Analysis of the epidemiological dynamic of monkeypox from 15th May to 31st August 2022

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Summary

We show that in all countries with more than 1000 monkeypox cases at the end of August 2022, the evolution of the total number of cases is described by the Gompertz growth model. Although the data collection has many temporal irregularities, we have been able to measure the order of magnitude of the number of new cases per day in each country until the end of the study period in August 2022, as well as to analyse its dynamics. In this way, it is easy to check whether the epidemiological situation is improving. If no new epidemic outbreaks appear, as of early September, the model predicts a rapid improvement in the epidemiological situation.

Key words:
Monkeypox.
Mathematical epidemiology.
Gompertz model.

Análisis de la dinámica epidemiológica de la viruela del mono del 15 de mayo al 31 de agosto de 2022

Resumen

Mostramos que todos los países que han registrado más de 1000 casos de viruela del mono a finales de agosto de 2022, tienen una evolución del número de casos que se describe correctamente con el modelo de Gompertz. Aunque la recogida de datos presenta muchas irregularidades temporales, hemos podido medir el orden de magnitud del número de nuevos casos diarios en cada país, hasta el fin del período de estudio en agosto de 2022, así como analizar su dinámica. De esta manera, puede constatarse fácilmente si la situación epidemiológica está o no en vías de mejora. Si no aparecen nuevos brotes epidémicos, a fecha de inicios de septiembre, el modelo prevé una rápida mejora de la situación epidemiológica.

Palabras clave:
Viruela del mono.
Epidemiología matemática.
Modelo de Gompertz.

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Introduction

While the COVID-19 pandemic is still ongoing, monkeypox (MPX) has spread through several non-endemic countries. The World Health Organization (WHO) declared MPX as a new Public Health Emergency of International Concern on 23rd July 2022[1]. At the end of August 2022, the total number of reported cases was above 1000 in 9 countries, between 100 and 1000 in 18 countries and less than 100 in 55 countries[2]. The case fatality ratio shows large differences between countries given the relatively low number of cases. It is currently 0.04% in Spain[3]. This is a case fatality ratio much lower than that of COVID-19 in the initial stages when in most countries only severe cases were detected. However, it is much closer to the estimated values of current Infection Fatality Ratios of COVID-19, especially since vaccines became available. Besides, unlike SARS-CoV-2, the monkeypox virus affects more severely young children, who have higher mortality rates.

Many cases in the current outbreaks of MPX have been traced to sexual transmission, especially among men who have sex with men. The virus can also be transmitted through direct contact with infectious sores, scabs, or body fluids, and shared bedding/clothing[4]. Tarín-Vicente, E.J. *et al.*[5] argue that skin-to-skin contact has been the dominant transmission route in this outbreak, while respiratory transmission would be less important.

The incubation period of MPX is usually from 6 to 13 days and its symptoms can last from 2 to 4 weeks. The infection has two periods, a first invasion period in which the patient may suffer from fever, headache, myalgia and lymphadenopathy, being the latter a distinctive characteristic; and a second period of skin eruption which usually begins within 1–3 days after the appearance of fever and when the disease is highly transmissible. This eruption, similar to that of smallpox, mostly affects the face, palms of the hands and soles of the feet. However, it has been found to also affect oral mucous membranes and genitalia, which is why, as stated, in some countries such as Spain, sexual transmission is the main mode of propagation[6].

The characteristic rash of MPX has a very specific evolution, with a few to hundreds of lesions starting from macules (flat lesions) to papules (raised), vesicles (filled with clear fluid), pustules (filled with pus or yellowish fluid), and crusts which dry up and fall off. Once the lesions become crusts, the disease is no longer transmissible.

The rapid spreading of MPX, causing several outbreaks in a wide range of geographic zones, raised the need for surveillance and control measures to prevent it from becoming a pandemic like COVID-19. In this regard, it was proved that vaccination against smallpox in the past is protective for current monkeypox, but there are also specific vaccines for MPX. In Spain, the available vaccines are IMVANEX® and JYNNEOS®[7].

