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Letter to the Editor

Global differences in natural transmission rates of Monkeypox virus

Dear editors,

In this journal, Usman Ayub Awan et al. highlighted the epidemiology of Monkeypox (MPX) and prompted public awareness of MPX as a zoonotic disease.¹ MPX has posed a serious public health threat worldwide since it was declared a Public Health Emergency of International Concern by the World Health Organization (WHO) on July 23, 2022. Monkeypox virus (MPXV) is characterized by complex transmission routes and concentrated on highrisk populations. Its effective reproduction number (R_{eff}) is still locally estimated to be greater than 1 (1.02-1.39) in people over 40 years old, even though the populations are partially vaccinated for smallpox, and already have some immunity.² As for the basic reproduction number (R_0) , previous estimations did not eliminate the impact of existing coverage of the smallpox vaccine and coupled with the imperfection of the MPX surveillance system, which makes the derived R_0 likely underestimated.³ Due to the varying distribution of exposed populations and high-risk populations, the region-wise R₀ is still unknown and requires a new round of estimation. Aimed to quantify the transmissibility of MPX for regions comprehensively and systematically, and provide evidence to explain the transmission characteristics and regional heterogeneity of MPX, this study estimates region-wise R₀, time-dependent reproduction number (R_t) , explains the high values of estimations and emphasis the important means against MPX.

By September 20, 2022, the MPX outbreak has rapidly spread to 100 locations. The current MPX outbreak is most severe in America and Europe (Fig 1), where high risks are assessed by the WHO.⁴ Among countries, the United States ranked first in the world with a total number of cases of 24,042, followed by Brazil (7115), Spain (7083), France (3898), and the United Kingdom (3591). Currently, the total number of cases of MPX worldwide has reached 64,208 (Fig 1). We selected 29 countries with a total number of MPX cases of more than 50 and stable case data to quantify the transmissibility of MPX. The uncertainties of R_0 due to data noise are quantified for each country using forward piecewise fitting, i.e. fitting in each time segment starting from the first observation gives one sample of R_0 in the specific region. The global median R_0 was 2.44 (interquartile range [IQR]: 2.06–3.06), with R_0 values of 3.54 (IQR: 3.04-3.91), 3.46 (IQR: 2.97-4.26), 2.38 (IQR: 1.86-2.57) for the United States, Brazil, and Spain, respectively. The median R_0 was highest in Peru (4.23 [IQR: 3.19-4.45]), and Greece was the

lowest $(3.77 \times 10^{-4}$ [IQR: 3.56×10^{-4} –0.59]) (Fig 1). The global mean value of median R_t is 1.29 (standard deviation [SD]: 0.87), and the mean value of median R_t value of 1.31 (SD: 0.54), 1.33 (SD: 0.50), 1.11 (SD: 0.47) for the United States, Brazil, and Spain, respectively. The mean value of median R_t was highest in Luxembourg (1.81 [SD: 2.51]), and Portugal was the lowest (1.03 [SD: 0.28]). In specific scenarios of severe outbreaks, the maximal global R_t can reach 7.90, 4.23 in the United States, 3.36 and 2.69 in Brazil and Spain respectively (Fig 2).

The results showed the mean value of median Rt value for MPX of 1.36 (SD: 0.21) and the median R_0 value of 1.63 (IQR: 1.34– 1.72) where the R_0 values we calculated were higher than the estimates listed on the WHO official website.⁵ Several experts have made it clear that MPX will not be the next Corona Virus Disease 2019 (COVID-19), but why the calculated R_0 is close to COVID-19 $(2.5 \text{ (range: } 1.8-3.6)) \text{ or even higher than influenza } (1.5)?^6 \text{ On one}$ aspect, the most important transmission route of MPX is through close physical contact, along with relatively few transmission by droplets under prolonged face-to-face conditions, however, the respiratory diseases COVID-19 and influenza, are mainly transmitted by droplet transmission route. The physical contact mode of transmission is the main reason for limiting the spread of MPX. On the other aspect, our model considers and eliminates the effect of smallpox vaccination, and calculates the idealized transmissibility of MPX in a group with high-risk behaviors for men who have sex with men (MSM) without any interventions. The variation of highrisk social networks in fixed local contact patterns will undoubtedly amplify the transmissibility of MPX in the specific community; whereas the transmissibility of COVID-19 and influenza are estimated on an average mixed pattern of population. Other disease involving similar high-risk physical contact behaviors, like AcquiredImmune Deficiency Syndrome (AIDS), is often taken up for exploration alongside MPX. The popular question about which has the higher reproduction number between MPX and AIDS means nothing because AIDS patients usually be infectious for their whole life, not as acute infectious disease as MPX is. The definition of reproduction number makes it not adequate for comparing the transmissibility between infectious and chronic diseases. Even if the transmission of MPX is unlikely to reach the same scale as COVID-19, the R_0 and R_t values derived from our study suggest an effective alert on the spread of MPX in high-risk population communities. The most important step against MPX is to raise public awareness of MPXV, especially in high-risk populations with highrisk behaviors, and to improve the case surveillance tracking system and vaccination strategies.

