




Letter to the Editor

Monkeypox testing delays: The need for drastic expansion of education and testing for monkeypox virus

Mindy M. Sampson DO^{1,2,3} , Christopher M. Polk MD^{1,2,3}, Robert T. Fairman MPH^{1,2,3,4}, Michael E. DeWitt MS^{1,2} ,
Michael K. Leonard MD^{1,3}, Lisa Davidson MD³, Lewis McCurdy MD³ and Catherine L. Passaretti MD³ 

¹Section on Infectious Diseases, Department of Internal Medicine, Wake Forest University School of Medicine, Winston-Salem, North Carolina, ²Center for the Study of Microbial Ecology and Emerging Diseases, Wake Forest University School of Medicine, Winston-Salem, North Carolina, ³Division of Infectious Diseases, Atrium Health, Charlotte, North Carolina and ⁴Department of Health Policy & Behavioral Sciences, School of Public Health, Georgia State University, Atlanta, Georgia

To the Editor—An outbreak of monkeypox (MPX) described initially in Europe in May 2022 has increased rapidly, with >30,000 cases diagnosed worldwide in <3 months. A public health emergency was declared by the World Health Organization on July 23, 2022, and in the United States on August 4, 2022.^{1,2} Classically, MPX presents with a prodrome of fevers, lymphadenopathy, and general malaise followed by development of a rash starting on the face and spreading to the rest of the body.³ However, during the 2022 outbreak many patients with MPX have presented with a variety of nontraditional symptoms.⁴ Specifically, many patients have relatively few skin lesions in atypical distributions, lesions limited to the genitals that may be easily confused with sexually transmitted infections (STIs) such as syphilis or herpes virus infection, or marked pain from proctitis or pharyngitis.⁴ Prodromal symptoms such as fever or lymphadenopathy may or may not be present.⁴ Additionally, many patients are presenting with STI coinfections, which can make recognizing MPX even more diagnostically challenging.⁵ The atypical presentation associated with the 2022 outbreak in addition to the rarity of prior cases of MPX seen in the United States and Europe has the potential to lead to delays in clinician recognition and diagnosis of cases.

We retrospectively analyzed all MPX cases diagnosed within our healthcare system as of August 8, 2022. We specifically examined potential delays in diagnosis given clinician unfamiliarity with MPX. Atrium Health is a large healthcare system in the greater Charlotte region offering MPX testing across a broad geographic footprint at 32 urgent cares, 20 emergency departments, and 1 infectious disease clinic. Using electronic health record (EHR) chart review of individuals who had a positive MPX result, we identified any prior encounter in our healthcare system in which clinical symptoms were consistent with MPX, as judged by our research team, in which MPX testing was not obtained. Following work estimating the incubation period by Muira et al,⁶ we fit 3 parametric models to estimate the distribution of time between symptom onset and seeking a test. The models were compared using Pareto-smoothed importance sampling to assess the best fitting distribution.⁷ We obtained approval from our institutional review board.

Author for correspondence: Mindy Sampson, DO, 1225 Harding Pl. Ste 2100, Charlotte, NC 28204. E-mail: mindy.sampson@atriumhealth.org

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As of August 8, 2022, 35 cases of MPX had been diagnosed in our health system. All were males and most (83%) were black, with 11% white and 6% other races or ethnicities. All the cases for which sexual history was known were in men who have sex with men. Overall, 30 (86%) had prodromal symptoms, most commonly fever or lymphadenopathy, and 15 (43%) had symptoms of proctitis or rectal pain. Only 20% of cases had >10 lesions documented at the time of testing. Of these 35 cases, 16 cases had a prior visit with a healthcare provider for complaints that in retrospect were unrecognized symptoms of MPX infection. The most common reasons for evaluation in encounters prior to diagnosis included painful genital lesions, proctitis, and sore throat. Of those who had multiple visits, the mean number of visits prior to MPX recognition was 1.6 visits, ranging up to 5. The visits during which MPX could have been diagnosed and recognized earlier occurred most frequently in emergency departments (52%), followed by urgent care clinics (17%), primary care offices (13%), and other outpatient clinics (17%). In addition to finding that our patients had often had an encounter with healthcare prior to being diagnosed, we also found an average of a 6-day delay (range, 2–14 days) in testing after symptom onset. Further modeling suggested that 95% of cases would be expected to seek testing within 12.4 days (95% credible interval, 9.7–17.1) with a lognormal distribution most closely fitting the data (Fig. 1). This delay could be due to several causes including lack of patient awareness of MPX, underrecognition by healthcare providers, and/or lack of availability of testing.