In cases of public health emergencies, surveillance of outbreaks and prediction of new infections can be very useful tools to control an epidemic too. We have seen so in the recent case of the SARS-CoV-2 pandemic. These tools were used to inform politicians and policymakers to help them decide which healthcare policies to apply. Mathematical models showed their value in this regard historically, with examples of SEIR compartmental models for Influenza[8,9] and COVID-19[10]. Even empirical models such as Gompertz have been applied to predict new daily or weekly infections of SARS-CoV-2 in different countries of Europe[11]. However, this field is yet pretty much unexplored concerning monkeypox, with articles mostly focused on transmission dynamics[12-14].

For this reason, in this work, we present a Gompertz model that describes the different outbreaks of monkeypox in countries that recorded more than 1000 cases and test possible scenarios behind the dynamics of their evolutions.

Material and method

We used the public data of new daily infections available in Our World in Data[2] to study the MPX outbreak in those countries with more than 1000 reported cases as of 9th September 2022. These countries are Brazil, Canada, France, Germany, The Netherlands, Peru, Spain, the United Kingdom and the United States of America (USA).

Using the Gompertz equation[15], we modelled the epidemiological dynamics of the virus in the aforementioned countries, from May 15th to August 31st 2022. This mathematical function was proposed by Benjamin Gompertz in the 19th Century to study the dynamics of human mortality, but has been historically applied to model tumour growth and epidemic peaks[16]. Hence, we use the Gompertz model to describe the evolution of the number of cumulative confirmed infections (N_c) of MPX. This growth model is similar to the logistic equation[17] and other growth models, but it has some distinctive features. It is described by the equation:

$$N_m = K\, e^{-\ln\left(\frac{K}{N_0}\right) e^{-a\,t}} \qquad \text{Eq. (1)}$$

Where N_m is the number of cumulative cases, K is the maximum cumulative cases that the epidemic reaches, i.e., the magnitude of the epidemic, N_0 is the number of infected people when the epidemic starts, and a is the rate of growth retardation of the epidemic curve. In comparison with a purely logistic growth, the Gompertz model corresponds to a growth dynamic

where the specific speed decreases exponentially over time. This feature is very characteristic in most epidemic evolutions. In all epidemics, eventually, there is a decrease in growth rate which appears naturally associated with the reduction in the number of people susceptible to the virus. But also, in situations where we have a large cohort of susceptible population, the growth rate can decrease due to an increase in the detection and surveillance of people that belong to risk groups. Similarly, the implementation of pharmacological (vaccination campaigns) and non-pharmacological interventions can reduce its growth rate.

We adjust this model to all countries with more than 1000 cumulated cases of monkeypox. We fit the model to observational data and find the values of the parameters K, N_0 and a that minimize the sum of squares of the distance between the prediction of the model (N_m) and the observational data (N_c). A standard solver[18] has been used for this task.

Results

As stated, the MPX epidemic has spread to many countries around the world. Figure 1 shows a timeline of the moment when 100 cases were detected in each country. The first country was the United Kingdom (UK). After that, many European countries immediately followed. A few weeks later, it had already reached other continents. The spread does not seem to follow a clear geographical pattern. This type of geographical spread highlights the highly integrated nature of international interchanges.

Figure 2 shows a satisfactory fit of the Gompertz model for the data of MPX infections in the UK, with a goodness of fit R^2 of 0.9991. With this approach, we can deduce the order of magnitude of the number of new daily cases. In the case of the UK, we can see that the maximum number of new daily cases was reached at the beginning of July.

We proceed to fit case count data from Brazil, Canada, France, Germany, The Netherlands, Peru, Spain, the United Kingdom and the United States of America (USA). These are the 9 countries reporting more than a thousand MPX infections as of 31st August 2022. The adjustments of the Gompertz model for each country are depicted in Figure 3. Besides, we also provide the adjustment for all diagnosed cases of MPX worldwide.

Remarkably, the goodness of fit in all the countries studied is very close to 1. We systematically obtain $R^2 > 0.99$. This shows that the Gompertz model correctly describes the evolution of newly confirmed cases of MPX worldwide. It, therefore, allows us to infer the number of new cases per day, or at least its order of magnitude. Furthermore, we can observe that in all the countries studied, the epidemic peak has passed. Peru and Brazil are the ones that are still close to the peak at the end of August 2022.

