5–1.7)**	**1.4 (1.3–1.5)**	**2.0 (1.9–2.1)**	**0.8 (0.7–0.9)**	**0.8 (0.7–0.9)**	**0.8 (0.7–0.9)**

Abbreviations: AI/AN = American Indian or Alaska Native; NH = non-Hispanic; NH/OPI = Native Hawaiian or other Pacific Islander.

* Cases per 100,000 population. Summed state-specific denominators from 2019–2021 U.S. Census Bureau data were used to calculate incidence for the total grouping for each year.

† Sex was missing for 68 cases, age was missing for 65 cases, and race and ethnicity were missing for 20,749 cases.

§ Sex was missing for five cases, age was missing for five cases, and race and ethnicity were missing for 497 cases.

¶ Race and ethnicity were missing for 48 cases.

** Calculated on the basis of two or more reported race categories.

Implications for Public Health Practice

Increased awareness is needed to improve prompt diagnosis and treatment of coccidioidomycosis, histoplasmosis, and blastomycosis, particularly during periods of increased incidence of other respiratory diseases. To reduce misdiagnosis of these three fungal infections, standardized diagnostic guidance and informational resources for pan-respiratory testing, including fungal diseases, are needed and could be incorporated into broader respiratory disease awareness and preparedness efforts. Education to help clinicians distinguish fungal pneumonia from other respiratory infections might improve accurate diagnosis. Enhanced and expanded surveillance can also improve understanding of risk factors and epidemiologic trends to help guide efforts to raise awareness and improve diagnosis, management, and patient outcomes.

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Summary

What is already known about this topic?

Coccidioidomycosis, histoplasmosis, and blastomycosis, fungal diseases that can cause severe respiratory illness or disseminated disease and death, are underdiagnosed and underreported.

What is added by this report?

Coccidioidomycosis and histoplasmosis case counts declined in 2020 compared with 2019, then increased in 2021. These case fluctuations, a high 2021 blastomycosis case fatality rate (17%), and atypical 2020 seasonality across diseases suggest that these infections might have been affected by changes in health care–seeking behavior, diagnostic testing, or underreporting related to the COVID-19 pandemic.

What are the implications for public health practice?

Increased clinician education for coccidioidomycosis, histoplasmosis, and blastomycosis, and integration of diagnostic guidance and informational resources for fungal diseases into broader respiratory disease awareness and preparedness efforts, might improve timely diagnosis, patient management, and outcomes.

Corresponding author: Samantha L. Williams, pog3@cdc.gov.

[1]Mycotic Diseases Branch, Division of Foodborne, Waterborne, and Environmental Diseases, CDC; [2]Delaware Department of Health and Social Services; [3]Illinois Department of Public Health; [4]Nebraska Department of Health and Human Services; [5]Department of Environmental, Agricultural & Occupational Health, University of Nebraska Medical Center, Omaha, Nebraska; [6]Kentucky Department for Public Health; [7]Louisiana Department of Health; [8]Ohio Department of Public Health; [9]Oregon Health Authority; [10]Division of Public Health, Wisconsin Department of Health Services; [11]Rhode Island Department of Health; [12]Minnesota Department of Health; [13]Arkansas Department of Health; [14]Indiana Department of Health; [15]Maryland Department of Health; [16]New Hampshire Department of Health and Human Services; [17]California Department of Public Health; [18]Washington State Department of Health; [19]Utah Department of Health and Human Services; [20]Kansas Department of Health and Environment; [21]Montana Department of Public Health and Human Services; [22]Michigan Department of Health and Human Services; [23]North Dakota Health and Human Services; [24]Pennsylvania Department of Health; [25]New Mexico Department of Health.

