Estimates of mpox effective reproduction number in Spain, April–August 2022

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Abstract

We analysed the transmission of the human mpox virus in Spain by estimating the effective reproduction number of the disease from official surveillance data. Our computations show that this decreased steadily after an initial burst phase, dropping below 1 on July 12, and thus the outbreak was expected to reduce in the following weeks. Differences in trends were found across geographical regions of the country and across MSM and heterosexual populations.

Introduction

Since April 2022, an increasing number of countries reported confirmed cases of the mpox virus (also known as the monkeypox virus) with transmission chains not linked to endemic countries [1, 2]. On 23 July 2022, the WHO Director-General determined that the mpox outbreak constituted a public health emergency of international importance [3]. As of August 16, 16162 mpox cases had been reported in Europe [4].

In Europe, Spain was the most affected country, followed by Germany and France. The epidemic curve followed similar trends in these countries, peaking in the first week of July and starting to decrease during the second half of the month [5]. The basic reproduction number R_0 of the disease has been computed for some European countries [6–8], and estimates on the effective reproduction number and instantaneous growth rate are available as well for some countries [9–11].

The first case in Spain was identified retrospectively on 25 April 2022 [12, 13]. Since then, 6284 confirmed cases had been notified to the National Epidemiological Surveillance Network (RENAVE [14, 15]) as of 19 August 2022. This made Spain the non-endemic country with the most confirmed cases in the European region at the time, reporting the second highest number of cases in the world [16]. The spatial distribution of these was not homogeneous: Madrid and Barcelona provinces hosted 35% and 28% of the total cases, respectively (Figure 1). To date, the disease is predominantly prevalent among men, with less than 2% of the cases being notified among women. Two patients under 3 years old have also been reported, as well as two deceased cases.

Even though the incidence of the disease decreased substantially in Europe after the autumn of 2022 winter of 2022, further epidemiological insights are still to be drawn from the outbreak [1, 2]. While several studies in the country have addressed the clinical characteristics of the disease [17–19], assessments of the factors relevant to the containment of the disease at the population level are still in need. These are expected to provide valuable guidance in the design of effective public health policies and improved preparedness for future outbreaks of the disease or other diseases sharing epidemiological features with it.

Here, we compute estimates of the effective reproduction number (R_t) during the mpox outbreak in Spain, to evaluate the evolution of its transmission and to investigate its possible differences across different subgroups of the population. In particular, we consider transmission across geographical regions of the country and transmission across men who have sex with men (MSM) and heterosexual individuals, as both the geographical setting [19–21] and sexual activity have been identified as relevant factors in the spread of the disease [1, 18, 22].