Figure 1. Timeline of the order in which countries have achieved 100 cumulative confirmed infections.

Figure 2. Representation of (A) red dots: cumulative cases of MPX in the United Kingdom. Dashed blue line: Gompertz model. Dashed black line: daily new infections according to the Gompertz model; and (B) Predicted cases (N_m, Gompertz) opposed to observed cases (N_c).

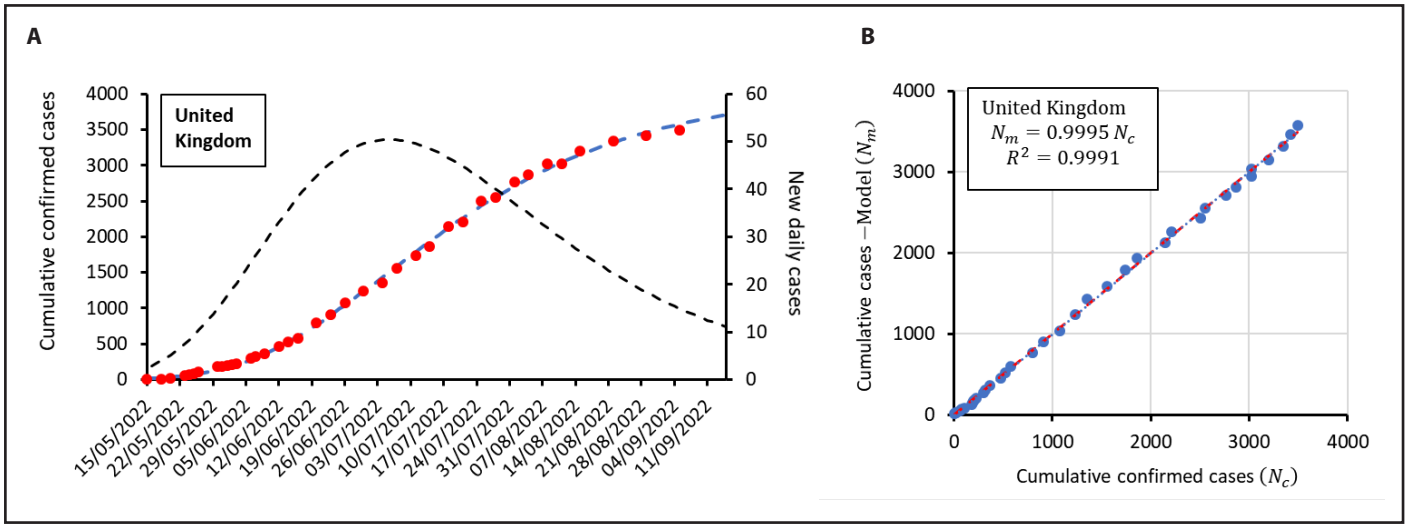


Table 1. Parameters of the Gompertz model and coefficient R^2 corresponding to countries that have reached 1000 diagnoses of MPX on 31st August 2022.

	a (days^{-1})	K (individuals)	R^2
Brazil	0.0344	9741	0.999
Canada	0.0253	1899	0.997
France	0.0296	5316	0.994
Germany	0.0444	3789	0.999
Netherlands	0.0430	1292	0.998
Peru	0.0325	3953	0.998
Spain	0.0377	7944	0.998
UK	0.0340	4038	0.999
USA	0.0311	39937	0.998

Table 1 shows the parameters obtained when adjusting the Gompertz equation to the empirical data of each country. As expected, the parameters that describe the curves in each country are different. They grow at different specific rates and the magnitudes of the epidemic reach different maximum values This raises the challenge of understanding what causes these differences.

We also focus on the growth dynamics when the case count raised from 100 to 1000 cases (Figure 4) in each of the nine countries under study. In Figure 4 we set the origin of time to the point where the case count crossed 100 cases. We note that the countries with the fastest growth were the United States and Brazil, which are also the biggest countries, but this relationship between size and speed is not generalisable. In fact, the case count is not large enough to consider that countries are homogeneous. Quite the opposite, the epidemics are concentrated in a few cities and their geographical scope is not large nor widespread among the population. The behaviour of the epidemics probably depends more on the number of cities where there have been epidemic outbreaks than on the size of the country or its total population.

