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Early estimates of the incidence trend and the reproductive number of the monkeypox epidemic in Brazil

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ABSTRACT

Background: We aimed to calculate the weekly growth of the incidence and the effective reproductive number (Rt) of the 2022 Monkeypox epidemic during its introduction in Brazil.
Method: We described the case distribution in the country and calculated the incidence trend and the Rt in the four geographical states with the highest case reports. By using two regression approaches, count model and the Prais-Winsten, we calculated the relative incidence increase. Moreover, we estimated the Rt for the period between the 24th and the 50th days after the first official report, using a serial interval reported in another population and two alternative values (± 3 days).
Results: Up to August 22, 3.896 Monkeypox cases were confirmed in Brazil. The weekly incidence increases were between 37.5% (95% CI: 20.7% - 56,6%) and 82.1% (95% CI: 59.5%–107.8%), and all estimates of Rt were significantly higher than 1 in the four states analyzed.
Conclusions: The Monkeypox outbreak in Brazil is a significant public health emergency that requires coordinated public health strategies such as testing, contact tracing, and vaccination.

1. Introduction

In July of 2022, the World Health Organization declared that the monkeypox outbreak was a public health emergency of international concern [1]. Up until August 22, 2022 there were 43.583 confirmed cases and 9 deaths worldwide [2]. In Brazil, the first case was confirmed on June 8, 2022, increasing to 3.896 confirmed cases until August 22, 2022 [3]. Brazil also registered one Monkeypox death, on July 29, 2022, in the state of Minas Gerais (MG).

Although this outbreak is unprecedented, Monkeypox is not a new disease. The virus was discovered in 1959 and the disease is endemic in Central and West Africa [4,5]. For decades, it has been warned about the risk of epidemics in the human population, since the virus might infect susceptible animals [6]. Outbreaks were reported in the Democratic Republic of the Congo in 2013 [7], as well as in non-endemic countries, such as the United States of America in 2003 and the United Kingdom in 2018 [8,9]. Along the side, the protection conferred by the smallpox vaccine decreased worldwide, mainly in young people, as the campaigns were interrupted with the eradication of this disease [10].

Incidence trends and reproductive number estimates are important to recognize the potential extension of an outbreak and to justify public health interventions [11]. In this work, we aimed to estimate the weekly incidence growth and the effective reproductive number (Rt) of the 2022 Monkeypox epidemic during its introduction in Brazil.

2. Material and methods

This was an ecological study based on surveillance data of the epidemiological reports posted by the Brazilian National Health Ministry [3]. We created a database with all the new and accumulated cases and deaths [12]. We focused on the four states with more than 150 cases up to August 22, 2022. These states were São Paulo (SP), Rio de Janeiro (RJ), Minas Gerais (MG) and Goiás, which geographically includes the Federal District of Brasília (GO-FD).

The Brazilian Health Ministry defined a suspected Monkeypox case as a case that shows one or more of the following criteria [13]:

- Prolonged exposure with no respiratory protection OR direct physical contact, including sexual contact, with multiple and/or

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unknown partner in the 21 days before the lesions and/or the onset of symptoms;
- Prolonged exposure with no respiratory protection OR close contact history, including sexual, with suspected or confirmed Monkeypox case in the 21 days before the lesions and/or the onset of symptoms;
- Contact with contaminated materials like sheets and bathroom towels or common use utensils that belong to a suspected or confirmed Monkeypox case in the 21 days before the lesions and/or the onset of symptoms;
- Health workers without proper use of protection equipment with history of contact with suspected or confirmed Monkeypox case in the 21 days before the lesions and/or the onset of symptoms.

Confirmed cases are defined by a suspected case with positive PCR result for the Monkeypox virus (MPXV) [13]. The Brazilian Health Ministry started the official case notifications on June 27, 2022. SP and RJ states already had cases on that data, MG had its first case notified on June 29, 2022 and GO-FD had their first cases notified on July 02, 2022.

Considering the confirmed cases, we performed two analyses. First, we estimated the weekly growth of the incidence of Monkeypox, starting one day after the first reported case in the corresponding state. For this, we grouped the cases by week and used two regression approaches: the count models of Poisson and negative binomial regression, reporting the last one when the alpha term differed significantly from zero [14,15]; and, the Prais-Winsten regression to the natural logarithm of the weekly case count [16,17]. We reported the relative incidence increase calculated as e^{β}-1, where β is the regression coefficient. We used both regressions to assess the consistency of the weekly growth estimates.