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References

1. Nnadi NE, Carter DA. Climate change and the emergence of fungal pathogens. PLoS Pathog 2021;17:e1009503. PMID:33914854 https://doi.org/10.1371/journal.ppat.1009503
2. Ashraf N, Kubat RC, Poplin V, et al. Re-drawing the maps for endemic mycoses. Mycopathologia 2020;185:843–65. PMID:32040709 https://doi.org/10.1007/s11046-020-00431-2
3. Smith DJ, Free RJ, Thompson III GR, et al.; Endemic Mycoses Diagnostic Algorithm Subject Matter Expert Group. Clinical testing guidance for coccidioidomycosis, histoplasmosis, and blastomycosis in patients with community-acquired pneumonia for primary and urgent care providers. Clin Infect Dis 2023;ciad619. PMID:37802909 https://doi.org/10.1093/cid/ciad619
4. CDC. Fungal diseases. Reportable fungal diseases by state. Atlanta, GA: US Department of Health and Human Services, CDC; 2023. https://www.cdc.gov/fungal/fungal-disease-reporting-table.html
5. Smith DJ, Williams SL, Benedict KM, et al.; Endemic Mycoses State Partners Group. Surveillance for coccidioidomycosis, histoplasmosis, and blastomycosis—United States, 2019. MMWR Surveill Summ 2022;71(No. SS-7):1–14. PMID:36006889 https://doi.org/10.15585/mmwr.ss7107a1
6. Czeisler MÉ, Marynak K, Clarke KEN, et al. Delay or avoidance of medical care because of COVID-19–related concerns—United States, June 2020. MMWR Morb Mortal Wkly Rep 2020;69:1250–7. PMID:32915166 https://doi.org/10.15585/mmwr.mm6936a4
7. Messina FA, Giusiano G, Santiso G. Endemic mycoses and COVID-19: a review. Curr Fungal Infect Rep 2022;16:98–106. https://doi.org/10.1007/s12281-022-00435-z
8. Gold JAW, Ahmad FB, Cisewski JA, et al. Increased deaths from fungal infections during the coronavirus disease 2019 pandemic—National Vital Statistics System, United States, January 2020–December 2021. Clin Infect Dis 2023;76:e255–62. PMID:35717660 https://doi.org/10.1093/cid/ciac489
9. Benedict K, Hennessee I, Gold JAW, Smith DJ, Williams S, Toda M. Blastomycosis-associated hospitalizations, United States, 2010–2020. J Fungi (Basel) 2023;9:867. PMID:37754975 https://doi.org/10.3390/jof9090867
10. Ahmad FB, Anderson RN, Knight K, Rossen LM, Sutton PD. Advancements in the National Vital Statistics System to meet the real-time data needs of a pandemic. Am J Public Health 2021;111:2133–40. PMID:34878853 https://doi.org/10.2105/AJPH.2021.306519

Notes from the Field

Expanded Laboratory Testing for Varicella — Minnesota, 2016–2023

Alison Ruprecht, MPH[1]; Mona Marin, MD[2]; Anna K. Strain, PhD[1]; Katie Harry, MS[1]; Cynthia Kenyon, PhD[1]

The U.S. varicella vaccination program, implemented in 1995, led to a >97% decline in varicella incidence (*1*). Clinical diagnosis continues to be the primary means for diagnosing varicella (*1*), although the modified signs and symptoms of disease (fewer skin lesions, mostly maculopapular) occurring in persons who have received varicella vaccine pose diagnostic challenges (*2*). Laboratory confirmation of varicella is increasingly necessary to guide clinical and public health management, understand varicella epidemiology, and evaluate vaccine effectiveness. In June 2023, the Council of State and Territorial Epidemiologists updated its varicella position statement to increase the specificity of confirmed varicella cases by including only cases with positive laboratory results or cases that have an epidemiologic link to a laboratory-confirmed varicella case or to a person with herpes zoster (*3*).

Public Health Intervention

In December 2016, the Minnesota Department of Health (MDH) established expanded laboratory testing for confirmation of varicella in Minnesota. A multipronged approach was used to promote testing. MDH implemented outreach to health care providers via newsletters, health advisories, webinars, and conferences describing the importance of laboratory testing for rash illnesses suspected to be varicella, the preferred testing method, and availability of free testing at MDH Public Health Laboratory (MDH-PHL). In addition, MDH implemented direct follow-up when needed with individual providers related to testing practices and provided specimen collection kits (containing a swab for collection of vesicular fluid and slides for collection of scabs or scraping of maculopapular lesions) to clinics interested in partnering with MDH-PHL. Through funding from CDC's Epidemiology and Laboratory Capacity Cooperative Agreement, MDH-PHL provided free testing for persons with suspected varicella, including clinically diagnosed, school- or child care–reported, and self-diagnosed cases. MDH-PHL performed polymerase chain reaction (PCR) testing for varicella-zoster virus (VZV), herpes simplex virus 1 (HSV-1), herpes simplex virus 2 (HSV-2), and enterovirus on all specimens received by MDH-PHL.

MDH also offered specimen collection kits directly to persons with suspected varicella identified through Minnesota's varicella case-based surveillance, allowing free access to testing across the state. Kits were also available to families through partnerships with schools and child care facilities. Lastly, MDH provided notification letters for families of children exposed to varicella, containing testing information to share with their providers. MDH describes the prevalence of laboratory-confirmed VZV, enterovirus, HSV-1 and HSV-2 infections among suspect varicella cases. SAS software (version 9.4; SAS Institute) was used for statistical analyses. This activity meets the regulatory definition of Public Health Surveillance as it seeks to improve varicella surveillance in Minnesota by way of PCR testing.* This activity was reviewed by CDC, deemed not research, and was conducted consistent with applicable federal law and CDC policy.†

Investigation and Outcomes

After the expanded laboratory program was initiated, the proportion of laboratory-confirmed varicella cases doubled, from 17% (235 of 1,426) during January 2013–November 2016 to 36% (619 of 1,717) during December 2016–March 2023 (p<0.001). The proportion of PCR-confirmed varicella cases increased 62%, from 29% in 2017 to 47% in 2022. Among the 619 patients who received a positive VZV PCR test result after program implementation, 157 (25%) had testing performed at MDH-PHL.