Material and methods

We used confirmed cases notified to the National Epidemiological Surveillance Network (RENAVE) from 25 April to 19 August 2022. These were used in the method of Cori et al. [23–25] to estimate the R_t of the disease. Several factors were taken into account for this:
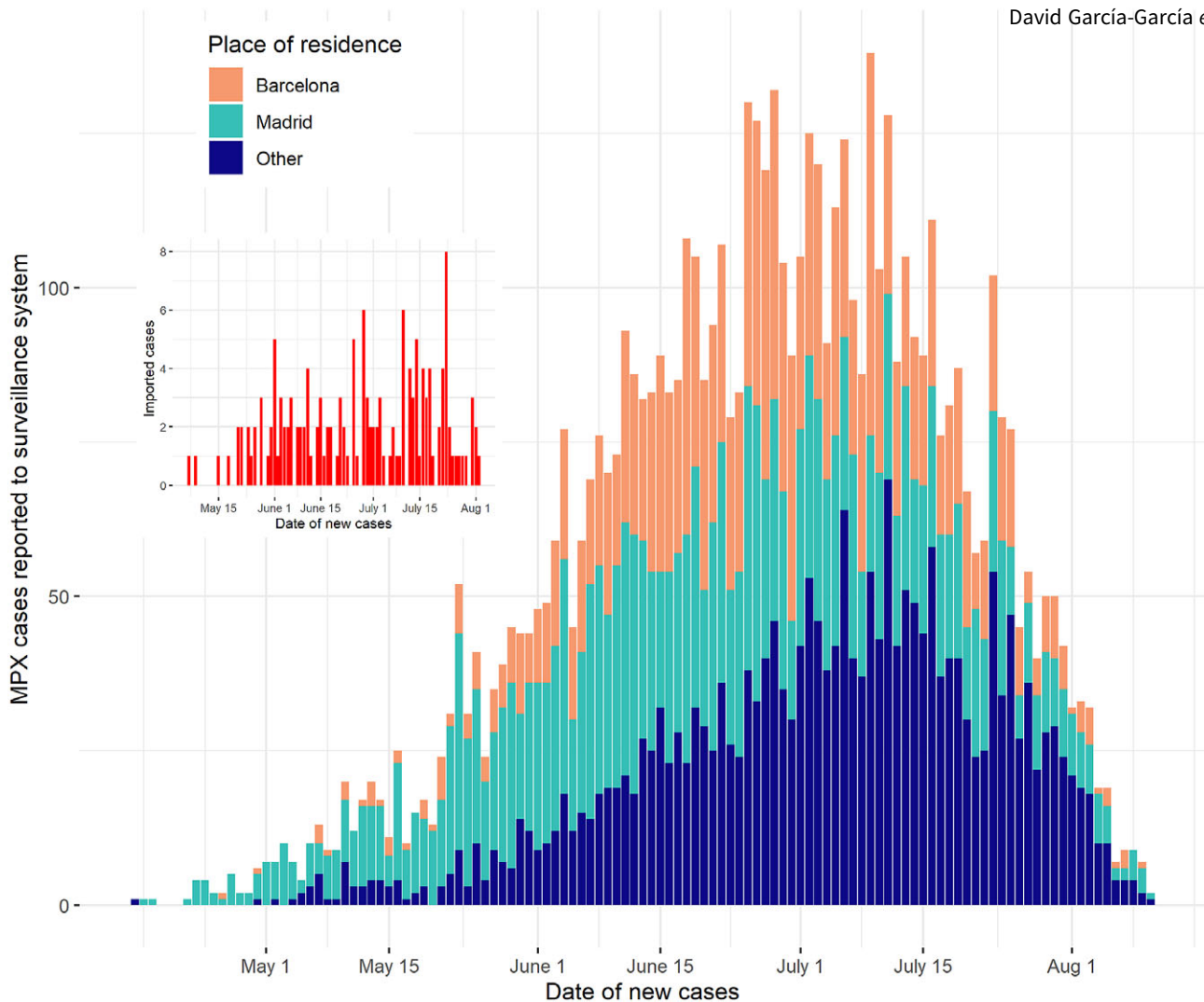
Figure 1. Epidemic curve of MPX in Spain, Madrid, and Barcelona, 25 April–19 August 2022. The date of new cases was obtained as the date of the onset of symptoms, offset by the incubation period.

–   The date for new cases was chosen to be the date of the onset of symptoms, offset by the incubation period (see the next item), as usual when computing R_t estimates [26]. No asymptomatic transmission was assumed in the model. While some instances of transmission from individuals presenting no mpox-related symptoms have been observed [27, 28], their occurrence has been rare. We thus assume that these do not represent a significant source of infection and that their possible effect on the model output can be disregarded.

–   The output dates of the model were offset by an incubation time of 9 days [25], in agreement with several findings in the literature [3, 6, 29].

–   The serial interval was assumed to be gamma-distributed with a 9.8-day average and a 3.875-day standard deviation, as estimated by WHO [3].

–   We performed a descriptive sensitivity analysis for the choice of the smoothing window. We computed R_t estimates for 3- to 13-day-long smoothing windows (leaving the rest of the parameters fixed) and chose the value that seemed to provide a more balanced compromise between detail and variability in the estimate upon visual examination of the resulting curves.

–   In total, 151 out of 6284 cases (2.4%) were notified as imported (a case is defined as imported in RENAVE if the probable place of infection was outside of the country). Although the

information on this variable is not always complete, these were included as imported cases in the method of Cori et al. In addition to this, the first recorded case in each of the regions under study was also labelled as imported when performing region-specific R_t estimates. This is a requirement of the method of Cori et al. [23, 24], which assumes that the first infection in each region was not caused by local transmission.

