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a major reservoir of group A streptococcus: up to 15–25% of asymptomatic school-aged children are colonised in their throat.<sup>4</sup> Children can transmit group A streptococcus to their pregnant mothers or to other contacts. Screening for children has not been found to be feasible or desirable.<sup>4</sup> However, screening of health-care givers who have cared for patients admitted with serious group A streptococcal infection has been recommended<sup>4</sup> to limit the spread of infection.

Group A streptococcal disease in pregnant women and young children is serious. Knowledge of the different clinical features of invasive group A streptococcal infection could lead to earlier recognition and treatment of infection, data on invasive disease would improve, and more correct estimates of disease would be available. Increased knowledge might improve the evaluation of treatment and the development of preventive strategies such as screening or vaccine development.

I declare no competing interests.

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## Monkeypox outbreaks outside endemic regions: scientific and social priorities



As the world recovers from the shock of the COVID-19 pandemic and reflects on lessons learnt from failure of global public health systems to contain the global outbreak of SARS-CoV-2,<sup>1</sup> new infectious disease threats, caused by movement of people globally, remain omnipresent, and repeated calls<sup>2</sup> for more proactive action go unheeded. This is aptly shown by the unprecedented and unexpected outbreaks of human monkeypox cases and clusters since May 7, 2022, across Europe, the Americas, and Australia,<sup>3</sup> which yet again, have taken global public authorities by surprise.

In the ongoing outbreak, the first monkeypox case reported by the UK Health Security Agency on May 7, had travel links to Nigeria.<sup>4</sup> On May 14, two more cases were identified in the UK, both lived in the same household but had no travel history to Africa and no contact with the case reported on May 7. Additional monkeypox cases have continuously been reported to WHO from 12 member states across three WHO regions. As of May 21, 2022, there have been 92 laboratory-confirmed cases and 28 suspected monkeypox cases reported to WHO from the UK, the USA, Canada, France,

Germany, Belgium, Spain, Portugal, Italy, Sweden, and Australia.<sup>3</sup> Detection of more cases is anticipated. The epidemiological links between these cases remain to be defined. Fortunately, there have been no deaths reported to date. However, there are several unusual, atypical, and perplexing aspects of these outbreaks that are of major scientific, public health, and social concern.

First, the number of monkeypox cases detected in this outbreak 2 weeks since first case detection<sup>3</sup> in the UK alone has, by far, surpassed the total number of cases detected in the UK<sup>5</sup> and outside monkeypox-endemic Africa zones<sup>2</sup> since the first discovery of monkeypox in 1970 as a human pathogen. The scientific, environmental, and social reasons for this phenomenal increase remain an enigma and require urgent delineation through a unified, universal One Health (human, environmental, and animal) approach.<sup>2</sup>

Second, it is very unusual and worrying that ongoing epidemiological investigations to date have revealed no substantial travel links of the cases to monkeypox-endemic areas in Africa.<sup>2,3</sup> This could indicate that the monkeypox virus might already have been spreading



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undetected in Europe for a while, with human-to-human transmission occurring due to close physical contact with infected asymptomatic or symptomatic people.

Third, whether these events are due to change in monkeypox virus transmission properties or increased virulence remains unknown. Compared with RNA viruses, the monkeypox virus is a large DNA virus, which makes itself more stable and efficient than RNA viruses at detecting and repairing mutations. Thus, it is unlikely that the virus has evolved to increase human transmission. Preliminary genomic sequence data indicate a relationship with monkeypox clades circulating in west Africa, which cause milder disease and have a lower death rate than clades in central Africa.<sup>3</sup>

Fourth, most monkeypox cases have been detected in men who have sex with men<sup>3</sup> and some cases in Europe occurred in men who have sex with men and bisexual men who travelled to recent festivals. Whether monkeypox is sexually transmitted requires further careful study in all geographical settings. Clusters of viral infections can occur in any group in close contact at mass gathering events.<sup>6</sup> The intense public and social media coverage regarding the spread of monkeypox in these contexts has generated hype in its various forms through use of language, conversation, and content, indirectly or directly negatively generating homophobic and racist stereotypes that exacerbate stigma.<sup>7</sup> This is prejudicial, unfair, stigmatising, and unacceptable.<sup>7,8</sup> Lessons from the HIV and AIDS response showed that stigma and blame undermines outbreak response,<sup>8</sup> highlighting the universal need for building human-rights-based, non-stigmatising outbreak responses and community-led epidemic prevention programmes.