To evaluate the hypothesis that the behaviour depends spatially on the number of epidemic outbreaks is at least feasible, we have represented the same evolution from 100 to 1000 cases by means of simulations using the Gompertz model (Figure 5). In the first simulation we have represented the growth from 100 to 1000 cases with the typical parameters that fit Canadian data ($a = 0.025$ days^{-1} and $K = 1900$ *individuals*). We then consider a country with two independent growths from 50 to 500 cases each, using the same parameters for the Gompertz model, and represent their joint evolution. The same has been done with 3 and more epidemic outbreaks, always satisfying that the total number of initial infections is 100 (i.e., 1 outbreak with 100 initial cases, 2 outbreaks with 50 initial cases, 3 outbreaks with 33 initial cases, 4 outbreaks with 25 initial cases, and so on). The similarity between the behaviour observed in the reported data and the behaviour of the jointed Gompertz models indicates that it is plausible that a determining factor in the parameters obtained for each country is the number of outbreaks they have had, which can be related with the number of affected cities.

Figure 3. Evolution of the data of cases registered in the 9 countries that have exceeded 1000 diagnoses of MPX by the end of August 2022 (A, B, C) and worldwide (D). The countries are ordered according to the date on which they reached 100 cases, from top to bottom and alphabetically (A), (B), (C). Red dots: cumulative confirmed cases of MPX. Dashed blue line: number of accumulated cases according to the Gompertz Model. Dashed black line: number of new cases per day according to the Gompertz Model.