A summary of the chosen parametrisation is shown in Table 1. We also estimated the R_t in specific groups from the entire set of cases, in search for epidemiologically relevant differences. For this, we computed the R_t considering as input data only those cases with particular features. The resulting curves describe how transmission evolves within distinct subgroups of the population. We then compared the resulting curves by visual inspection and looked for apparent differences between them. This was done for three different groupings of the population:

–   *Madrid and Barcelona provinces.* These two provinces hosted most of the mpox cases in the country, especially during the initial burst phase of the outbreak. National transmission trends were thus expected to be dominated by cases residing in these provinces.

–   *Mobility-based communities.* We divided the total population of the country into seven 'communities', comprising several provinces. These communities were identified using clustering

Table 1. Model parametrisation

Parameter	Value	Notes
Date of new cases	Date of the onset of symptoms, offset by incubation period	
Incubation period	9 days	[3, 6, 29]
Serial interval	Average = 9.8 days Standard deviation = 3.875 days	Gamma-distributed [3]
Smoothing window	5 days	Chosen from sensitivity analysis (see Supplementary material)
Imported cases	Whenever the probable place of infection was not in Spain	Manually labelled first case in each region as imported (method requirement)

Summary of the parameter values used in the method of Cori et al. [23] to estimate the effective reproduction number.

algorithms on a large data set of mobility data based on cellular network data, published by the Spanish Ministry of Transport, Mobility and Urban Agenda [30]. These communities should be understood as mobility clusters, in the sense that intracommunity movement is significantly more likely than intercommunity displacement. The role played by these communities in disease spread has been verified for other infectious diseases [31]. See Supplementary Table S1 and Supplementary Figure S2 for explicit descriptions of the communities.

- *MSM and heterosexual population.* Transmission across individuals who identified themselves as heterosexual and MSM was also computed. MSM who declared having a female sexual partner during the 21 days previous to the onset of symptoms were removed from this grouping.

Results

After a steady increase in the number of weekly declared cases of the disease, the outbreak seemed to stabilise and slightly decrease in July and August, by looking at the number of new daily cases (Figure 1). The sensitivity analysis showed qualitatively similar results, with longer smoothing windows leading to estimates with smaller short-term variations, as expected (Supplementary Figure S1). We chose a 5-day-long smoothing window after inspecting the resulting curves. The results reported in the article were consistent upon variations in this parameter and showed little or no change for different choices of it. In particular, we found a generally decreasing trend in R_t, with a decrease below 1 on July 12 when using a 5-day smoothing window (Figure 2), and at most a 1-day variation on this date for 3- to 13-day smoothing windows (Supplementary Figure S1).

The evolution of the R_t for cases located in Madrid and Barcelona presented apparent differences during the first month of the
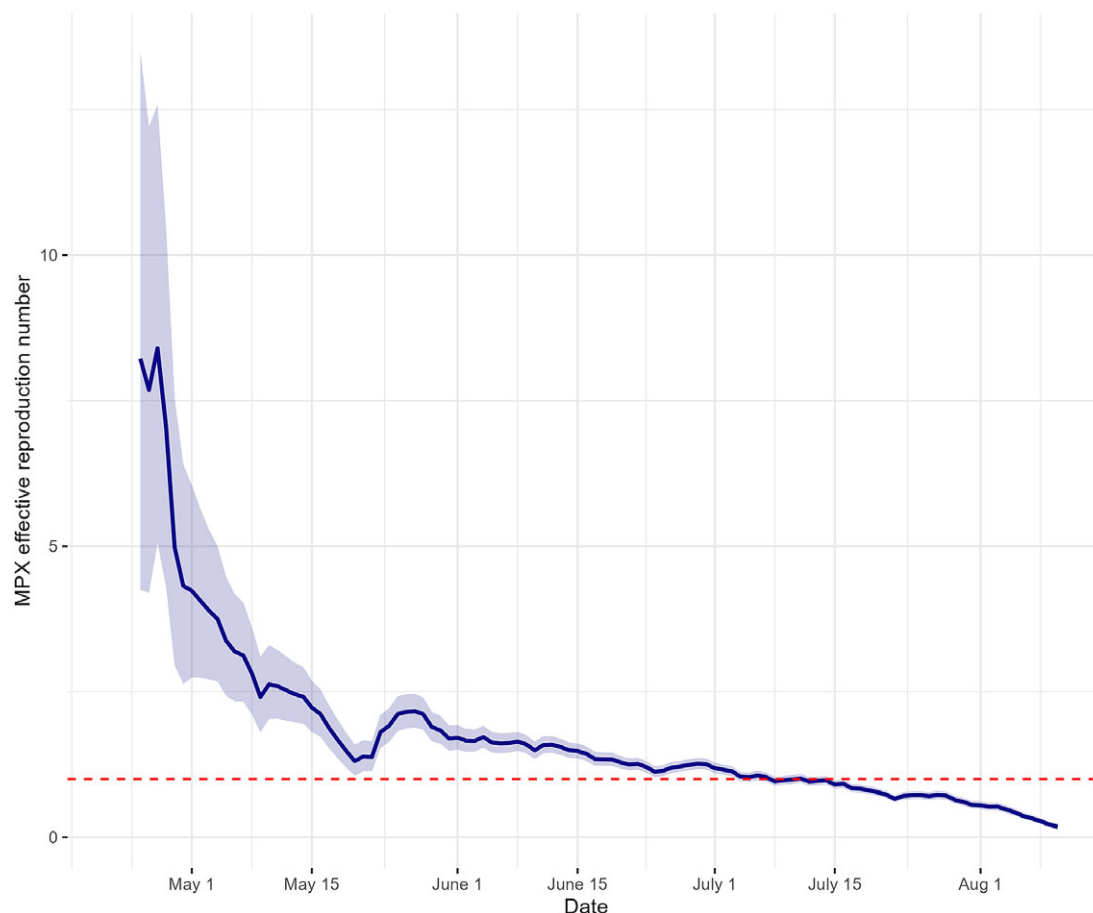