Second, we estimated the Rt in each of the four states aforementioned by using the "estimate_R" function contained in the "EpiEstim" package of the R programming language [18,19]. We used the "parametric_si" configuration of the package (script available as supplementary material). One of the parameters necessary to estimate the Rt is the serial interval (SI) of the disease. The SI consists of looking at a pair of cases and extracting the number of days between the disease onset on the primary case and that on the secondary case. Since the microdata of Monkeypox cases in Brazil are unavailable, we do not have the local SI data, so we used a value recently calculated in the United Kingdom [20]. This SI was obtained from 17 pairs of cases (primary - secondary) of the United Kingdom. The mean SI calculated in this study is 9.8 days, and the standard deviation (SD) is 9.1 days [20]. Since SI can be different from one location to another, we also calculated the Rt for two more SI values defined by subtracting and adding three days to the reference (SIs of 6.8 and 12.8 days with SDs of 6.1 and 12.1, respectively) [20].

For each day since July 26, the Rt was estimated on weekly sliding windows, given by the parameters "t_start" and "t_end". Therefore, the first estimates of Rt based on new cases notified between July 20 and 26, 2022, i.e., between the 24th and 30th day after the first report in Brazil. We chose that starting point because it was when we observed that the Rt values became more stable. We also calculated a summary estimate of the Rt for each state by widening the viewing window from July 20 to August 22, 2022.

This study used public data, and the analysis was performed using R (version 4.2.1) and Stata (version 17.0, Stata Corp LP, College Station, TX, USA).

3. Results

The 3.896 confirmed Monkeypox cases in Brazil up to August 22, 2022, almost doubled when compared to the 2.004 cases that were notified up to August 5, 2022. The state with the most reported cases was SP, followed by RJ and GO-FD (Figs. 1 and 2). The highest relative increase of incidence was observed in GO-FD, being 74.7% per week using the count model and 82.1% using the Prais-Winsten regression. In all states, the increasing trend was statistically significant with both regression approaches (Table 1).

The summary Rt was also higher in GO-FD, with 2.07 (95% CI: 1.98–2.16), followed by SP with 1.70 (95% CI: 1.68–1.72), RJ with 1.65