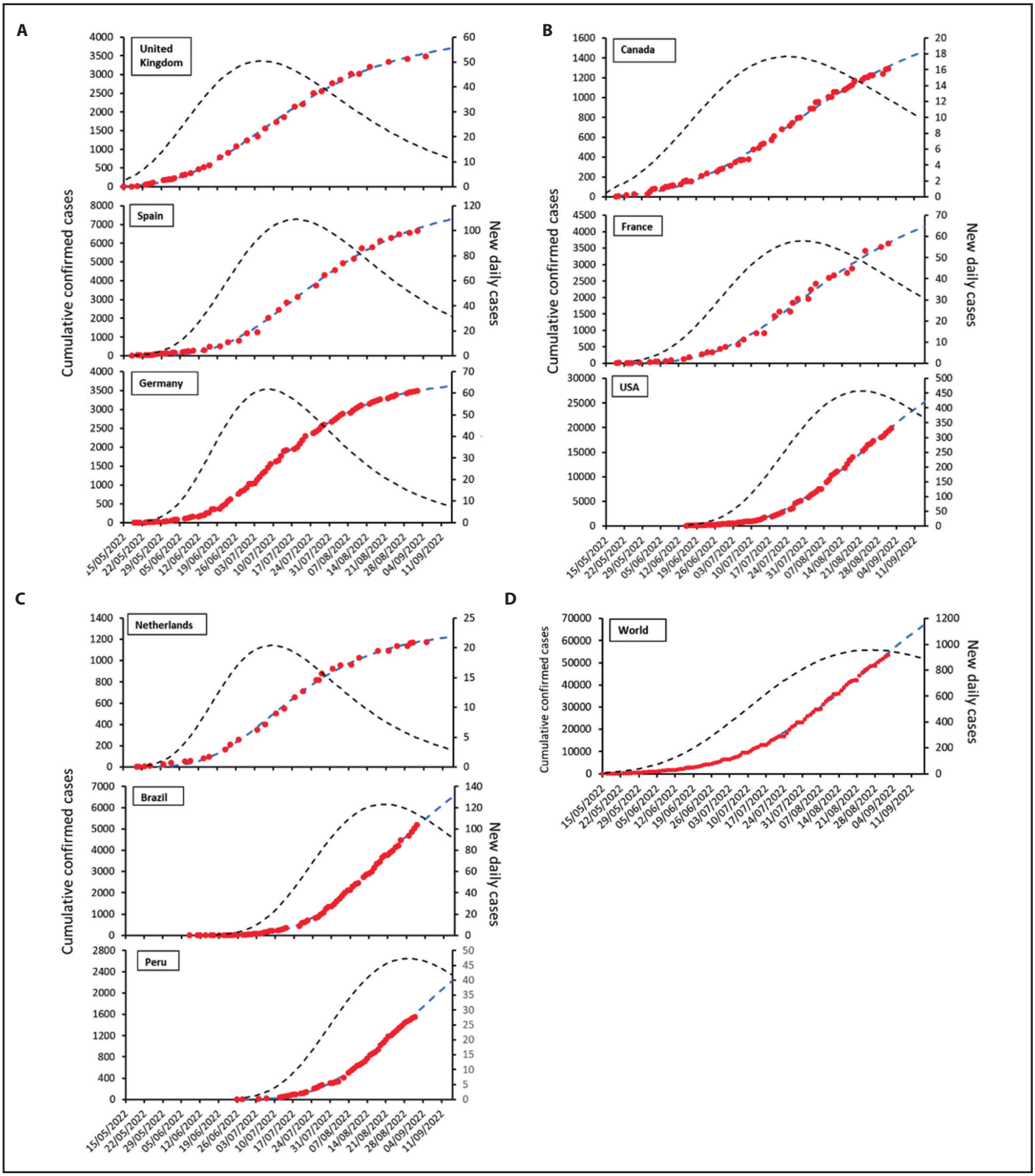


Figure 4. Evolution of the growth from 100 to 1000 cases of MPX in each of the studied countries.