Figure 2. MPX effective reproduction number (R_t) in Spain, 25 April 2022–10 August 2022. Shaded area represents 95% confidence interval.

outbreak: transmission in Madrid seemed to decrease from an initial maximum peak, while transmission in Barcelona seemed to start at a low point, then increased quickly, and decreased again afterwards, although higher uncertainty was found for the estimate in Barcelona (Figure 3). After May 25, both curves seemed to stabilise in a slowly decreasing trend.

Several transmission patterns were found for the transmission in mobility-based communities (Figure 4). Three communities (Central East, Central West, and Canary Islands) showed a general decrease with some oscillations after an initial peak, similarly to Madrid. The transmission dynamics in two communities (Northeast and South) were similar to that found in Barcelona, following an initial increase and a subsequent decrease, with another mild increase in transmission before the final decrease. Two communities (North and Northwest) seemed to follow a different, more variable pattern, probably due to the smaller number of cases declared in these regions (see Supplementary Table S1 and Supplementary Figure S3).

While transmission across the MSM population resembled closely the global dynamics (as expected, since 75% of the patients identified themselves as MSM), the dynamics of infection across the heterosexual population seemed to be qualitatively different, with several peaks and valleys in the curve before the final decrease (Figure 5).

Discussion

Several factors might have contributed to the decrease in R_t. Since July, institutional and NGO campaigns have also been launched in order to increase awareness in the LGBTIQ community and to promote preventive measures, which may have caused changes in the behaviour of the at-risk population. The reduction in the susceptible population due to natural or acquired immunity may also be a relevant factor for reducing the transmission. Indeed, contact networks among MSM are known to be governed by a smaller number of individuals who concentrate on a larger proportion of contacts [32]. This relatively small group of the population may have been more exposed to the disease during the first weeks of the outbreak, acquiring immunity at a higher pace. Post-exposure vaccination to close contacts of the confirmed cases was prioritised in Spain on June 9 [33], and this recommendation was extended to pre-exposure vaccination of the most-at-risk population on July 12 [34]. However, the expected time required to develop immunity makes it unlikely for vaccination to have contributed significantly to the reduced transmission.