During December 2016–March 2023, MDH-PHL performed testing on specimens for 420 patients with suspected varicella; the median patient age was 5 years (range = 0–68 years), and 95 (23%) provided specimens collected at home. Nearly one half (194; 46%) of patients tested received a negative test result, including 108 (56%) who had received at least 1 dose of varicella vaccine, and two had indeterminate test results for all four viral targets. VZV was detected in 157 (37%) specimens, including 32 (20%) from patients who had received at least 1 dose of varicella vaccine; enterovirus was detected in 47 (11%), and HSV-1 in 20 (5%). No HSV-2 or viral coinfections were identified.

Among 208 patients with an in-person clinical diagnosis of varicella at a medical facility, 45% (93), 13% (26), and <1% (one) received positive VZV, enterovirus, and HSV-1 test results, respectively. VZV detection was significantly lower in specimens from patients who had received varicella vaccine (22 of 100; 22%) than among those from patients who were unvaccinated (68 of 103; 66%) (p<0.001, Bonferroni adjusted). The proportion of patients with positive enterovirus test results did not differ between patients who had received varicella vaccine (10%) and those who had not (16%) (p = 1.0, Bonferroni adjusted).

* 45 CFR 46.102(l)(1).
† 45 C.F.R. part 46.102(l)(2), 21 C.F.R. part 56; 42 U.S.C. Sect. 241(d); 5 U.S.C. Sect. 552a; 44 U.S.C. Sect. 3501 et seq.

Summary

What is already known about this topic?

Varicella can manifest with fewer, mostly maculopapular, skin lesions among persons who have received varicella vaccine; this modified clinical appearance can pose diagnostic challenges.

What is added by this report?

In December 2016, the Minnesota Department of Health expanded laboratory testing for varicella. Among 208 patients receiving a clinical diagnosis of varicella at a medical facility, 45% had positive varicella-zoster virus (VZV) test results. VZV detection was lower in those who received varicella vaccine (22%;100) compared with those who did not (66%;103).

What are the implications for public health practice?

Clinical diagnosis of varicella can be unreliable, especially in vaccinated patients. Laboratory confirmation is important to guide clinical and public health management, understand varicella epidemiology, and evaluate vaccine effectiveness.

Preliminary Conclusions and Actions

These findings suggest that the clinical diagnosis of varicella can be unreliable, especially in vaccinated patients, and underscore the importance of laboratory confirmation of varicella. PCR testing of appropriately collected skin lesion specimens has demonstrated high reliability in detection of VZV in vaccinated and unvaccinated persons (*4*). Because recommended clinical and public health management of varicella differs from that of other rash illnesses (*5*), not performing testing can result in nonrecommended clinical management of suspected varicella cases and exposed contacts, as well as incorrect recommendations regarding the need for exclusion from school or work. Education and engagement with health care providers, partnership development and maintenance with schools and child care facilities, and opportunities for free testing and at-home specimen collection might have contributed to an increase in varicella testing and confirmation rates in Minnesota. This increase in varicella testing likely also contributed to an increase in appropriate clinical management and school exclusion recommendations for suspect varicella cases.

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Corresponding author: Alison Ruprecht, ali.ruprecht@state.mn.us.

[1]Minnesota Department of Health; [2]Division of Viral Diseases, National Center for Immunization and Respiratory Diseases, CDC.

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References

1. Marin M, Leung J, Anderson TC, Lopez AS. Monitoring varicella vaccine impact on varicella incidence in the United States: surveillance challenges and changing epidemiology, 1995–2019. J Infect Dis 2022;226(Suppl 4):S392–9. PMID:36265855 https://doi.org/10.1093/infdis/jiac221
2. Dooling K, Marin M, Gershon AA. Clinical manifestations of varicella: disease is largely forgotten, but it's not gone. J Infect Dis 2022;226(Suppl 4):S380–4. PMID:36265857 https://doi.org/10.1093/infdis/jiac390
3. Council of State and Territorial Epidemiologists. Update to public health reporting and national notification of varicella. Atlanta, GA: Council of State and Territorial Epidemiologists; 2023. https://cdn.ymaws.com/www.cste.org/resource/resmgr/ps/ps_2023/23-ID-09_Varicella.pdf
4. Leung J, Harpaz R, Baughman AL, et al. Evaluation of laboratory methods for diagnosis of varicella. Clin Infect Dis. 2010;51(1):23–32. PMID:20504232 https://doi.org/10.1086/653113
5. American Academy of Pediatrics Committee on Infectious Diseases. Varicella-zoster virus infections. In: Red Book: 2021–2024 report of the Committee on Infectious Diseases. 32nd ed. Itasca, IL: American Academy of Pediatrics; 2021:831–43.

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