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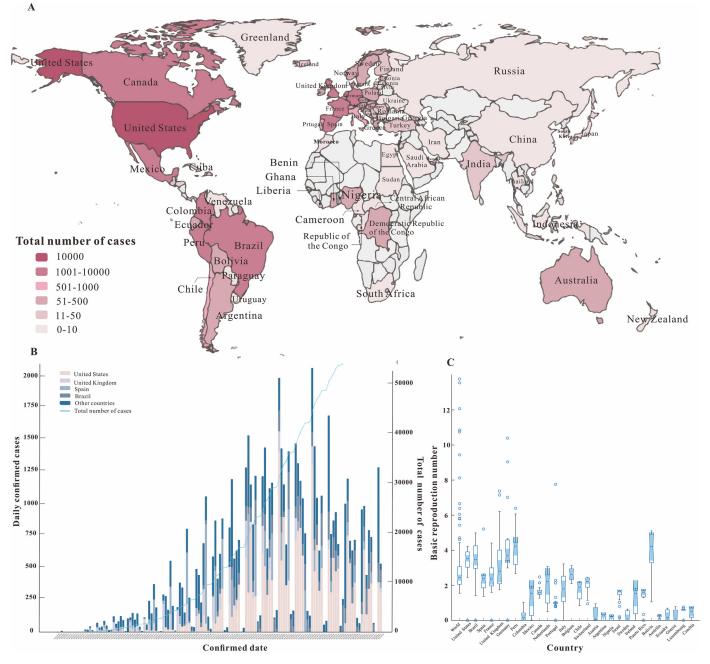


Fig. 1. Epidemic situation and calculation of transmissibility of monkeypox (A: The spatial distribution of monkeypox cases in different countries. B: Outbreak curve of confirmed monkeypox cases in global from 6 May, 2022, to 20 Sept, 2022. C: Box plots of basic reproduction numbers for global and multiple countries).

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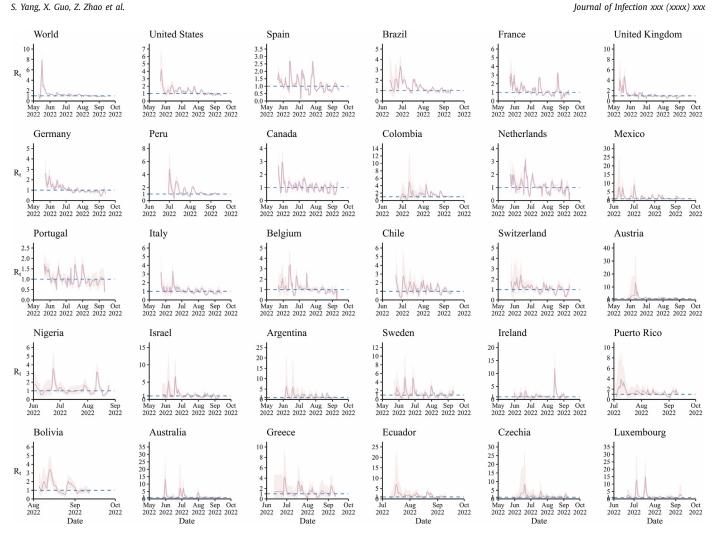


Fig. 2. Estimated time-dependent reproduction numbers from May 6, 2022, to September 20, 2022, globally and for 29 countries (The pink dash indicates the median R_t , the light pink interval indicates the 95% confidence interval, and the blue dashed line indicates R_t equal to 1. R_t calculated by the serial interval (mean: 4.0, standard deviation: 1.5)). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Ethical approval

The data we obtained are from the public database (Our world in data), therefore institutional review board approval and informed consent were not required. All data analyzed were anonymized.

Data availability

The data we obtained are from the public database (Our world in data, https://ourworldindata.org/monkeypox).

Competing interests

All authors declare no competing interests.

CRediT authorship contribution statement

Shiting Yang: Conceptualization, Methodology, Visualization, Writing – original draft. Xiaohao Guo: Methodology, Software, Writing – original draft. **Zeyu Zhao:** Conceptualization, Methodology, Writing – review & editing. **Yichao Guo:** Software. **Guzainuer Abudurusuli:** Writing – review & editing. **Tianmu Chen:** Conceptualization, Validation.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jinf.2022.10.032.

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