Elsevier has created a Monkeypox Information Center in response to the declared public health emergency of international concern, with free information in English on the monkeypox virus. The Monkeypox Information Center is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its monkeypox related research that is available on the Monkeypox Information Center - including this research content - immediately available in publicly funded repositories, with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the Monkeypox Information Center remains active.

Monkeypox in the UK: arguments for a broader case definition

Monkeypox cases are increasing rapidly in the UK. The UK Health and Safety Agency (UKHSA) defines a probable case of monkeypox as "a person with an unexplained rash on any part of their body plus one or more classical symptom or symptoms of monkeypox infection since March 15, 2022 and either: has an epidemiological link to a confirmed or probable case of monkeypox in the 21 days before symptom onset; or reported a travel history to west or central Africa in the 21 days before symptom onset; or is a gay, bisexual or other man who has sex with men". However, confirmed cases lack a travel history or contact with travel-related cases or with west or central Africa, so we strongly urge for the UKHSA's case definition to be re-evaluated.

Transmission within the community is already taking place. To untrained eyes, monkeypox could easily be mistaken for other dermatological diagnoses within sexual health clinics or primary care (eg, chickenpox, varicella zoster, herpes simplex, syphilitic chancre, gonorrhea, or molluscum contagiosum). An emergency drill in the USA showed that six of 13 patients with simulated smallpox were discharged with diagnoses that included West Nile virus and upper respiratory infections.[1] In February, 2020, the case definition of SARS-CoV-2 required previous exposure to a confirmed case, or recent travel to Wuhan, China, or Lombardy, Italy, when there was already significant community transmission within the UK.[2] Current case definitions of monkeypox would miss the case of a heterosexual patient with a characteristic vesicular-pustular rash but no travel history or contact with confirmed infection. The latter description best fits those people who most typically become infected in endemic areas.

Literature on monkeypox transmission is severely lacking. In a PubMed search for "monkeypox AND transmission" that yielded only 224 manuscripts, published from 1962 to 2022, we found more reviews published on the subject than original research studies in humans (appendix). 15 of the studies involving humans investigated transmission, the largest study being that of 2510 contacts of 214 patients with monkeypox in Zaire from 1980 to 1984; here the investigators reported infected cases without exanthema.[3] In 2005, smallpox-vaccinated individuals with monkeypox breakthrough infection were reported to have few or no skin lesions.[4] Prolonged upper respiratory tract viral DNA shedding after skin lesion resolution was also seen in patients with monkeypox admitted to dedicated high consequence infectious diseases centres between 2018 and 2021.[5] Early on in the COVID-19 pandemic, SARS-CoV-2 was assumed to spread through droplets from symptomatic patients, whereas overwhelming evidence now exists of aerosol (long distance) transmission, with asymptomatic or pre-symptomatic patients dominating transmission chains.[6] Although assumptions of asymptomatic and airborne transmission of monkeypox might be premature, in the context of yet another outbreak rapidly spreading across the world, the possibility of such transmission modalities must be considered. We must take a precautionary infection control approach to control the spread of the virus while completing urgent research to understand better the human-to-human monkeypox transmission process.

Although most cases in the current outbreak are in men who have sex with men (MSM), monkeypox has not historically been a sexually transmitted disease. It is possible the number of onward transmissions per case is artificially elevated because of the settings in which the virus is currently being transmitted (high rates of close contact). However, if this is the case, it is possible that other vulnerable groups would be similarly at risk of infection. Of note, although smallpox virus in the urine, throat, and conjunctival secretions has been found to diminish rapidly with time, the quantity of virus in scabs (dried pustules) does not.[7] Early on in the COVID-19 pandemic, people from minority ethnic groups were disproportionately affected by COVID-19,[8] not because of an inherently higher risk of developing severe disease from the virus, but because of a higher risk of coming into contact with an infectious person with SARS-CoV-2.[9] Patients from vulnerable groups, such as those from minority ethnic groups, might therefore also be at elevated risk of monkeypox infection, should the number of cases continue to increase. In addition to ensuring that case definitions for monkeypox do not overlook at-risk groups, it is also vital that these definitions do not further stigmatise or marginalise communities. In the COVID-19 pandemic, foreign born and minority ethnic communities faced stigma and discrimination due to erroneous assumptions around their increased risk of infection; our public health response to monkeypox must learn from these mistakes to achieve rapid identification of key risk groups without placing blame on these communities.

Current case definitions of monkeypox do not take into account the significant community transmission that is almost certainly occurring in the UK. Although monkeypox is unlikely to cause as much harm to the general public as COVID-19 did, lessons learned from the recent past with SARS-CoV-2 must still be applied; early spread of SARS-CoV-2 could have been mitigated if initial case definitions had been less stringent and extensive community testing implemented sooner. We propose that probable case definitions of monkeypox be broadened to include anyone with an unexplained vesicular-pustular rash on any part of their

Published Online
June 15, 2022
https://doi.org/10.1016/S0140-6736(22)01101-1

See Online for appendix

For **monkeypox guidance** see https://www.gov.uk/guidance/monkeypox

body with associated prodrome of fever, malaise, and lymphadenopathy so that fewer cases are missed in the community. Although this might initially increase the public health workload substantially, the probable case definition can be refined over the coming weeks and months, once the factors that make an individual infectious, locations where exposures are likely to occur, and the viral incubation period are better understood.

We declare no competing interests.