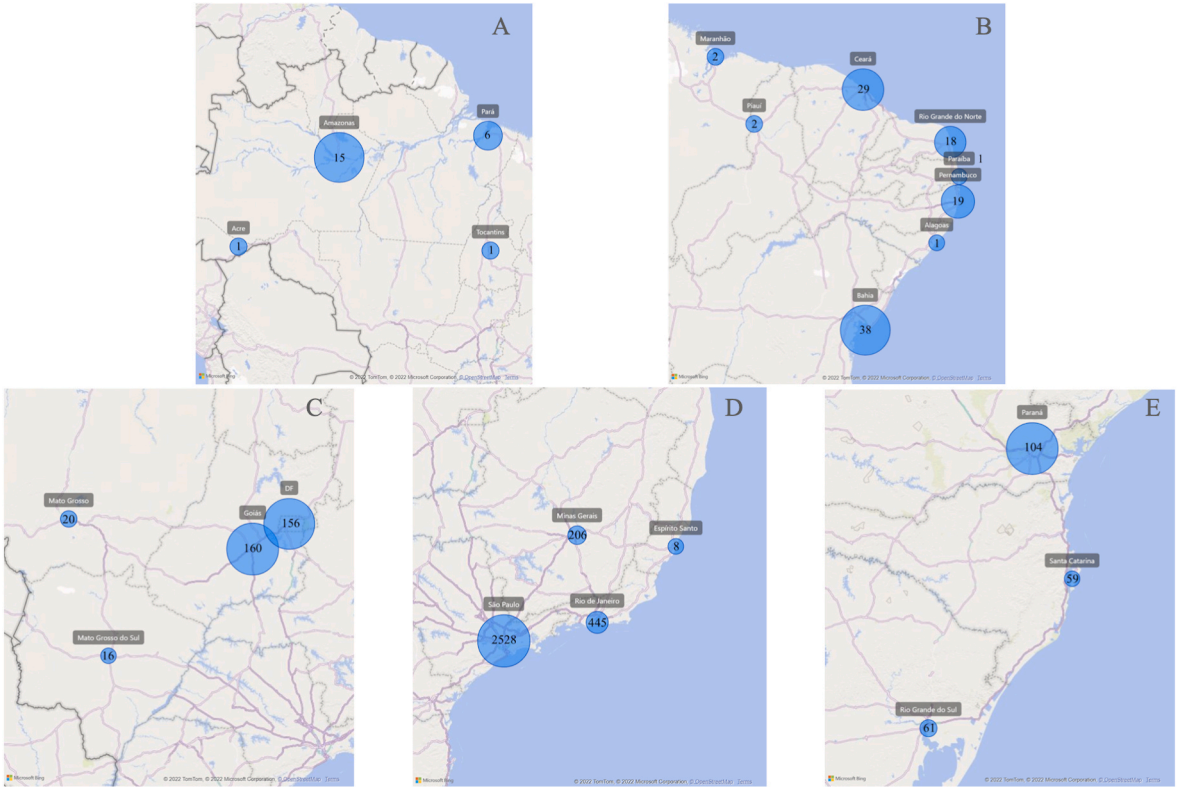

Fig. 1. Brazil maps with Monkeypox incidence by region: North (A), Northeast (B), Center West (C), Southeast (D) and South (E).

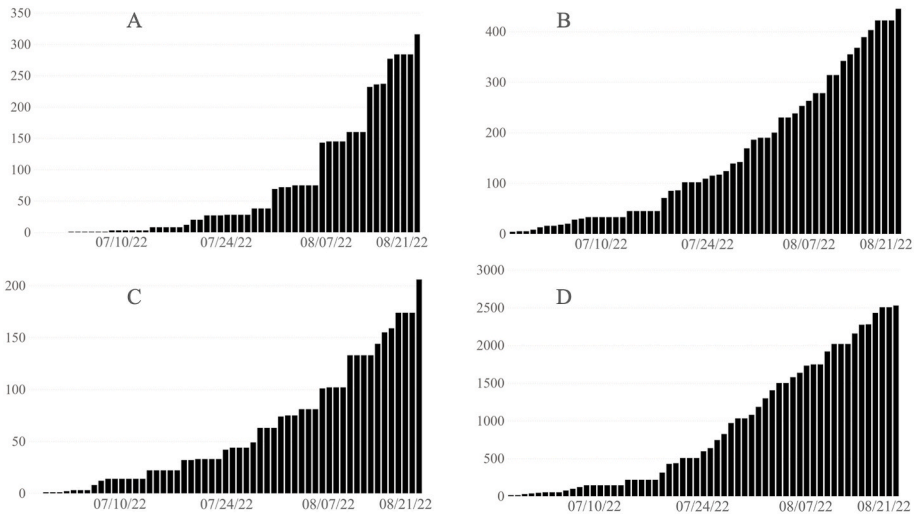

Fig. 2. Epidemic curve of the four analyzed states: GO-FD (A), RJ (B), MG (C) and SP (D).

Table 1
Relative incidence increases and reproductive number of monkeypox epidemic in the most affected states of Brazil.

State	Weekly incidence increase (95% CI)		Rt-mean (95% CI) according to serial interval (SI)		
	Count model[a]	Prais–Winsten	SI:9.8 days	Sensitivity analysis:	
				SI:6.8 days	SI:12.8 days
GO–FD[b]	74.7% (52.5%–100.2%)	82.1% (59.5%–107.8%)	2.07 (1.98–2.16)	1.73 (1.66–1.80)	2.42 (2.31–2.52)
SP[c]	45.5% (21.9%–73.7%)	45.6% (15.5%–83.6%)	1.70 (1.68–1.72)	1.46 (1.45–1.48)	1.94 (1.92–1.96)
RJ[d]	37.5% (20.7%–56.6%)	40% (18.4%–65.6%)	1.65 (1.61–1.70)	1.44 (1.40–1.48)	1.87 (1.82–1.92)
MG[e]	41.5% (31.7%–52%)	42.9% (39%–46.9%)	1.64 (1.57–1.72)	1.43 (1.37–1.50)	1.86 (1.78–1.94)

[a] Estimate for MG was obtained using Poisson, and for the other states using negative binomial regress (p-value <0.001 of alpha = 0).
[b] GO-FD: the state of Goiás plus Federal District (Brasília).
[c] SP: São Paulo.
[d] RJ: Rio de Janeiro.
[e] MG: Minas Gerais.