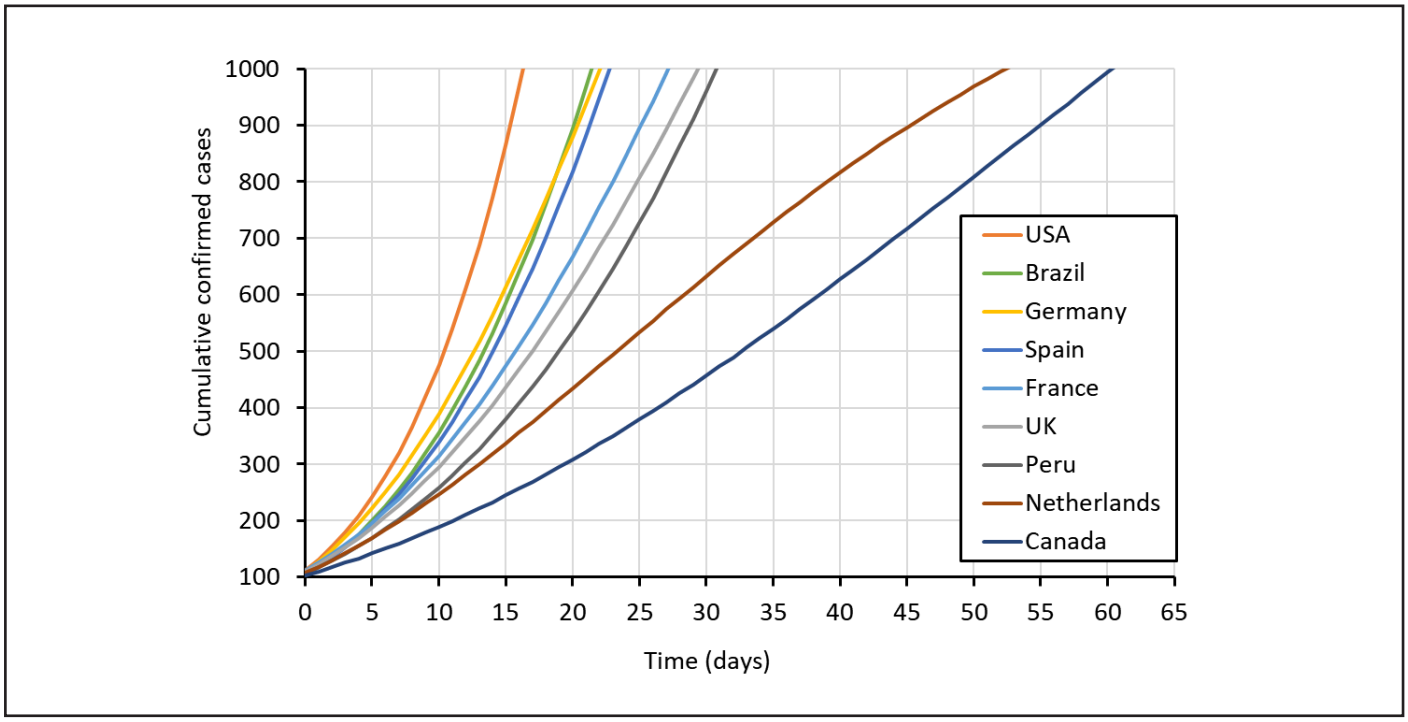
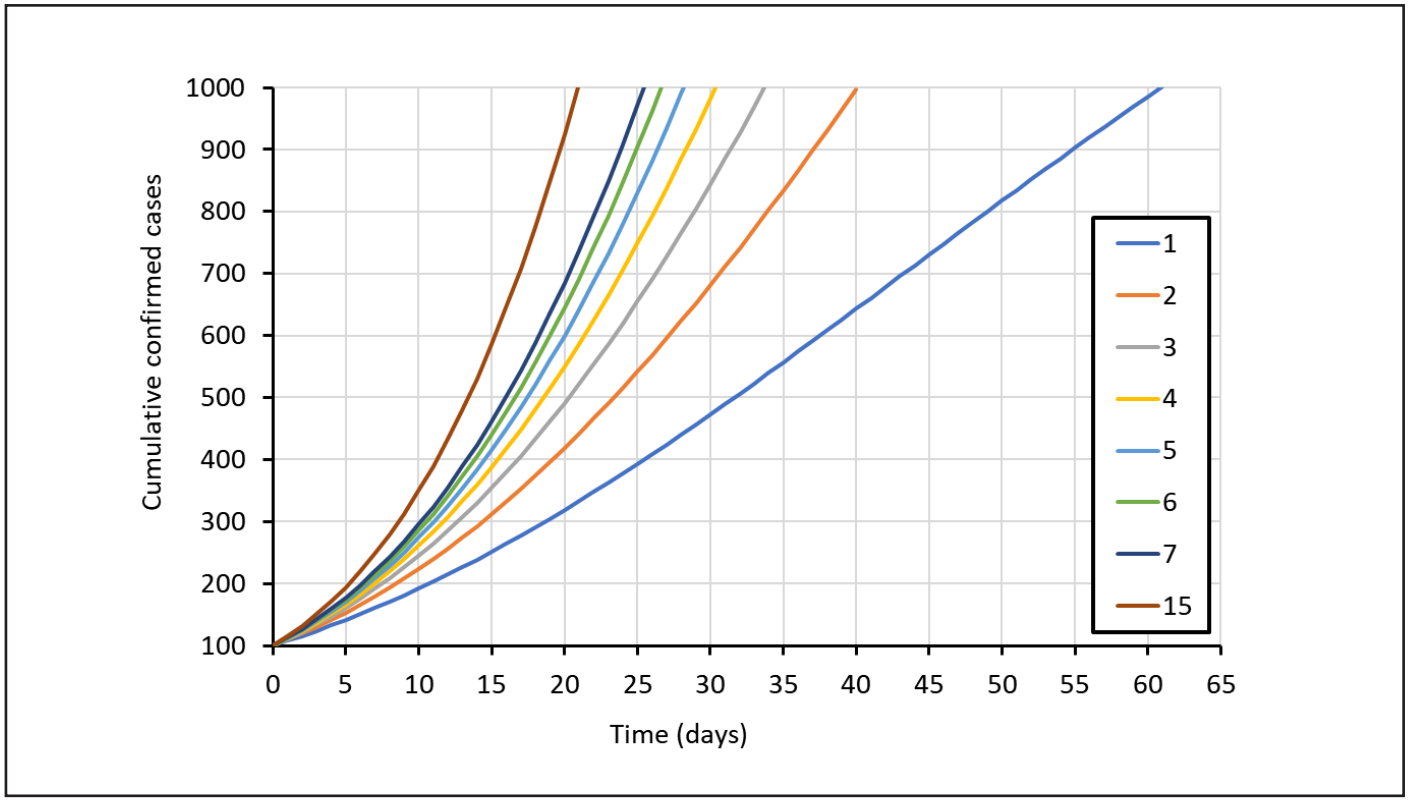


Figure 5. Simulations of the growth of infections performed with Gompertz functions for different numbers of independent outbreaks (N) in different countries. The legend in the image indicates the number of simultaneous outbreaks in the same country. We consider that all countries have the same initial number of cases n_0, so the initial number of cases of each independent outbreak is n_0/N.