Transmission in Madrid and Barcelona seemed to follow different initial trends. In Madrid, it steadily decreased from an initial peak, while in Barcelona a bell-shaped curve was found for the first month of the outbreak. In addition to the different infection dynamics that may have taken place in the two provinces, the substantially higher estimates for the first days in Madrid may represent an overestimation due to the new incorporation of the disease in the surveillance system [25]. No apparent relations between the variations in these curves and the dates of events expected to be associated with a higher risk of infection
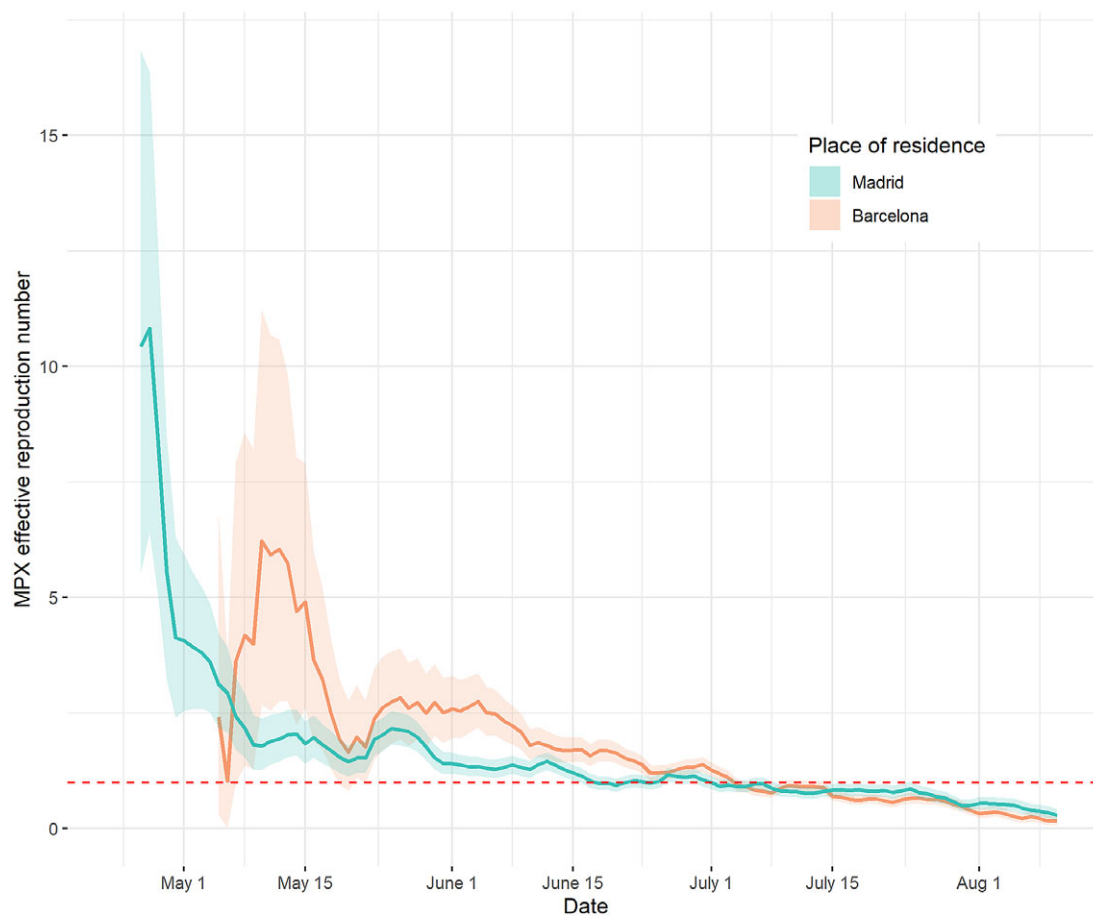

