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## Asymptomatic monkeypox infection: a call for greater control of infection and transmission

Effective public health response to the current monkeypox virus global health emergency requires quantification of asymptomatic infections. We collected evidence on the prevalence of asymptomatic infections through a literature search of five databases (Web of Science, Google Scholar, PubMed, Scopus, and Virtual Health Library) on Aug 30, 2022, with no restrictions on country of publication, using the following search terms: (“asymptomatic” OR “no symptom”) AND (“monkeypox” OR “MPV” OR “MPX” OR “monkey pox” OR “monkeypox virus”). We included only studies that recruited patients from the current outbreak, which began in May, 2022. Both authors were involved in the screening process in addition to another phase of manual searches to avoid missing any relevant publications, including cohort, cross-sectional, case series, and case report studies. Of the 837 reports screened, we found two studies that assessed asymptomatic infection among cases of monkeypox virus infection: a study by De Baetselier and colleagues<sup>1</sup> and another by Ferré and colleagues.<sup>2</sup> Across the two studies, among 807 participants who underwent PCR testing for monkeypox virus infection, 288 (36%) cases of monkeypox virus infection were detected (table). Among these cases, the prevalence of asymptomatic monkeypox virus infection was 6% (three [75%] of four participants in De Baetselier and colleagues’ study<sup>1</sup> and 13 [5%] of 284 participants in Ferré and colleagues’ study).<sup>2</sup>

The current evidence of asymptomatic monkeypox virus infections from our study supports the need for universal infection and transmission control efforts to curb increased transmission by undetected monkeypox virus carriers. This need

has also been shown by Maruotti and colleagues’ study,<sup>3</sup> which used a capture–recapture–based estimation of the true monkeypox cases and indicated that the true number of cases might be 3.16 times the number of announced cases. Maruotti and colleagues suggested that this underestimation of the actual number of cases might be due to undetected spread of monkeypox virus outside of the African continent, the historical origin of the disease. Furthermore, data from previous outbreaks<sup>4,5</sup> have shown that monkeypox cases can be asymptomatic, although this evidence was based on a serological diagnosis with no molecular testing of the presence and replication-competence reported by De Baetselier and colleagues.<sup>1</sup>

According to previous studies, the role of asymptomatic transmission of orthopox viruses is negligible.<sup>6,7</sup> Although the smallpox virus could be detected in the upper respiratory tract of asymptomatic contacts of smallpox cases, quarantine and contact tracing

were the most effective measurements in eradicating the disease, together with vaccination. Similarly, containing previous monkeypox outbreaks was achievable by such measures in endemic areas.<sup>8</sup> However, these measures might not be adequate in controlling the current outbreak because sexual activity seems to be the main mechanism of transmission for monkeypox, and contact tracing might not be feasible in situations involving frequent sexual activities with anonymous partners.

National surveillance programmes should be conducted, particularly among populations at high risk of infection, to detect asymptomatic cases. Such surveillance will require rapid diagnostic or home-based tests that could identify undiagnosed infections. Surveillance at a country’s entry points (eg, airports) might be effective, particularly in non-endemic countries with little evidence of local transmission, similar to approaches previously suggested for asymptomatic COVID-19 transmission.<sup>9,10</sup> Health-care



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	De Baetselier et al (2022) <sup>1</sup>	Ferré et al (2022) <sup>2</sup>
Country	Belgium	France
Study population	Men undergoing anorectal or oropharyngeal sampling for gonorrhoea or chlamydia testing at a large sexual health clinic in Belgium	Men who have sex with men undergoing regular screening for gonorrhoea or chlamydia under programme for people receiving pre-exposure prophylaxis or antiretroviral treatment for HIV
Number of participants tested for monkeypox virus	224	583
Diagnostic method	PCR	PCR
Cases of monkeypox virus infection, n/N (%)	4/224 (2%)	284/583 (49%)
Asymptomatic infections among cases of monkeypox virus infection, n/N (%)	3/4 (75%)	13/284 (5%)
Characteristics of asymptomatic cases		
Vaccinated against smallpox, n/N	0/3	..
Orthopox-directed IgG antibody titres*, range	1:40–1:320	..
Sexual activity without condom in month before testing, n/N (%)	3/3 (100%)	..
Sexual contact during foreign travel in 2 weeks before testing, n/N (%)	2/3 (67%)	..
Monkeypox virus replication competence (by culture), n/N (%)	2/3 (67%)	..
*Serum samples obtained between days 21 and 37 after initial PCR testing; lower limit of detection 1:20.		

**Table: Characteristics of included studies**

providers should also establish a proper differential diagnosis before excluding monkeypox, especially considering the increasing non-specific presentations of the disease. Finally, cases could be decreased and the processes of case identification and contact tracing could be facilitated by individuals limiting their numbers of sexual partners and by limitations on areas and gatherings where people commonly engage in anonymous sexual activities.

We declare no competing interests.

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