Discussion

After the worst stages of COVID-19, the rapid progress of monkeypox caused concern. However, it quickly became clear that the ability of this disease to spread was not comparable to COVID-19. We have found that the evolution of the number of cumulative cases until the end of August in all countries with more than 1,000 cases is very well described by the Gompertz model. This model is characterised by an exponential decrease in the propagation velocity over time. We therefore confirm that the limited number of accessible susceptible people and the preventive measures (behaviour, vaccination) have made it possible to control the spread of the disease. It is also noted that in all cases the maximum number of cases expected in each country is not large, between 1,300 and 40,000 cases.

Given that the collection of data presents many temporal irregularities, the model allows for estimating the order of magnitude of the number of new cases per day in each country. Both the processed data and the fitted model show that, at the end of the study period, in most of the studied countries the situation was already improving or was expected to do so in the upcoming weeks. The first countries to report cases had the highest number of daily cases in early July (UK) or mid-July (Spain). Globally, the maximum number of daily cases was reached at the end of August.

Currently, one month after the period analysed, at the beginning of October, the behaviour is still the same. All the countries studied continue to improve. In Peru, the improvement is slower than what had been observed. Besides, last month two new countries have reached the threshold of 1,000 cumulative cases, Colombia and Mexico.

It is of special interest that the initial dynamics observed in the different countries are diverse. Gompertz simulations allow for a possible interpretation where these different dynamics are compatible with a different number of independent outbreaks with limited geographical scope. If this was the case, the number of independent outbreaks could be more informative than the incidence. In some cases, we could identify specific events that gave rise to these local outbreaks such as mass gatherings.

The fact that the Gompertz model correctly describes independent outbreaks is of real interest. The sum of independent Gompertz growths can help us to understand the behaviour observed in this or other infectious diseases. In the monkeypox epidemic, most countries can be interpreted as quasi-synchronous independent outbreaks. In some cases, the appearance of a new outbreak at a certain moment can explain the variations in behaviour observed, as in the case of Peru at present.

The concept of reproductive number R_t depends significantly on the duration of the incubation phase of the disease, the duration of this phase for monkeypox is between 6 and 13 days. Therefore, we cannot speak rigorously about the value of R_t due to this variability. However, calculating its value when the countries initially have reached 100 cumulative cases, using a latency phase of 7 days, the average R_t calculated is 2.4.

The analysis conducted indicates that the monkeypox epidemic, that is currently affecting a large number of countries, can be hopefully brought under control in the coming months. We must try to understand the factors that have made the spread of the epidemic possible. Our analysis suggest that relatively isolated clusters drive the dynamics. This seems important in order to control its spread i not only in countries with robust public health systems that allow to track these local episodes but also in countries with low human development index (HDI) where it may be more difficult to do so.