(95% CI: 1.61–1.70) and MG with 1.64 (95% CI: 1.57–1.72). The weekly Rt, estimated with a SI of 9.8 days, oscillates between 1.86 and 2.62 in GO-FD, 1.54 and 2.00 in RJ, 1.56 and 1.77 in MG and 1.48 and 2.16 in SP (Fig. 3). With SIs of 6.8 days and 12.8 days (−3 and +3 days) all the Rt estimates stayed significantly above 1 (Fig. 4).

4. Discussion

In the present study, we illustrated a significant increase of confirmed Monkeypox cases in the most affected states of Brazil up to August 22, 2022. We are also observing a similar pattern in other states (data not shown), like Paraná and Rio Grande do Sul, even with lower numbers of cases (104 and 61, respectively). The values of Rt estimated for four states are considerably high and consistently above the level of

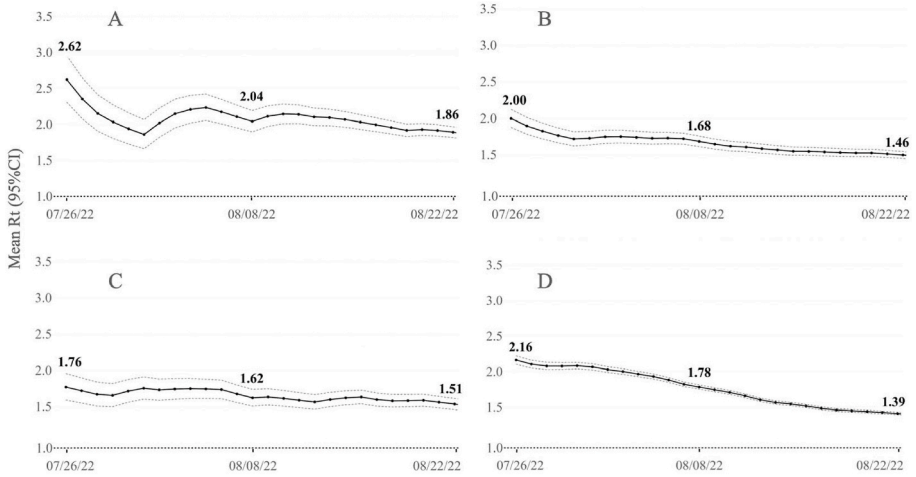

Fig. 3. Rt estimates from GO-FD (A), RJ (B), MG (C) and SP (D) with an SI of 9.8 days.

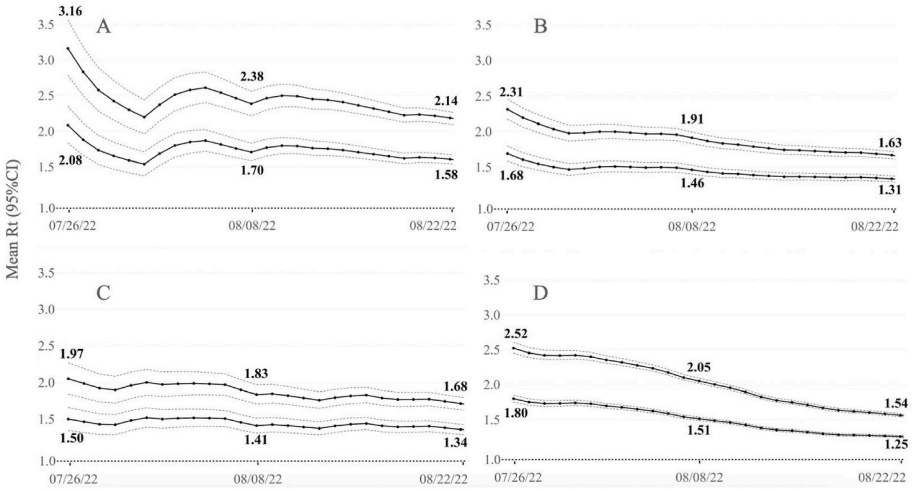

Fig. 4. Rt estimates with SIs of 12.8 (top line) and 6.8 days (bottom line) for GO-FD (A), RJ (B), MG (C) and SP (D).

control (i.e., Rt > 1). The Rt value obtained in the present work is consistent with other findings. Kwok et al. (2022) estimated a Ro of 1.6 (1.5–1.7) in England, 1.4 (1.2–1.6) in Portugal and 1.8 (1.7–2.0) in Spain [20]. Despite the differences among these populations, these data indicate the increasing transmission of Monkeypox in human populations during the current epidemic. Therefore, it is urgent to identify and interrupt the main transmission routes.