Figure 3. MPX effective reproduction number (R_t) in Madrid and Barcelona, 25 April 2022–10 August 2022. Shaded areas represent 95% confidence intervals.
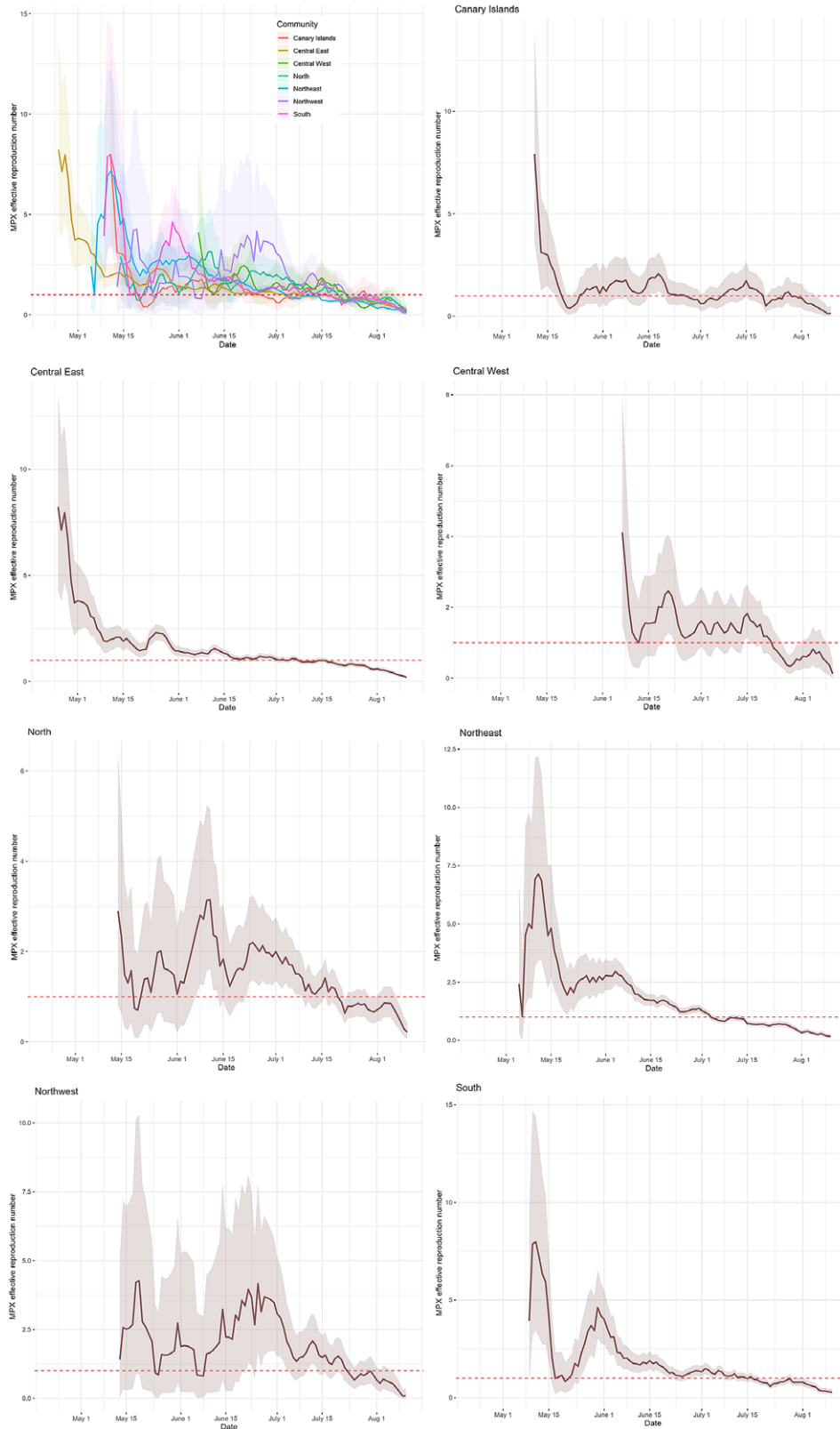
Figure 4. MPX effective reproduction number by mobility-based community in Spain, 25 April–10 August 2022. Shaded areas represent 95% confidence intervals.

were found (for instance, Madrid Pride during 1–10 July 2022), hinting towards the role of continued transmission in the spread of the outbreak (see below, however, for the limitations of this estimate).