Bibliography

1. Monkeypox [Internet]. [cited 2022 Sep 28]. Available from: https://www.who.int/news-room/fact-sheets/detail/monkeypox
2. Edouard Mathieu, Fiona Spooner, Saloni Dattani, Hannah Ritchie and Max Roser (2022) - "Monkeypox". Published online at OurWorldInData.org. Retrieved from: 'https://ourworldindata.org/monkeypox' (Online Resource)
3. 2022 Monkeypox Outbreak Global Map | Monkeypox | Poxvirus | CDC [Internet]. [cited 2022 Sep 30]. Available from: https://www.cdc.gov/poxvirus/monkeypox/response/2022/world-map.html
4. Rizk JG, Lippi G, Henry BM, Forthal DN, Rizk Y. Prevention and Treatment of Monkeypox. *Drugs* [Internet]. 2022 Jun 1 [cited 2022 Oct 10];82(9):957–63. Available from: https://link.springer.com/article/10.1007/s40265-022-01742-y
5. Tarín-Vicente EJ, Alemany A, Agud-Dios M, Ubals M, Suñer C, Antón A, *et al*. Clinical presentation and virological assessment of confirmed human monkeypox virus cases in Spain: a prospective observational cohort study. *Lancet* [Internet]. 2022 Aug 27 [cited 2022 Oct 13];400(10353):661–9. Available from: http://www.thelancet.com/article/S0140673622014362/fulltext
6. Català A, Clavo-Escribano P, Riera-Monroig J, Martín-Ezquerra G, Fernandez-Gonzalez P, Revelles-Peñas L, *et al*. Monkeypox outbreak in Spain: clinical and epidemiological findings in a prospective cross-sectional study of 185 cases. *Br J Dermatol* [Internet]. 2022 [cited 2022 Sep 28]; Available from: https://pubmed.ncbi.nlm.nih.gov/35917191/
7. Viruela del mono | Comunidad de Madrid [Internet]. [cited 2022 Sep 28]. Available from: https://www.comunidad.madrid/servicios/salud/viruela-mono
8. Shao Q, Jia M, Tang Z. Application of an improved individual contact SEIR model in the influenza spread simulations inside terminal. *Adv Mater Res*. 2013;663:238–44.
9. Dukic V, Lopes HF, Polson NG. Tracking epidemics with Google Flu trends data and a state-space SEIR model. *J Am Stat Assoc*. 2012;107(500):1410–26.

10. Kuniya T. Prediction of the epidemic peak of coronavirus disease in Japan, 2020. *J Clin Med.* 2020;9(3):1–7.

11. Català M, Alonso S, Alvarez-Lacalle E, López D, Cardona PJ, Prats C. Empirical model for short-time prediction of COVID-19 spreading. *PLOS Comput Biol* [Internet]. 2020 Dec 9 [cited 2021 Dec 29];16(12):e1008431. Available from: https://journals.plos.org/ploscompbiol/article?id=10.1371/journal.pcbi.1008431

12. Peter OJ, Kumar S, Kumari N, Festus ·, Oguntolu A, Oshinubi K, *et al.* Transmission dynamics of Monkeypox virus: a mathematical modelling approach. *Model Earth Syst Environ* [Internet]. 2022;8:3423–34. Available from: https://doi.org/10.1007/s40808-021-01313-2

13. Lasisi NO, Akinwande NI, Oguntolu FA. Development and exploration of a mathematical model for transmission of monkey-pox disease in humans. *Math Model Eng* [Internet]. 2020 Mar 31 [cited 2022 Sep 28];6(1):23–33. Available from: https://www.extrica.com/article/21234

14. Khan A, Sabbar Y, Din A, Khan A, Sabbar Y, Din A. Stochastic modeling of the Monkeypox 2022 epidemic with cross-infection hypothesis in a highly disturbed environment. *Math Biosci Eng* 2022 1213560 [Internet]. 2022 [cited 2022 Sep 28];19(12):13560–81. Available from: http://www.aimspress.com/article/doi/10.3934/mbe.2022633

15. Gompertz B. XXIV. On the nature of the function expressive of the law of human mortality, and on a new mode of determining the value of life contingencies. In a letter to Francis Baily, Esq. FRS &c. *Philosophical transactions of the Royal Society of London.* 1825;(115):513–83.

16. Vaghi C, Rodallec A, Fanciullino R, Ciccolini J, Mochel JP, Mastri M, *et al.* Population modeling of tumor growth curves and the reduced Gompertz model improve prediction of the age of experimental tumors. *PLOS Comput Biol* [Internet]. 2020 [cited 2022 Oct 10];16(2):e1007178. Available from: https://journals.plos.org/ploscompbiol/article?id=10.1371/journal.pcbi.1007178

17. Kucharavy D, De Guio R. Application of Logistic Growth Curve. *Procedia Eng.* 2015 Jan 1;131:280–90.

18. Delgado-Aguilar M, Valverde-Som L, Cuadros-Rodríguez L. Solver, an Excel application to solve the difficulty in applying different univariate linear regression methods. Chemom. Intell. Lab. Syst. [Internet]. 2018 July 15 [cited 2022 Sep 28]; 178:39-46. Available from: https://doi.org/10.1016/j.chemolab.2018.04.018