*Daniel Pan, Shirley Sze, Joshua Nazareth, Christopher A Martin, Amani Al-Oraibi, Rebecca F Baggaley, Laura B Nellums, T Déirdre Hollingsworth, Julian W Tang, *Manish Pareek*

manish.pareek@leicester.ac.uk

Department of Respiratory Sciences (DP, JN, CAM, AA-O, RFB, JWT, MP) and Department of Life Sciences (SS, RFB), University of Leicester, Leicester LE1 9HN, UK; Department of Infectious Diseases and HIV Medicine (DP, JN, CAM, MP) and Department of Virology (JWT), University Hospitals of Leicester NHS Trust, Leicester, UK; Lifespan and Population Health, School of Medicine, University of Nottingham, Nottingham, UK (AA-O, LBN); Oxford Big Data Institute, Oxford, UK (TDH);

1 Klein K, Atas J, Collins J. Testing emergency medical personnel response to patients with suspected infectious disease. *Prehosp Disaster Med* 2004; **19:** 256–65.

2 Chappell JG, Tsoleridis T, Clark G, et al. Retrospective screening of routine respiratory samples revealed undetected community transmission and missed intervention opportunities for SARS-CoV- 2 in the United Kingdom. *J Gen Virol* 2021; **102:** 001595.

3 Jezek Z, Marennikova SS, Mutumbo M, Nakano JH, Paluku KM, Szczeniowski M. Human monkeypox: a study of 2510 contacts of 214 patients. *J Infect Dis* 1986; **154:** 551–55.

4 Hammarlund E, Lewis MW, Carter SV, et al. Multiple diagnostic techniques identify previously vaccinated individuals with protective immunity against monkeypox. *Nat Med* 2005; **11:** 1005–11.

5 Adler H, Gould S, Hine P, Snell L, Wong W, Houlihan C. Clinical features and management of human monkeypox: a retrospective observational study in the UK. *Lancet Infect Dis* 2022; published online May 24. https://doi.org/10.1016/S1473-3099(22)00228-6.

6 Greenhalgh T, Jimenez JL, Prather KA, Tufekci Z, Fisman D, Schooley R. Ten scientific reasons in support of airborne transmission of SARS-CoV-2. *Lancet* 2021; **397:** 1603–5.

7 Mitra AC, Sarkar JK, Mukherjee MK. Virus content of smallpox scabs. *Bull World Health Organ* 1974; **51:** 106–07.

8 Pareek M, Bangash M, Pareek N, et al. Ethnicity and COVID-19: an urgent public health research priority. *Lancet* 2020; **395:** 1421–22.

9 Sze S, Pan D, Nevill CR, et al. Ethnicity and clinical outcomes in COVID-19: a systematic review and meta-analysis. *EClinicalMedicine* 2020; **29:** e100630.

Global burden of antimicrobial resistance: essential pieces of a global puzzle

Christopher J L Murray and colleagues[1] provide a compelling contribution to the understanding of the burden of disease attributable to bacterial antimicrobial resistance (AMR) in 2019. Focusing on 23 bacterial pathogens, they used two-stage spatiotemporal modelling to estimate this burden to be larger than diseases such as HIV and malaria, with the highest rates in sub-Saharan Africa. This new information should raise this issue higher on the global health agenda. They also, however, highlight the scarcity of high-quality data for infectious diseases and antibiotic consumption, with the authors having to rely on antibiotics sales data for an indication of antibiotic consumption.

Unfortunately, as we have described previously,[2] equitable and accessible strategies to optimise antibiotic prescribing and consumption remain out of reach. This gap is a major concern because of increasing threats to the sustained and safe supply of antibiotics globally, compromising access to effective therapies and leading to their sub-optimal use.[3]

There is widespread agreement on some things that must be done, including taking a One Health approach to reduce emergence of resistance and investing in research and development to develop new antibiotics. We have also identified a need for research that offers greater understanding of how we can preserve and sustain the efficacy of existing and future antibiotics in countries with differing resources and governance systems, recognising how the goals of antibiotic stewardship and infection prevention and control efforts are threatened by crucial population and geographical inequities.[4] We concur with Murray and colleagues when they highlight the disproportionate burden of AMR faced by low-income and middle-income countries. Addressing these inequities requires a systems approach to research and implementation strategies for AMR that incorporates an understanding of four aspects: (1) diversity of national and international policies and their implementation in different sectors; (2) fragmented health care; (3) complexity of human behaviours; and (4) differences in access to expertise and resources.[5] It will also require a long-term commitment to build capacity for locally driven research that draws on and supports existing expertise and talent. Supporting strategies that address these gaps should be a priority for funders engaged in global health in general and in AMR in particular.

From a research and policy perspective, addressing the burden of AMR requires development of economic and contextually appropriate AMR-specific policy interventions, better use of data and prescribing systems across health-care settings, appropriate and scalable technological innovation and data linkage and evaluation, and a better understanding and consideration for sociocultural and behavioural factors.[2] However, above all, this agenda must be developed in partnership with those most affected—namely, the patients and prescribers.

We declare no competing interests.

**Esmita Charani, Martin McKee, Manica Balasegaram, Marc Mendelson, Sanjeev Singh, Alison H Holmes*

e.charani@imperial.ac.uk

National Institute for Health Research Health Protection Research Unit in Healthcare Associated Infections and Antimicrobial Resistance, Imperial College London, Hammersmith Hospital Campus, London W12 0NN, UK (EC, AHH); Department of Medicine, London School of Hygiene & Tropical Medicine, London, UK (MMc); Global Antibiotic Research and Development Partnership, Geneva, Switzerland (MB); Division of Infectious Diseases and HIV Medicine, Department of Medicine, University of