As with any surveillance system, delays and incomplete information may occur and distort our estimates. This is particularly relevant for the first few days of the outbreak, where an exceptionally high R_t was obtained, possibly due to an accumulation of
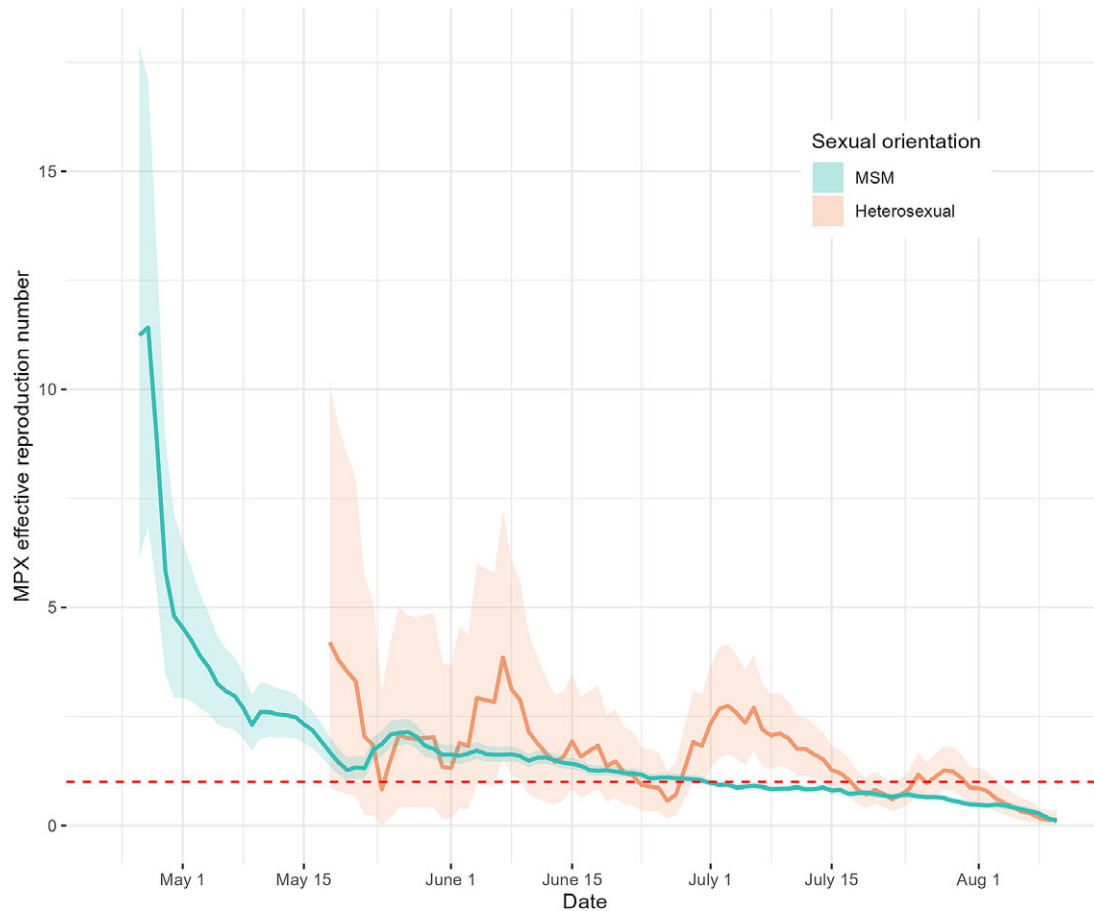
Figure 5. MPX effective reproduction number across the MSM and heterosexual populations in Spain, 25 April–10 August 2022. Shaded areas represent 95% confidence intervals.

cases of a previously non-prevalent disease and the known initial overestimation of the R_t [26]. A smaller value should be expected during these days, close to the basic reproduction number of the disease R_0 [6, 29]. A slightly lower value for the R_t may also be found in the last few days due to possible reporting delays during a holiday period, as usual when using the method of Cori et al. [23]. Finally, some cases during the last observed days may be missing due to delayed updates in the database, as the final date of update of the data set was 23 August 2022.

The estimates for the different groupings of the population should also be interpreted with care, due to the following limiting factors. First, the notification of imported cases is not always complete. In addition to this, geographical mixing is expected to occur between the regions considered in the analysis (both between Madrid and Barcelona and the mobility-based communities). These facts could cause variations in the estimates, in particular overestimations of the effective reproduction number during the first stages of the outbreak. Finally, the variable recording the sexual orientation of the cases is subject to considerable underreporting (23% empty records; only 149 out of 6284 cases identified as heterosexual), which manifests the possible inaccuracy of the estimate found for the heterosexual population, seen also in the large confidence intervals found for this estimate. Possible mixing between the MSM and the heterosexual populations could also be overlooked in our analysis due to incomplete declaration of the previous sexual partners.

Two different estimates for the mean generation interval are available in the literature [3, 6, 9], to our best knowledge. These were computed from 17 and 16 identified pairs of a secondary case and its primary case from the UK and Italy, respectively, and both report a wide 95% confidence interval. Interestingly, we found that the Rt decreased below 1 on the same date (July 12) when using both of these parametrisations. It would be desirable to further support our computations when estimates for this parameter computed from a larger amount of data are available. While estimates based on a larger number of cases are available for the incubation period [3, 6, 17, 29], a more accurate description of this parameter's distribution is still of need.

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