To put our findings in perspective, we consider that the Rt estimates may be comparable with some calculated for COVID-19 [21]. This comparison takes place in a scenario where the impacts of COVID-19 need further comprehension. It is important to highlight that MPXV and SARS-CoV-2 have significant differences in the predominant transmission routes. SARS-CoV-2 can be transmitted by exposure to small droplets and aerosols in short and long distances from the emission source [22–24], while MPXV can be transmitted by close contacts, especially with skin lesions, such as intimate or prolonged face-to-face contact, as well as by touching surfaces and objects with viable viral particles [25–29]. Nevertheless, the comparable Rt values could be explained by different combinations of the determinants of the reproductive number (duration of the infectious period, rate of contacts and the transmission probability) [30]. In that sense, an infectious disease with relative few transmission routes can even have a high reproductive number if either specific contact rate or infectious period duration are elevated [30,31].

Regarding Monkeypox, direct contact might be the predominant source of transmission in the current outbreak, hence the high viral loads detected on skin lesions [32,33]. Moreover, viral DNA can be detected by PCR test in skin samples from up to 21 days, according current evidence [26]. Therefore, even if the ways of transmission were limited, we hypothesize that a prolonged infectious period could explain high Rt values. If this hypothesis is confirmed with further studies, it could guide assertive public health interventions, such as prolonged isolation, to counteract the current epidemic. It is important to highlight that the currently available data is not enough to establish or discard the role of aerosols or other types of transmission, like fomites, in Monkeypox transmission. Even so, strategies focusing on isolation of suspect cases and contacts, ring vaccination and awareness about the transmission routes can be effective to control the current outbreak [34,35].

The monkeypox outbreak arrived in a different context than that of COVID-19, since approved vaccines against Smallpox can confer protection against Monkeypox in both pre-exposure and post-exposure contexts [36]. Moreover, tecovirimat, an antiviral drug, which might present a potential use to treat some cases of Monkeypox, is showing preliminary positive results in placebo-controlled pharmacokinetic and safety trial [37] and observational studies [38,39]. It is important to highlight that the coronavirus pandemic promoted preparedness against emerging pathologies [40]. However, besides this context, the Monkeypox outbreak growth in different countries, such as Brazil, asks for assertive and coordinated actions.

Our study had some methodological limitations. The sample size was limited and Rt can be unstable during the early stages of the epidemic [41]. Therefore, we restricted our analysis to four states and the Rt was estimated after the 24th day of the first official case notification. Another limitation is the potential delay in both notification and testing, affecting the real-time monitoring of the incidence.

On the other hand, we estimated the Rt with a preset SI obtained from another population, from the United Kingdom, since the Brazilian microdata was unavailable [20]. Even so, we believe this value could be compatible with that expected in Brazil since it was recently calculated in the context of the current epidemic. On the other hand, the sensitivity analysis, with alternative values of SI, supports robust conclusions regarding the lack of transmission control. In that sense, our Rt estimates correlated well with the observed upward trends across the states, which give a reference of the potential transmissibility of Monkeypox in Brazil.

5. Conclusions

Our results illustrated the growth of the incidence and the lack of control during the introduction of the MPXV in Brazilian states. These findings highlight the need for effective public health actions such as testing, contact tracing and isolation of the confirmed cases. There is also a need for smallpox vaccination in risk groups which could protect against Monkeypox [42], in spite of the fact that we do not have a specific Monkeypox vaccine at this moment. Finally, this work also reinforces the importance of surveillance and more detailed public data to ensure timely analyzes that guide decisions to control the epidemic.

Credit author statement

Isaac Schrarstzhaupt: Conceptualization; Methodology; Software; Writing - Original Draft.

Mellanie Fontes-Dutra: Resources; Writing - Review & Editing.

Fredi Alexander Diaz-Quijano: Conceptualization; Methodology; Writing - Review & Editing; Supervision.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.tmaid.2022.102484.

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