Fifth, the monkeypox outbreaks expose major gaps in understanding the dynamics of viral transmission and continuously evolving epidemiological characteristics of the disease,<sup>2,5,9</sup> and a more coordinated approach to epidemic preparedness is long overdue.<sup>12</sup> Most monkeypox cases in the current outbreak are in men aged 20–50 years. Smallpox vaccination was discontinued worldwide in the 1980s and cases of monkeypox in Africa were comparatively small before this.<sup>2,9,10</sup> This increase in numbers in this age group might reflect the loss of cross-protective immunity to monkeypox from not receiving the smallpox vaccination.<sup>2,10</sup> The antiviral tecovirimat for treatment of

seriously ill monkeypox cases, and the third-generation smallpox vaccine Imvanex (Bavarian Nordic, Hellerup, Denmark) for use as prophylaxis in all close and high-risk case contacts, together with specific guidelines for their use, need to be made available urgently universally at affordable cost.

Sixth, the appearance and rapid spread of monkeypox in Europe has generated intense scientific, political, and media activity. The rapid pace of developments, increasing case-detection rates, and accumulating real-time evolving data from global public health authorities have fuelled public anxieties. Two-way communication on monkeypox-related risks and engagement of affected communities on prevention, detection, and care becomes important for preventing further spread of monkeypox.

Seventh, in nature, the monkeypox virus transmits to humans from either rodents or from infected humans. Hundreds of cases of human monkeypox are detected in west and central Africa annually. The few cases seen outside Africa have all been associated with travel to Africa or contact with imported infected rodents.<sup>2,5,9</sup> The role of rodents in the UK monkeypox cases with history of travel to Africa<sup>4,5,9</sup> might reflect the current wave of human monkeypox infections occurring in Nigeria consequential to increased exposures to rodents during the COVID-19 lockdown periods. These secondary epidemiological cycles with human-to-human spread might be affecting international travellers. Further study on rodent dynamics and monkeypox cases inside and outside endemic regions aligned to viral genomics is required to detect possible drivers for the current monkeypox epidemic.

Priority for the current monkeypox outbreak should be on stopping further spread and protecting frontline health-care workers, and those most at risk globally. The unprecedented manifold increase in monkeypox cases seen in the past 3 weeks outside Africa yet again highlights that developing effective capacity at source is crucial for effective global public health preparedness and surveillance for zoonotic threats to global health security.<sup>12</sup> Rapid garnering of financial and political support for this is required to fuel reassurance, rather than fear and stigmatisation.

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## COVID-19 vaccine effectiveness against the omicron (BA.2) variant in England



The omicron (B.1.1.529) variant, first detected in the UK on Nov 27, 2021, rapidly became the dominant strain, due in part to reduced vaccine effectiveness.<sup>1</sup> An increase in sequenced cases of the omicron sub-lineage BA.2 was observed in the week beginning on Jan 3, 2022.<sup>2</sup> BA.2 has a growth advantage over BA.1<sup>3,4</sup> and has become the dominant strain in the UK at the time of writing. Neutralisation assays using monoclonal antibodies have suggested a small antigenic difference between BA.1 and BA.2, although sera from individuals with booster vaccinations neutralise both variants similarly.<sup>3</sup>

The UK COVID-19 vaccination programme has been in place since Dec 8, 2020, with primary courses of two doses of either BNT162b2 (Comirnaty, Pfizer–BioNTech), ChAdOx1-S (Vaxzevria, Oxford/AstraZeneca), or mRNA-1273 (Spikevax, Moderna). Booster vaccination with either BNT162b2 or a half dose (50 µg) of mRNA-1273 was introduced on Sept 14, 2021, to adults older than 50 years and those in risk groups, and on Nov 29, 2021, to all adults.

In this Comment, we estimate vaccine effectiveness against symptomatic disease and hospitalisation with BA.1 and BA.2 after one or two doses of BNT162b2,

ChAdOx1-S, or mRNA-1273, and after booster doses of BNT162b2 or mRNA-1273 during a period of co-circulation. We used a test-negative case-control study design.<sup>5–8</sup> Our analysis included all vaccines used in the UK. Vaccination status was included as an independent variable and effectiveness defined as 1 minus the odds of vaccination in cases, divided by the odds of vaccination in controls (appendix pp 1–3).

Between Jan 17 and March 31, 2022, there were 1127517 eligible tests from symptomatic individuals, of which 265 820 were positive for BA.1, 246 069 were positive for BA.2, and 615 628 were negative (controls). The hospitalisation analysis included 15043 eligible tests, of which 1662 were positive for BA.1, 623 were positive for BA.2, and 12758 were controls (appendix pp 4–7).

There was no evidence of reduced vaccine effectiveness against symptomatic disease with BA.2 compared with BA.1 (figure; appendix p 9). 25 weeks or more after two doses, vaccine effectiveness was 14.8% (95% CI 12.9–16.7 against BA.1 and 27.8% (25.9–29.7) against BA.2. Booster immunisation increased protection after a week to 70.6% (68.9–72.2)

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See Online for appendix