These delays resulted in 222 potential healthcare worker (HCW) exposures, with a median of 5 exposures per encounter (range, 0–23). Among these HCWs, 63 (28%) were considered high or intermediate risk according to per Centers for Disease Control and Prevention guidelines.⁸ Also, 3 individuals received vaccination after exposure. Simple linear regression was used to test the number of HCWs exposed as a function of number of encounters. Each healthcare encounter prior to MPX testing resulted in an estimated 3.2 additional exposures (95% confidence interval, 1.7–4.7; $P < .001$), of which 2.3 were considered high or intermediate risk ($P < .001$).

Our observed delays in testing for MPX could be due to several factors including lack of patient awareness of MPX, underrecognition by healthcare providers, and/or lack of availability of testing. Early in the testing period, not all emergency departments in our healthcare system had access to testing supplies, which might have particularly affected our findings. Delays in recognition of symptoms of MPX have multiple implications. For the patient, delayed recognition and testing leads to delays in treatment with antiviral agents as well as increased

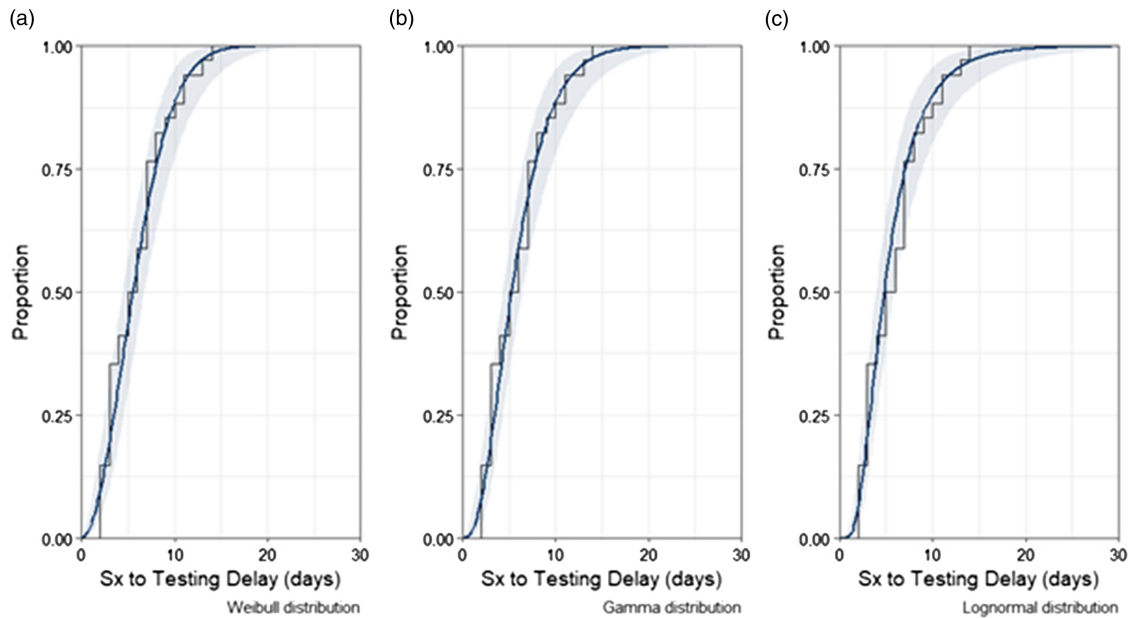


Fig. 1. Estimated cumulative density functions according to different parametric distributions and empirical distributions of time between symptom (Sx) onset and testing for monkeypox-positive cases.

cost of care due to multiple visits to healthcare. For the HCWs, lack of early recognition of MPX symptoms may lead to increased exposures due to lack of use of appropriate personal protective equipment. Aggressive education on the clinical presentation of MPX cases including visuals of the myriad skin presentations is urgently needed, particularly in emergency department and urgent care settings. In addition to further clinical education on the current atypical presentation of MPX in the 2022 outbreak, reinforcement of the use of standard precautions with all patients and adherence to universal mask protocols in healthcare are needed to prevent HCW exposure to patients with MPX while infectious.

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