

The impact of the distributions of the latent and infectious periods on epidemic dynamics

Paulo C. Ventura

Laboratory for Computational Epidemiology and Public Health, Department of Epidemiology and Biostatistics, Indiana University School of Public Health, Bloomington, IN, USA <https://orcid.org/0000-0001-8441-9359>

Allisandra G. Kummer

Laboratory for Computational Epidemiology and Public Health, Department of Epidemiology and Biostatistics, Indiana University School of Public Health, Bloomington, IN, USA <https://orcid.org/0000-0002-1076-3410>

Yong-Dam Jeong

Department of Applied Mathematics, Pukyong National University, Busan, Republic of Korea; interdisciplinary Biology Laboratory (iBLab), Division of Biological Science, Graduate School of Science, Nagoya University, Nagoya, Japan

Shreeya Mhade

Laboratory for Computational Epidemiology and Public Health, Department of Epidemiology and Biostatistics, Indiana University School of Public Health, Bloomington, IN, USA <https://orcid.org/0000-0002-3050-802X>

Shingo Iwami

interdisciplinary Biology Laboratory (iBLab), Division of Biological Science, Graduate School of Science, Nagoya University, Nagoya, Japan

Stefano Merler

Center for Health Emergencies, Bruno Kessler Foundation, Trento, Italy

Hongjie Yu

Shanghai Institute of Infectious Disease and Biosecurity, Department of Epidemiology, School of Public Health, Fudan University, Shanghai, China; Department of Epidemiology, School of Public Health, Fudan University, Key Laboratory of Public Health Safety, Ministry of Education, Shanghai, China

Keisuke Ejima

Lee Kong Chian School of Medicine, Nanyang Technological University, Singapore, Singapore

Maria Litvinova

Department of Epidemiology and Biostatistics, Indiana University School of Public Health, Bloomington, IN, USA <https://orcid.org/0000-0001-6393-1943>

Marco Ajelli

marco.ajelli@gmail.com

Laboratory for Computational Epidemiology and Public Health, Department of Epidemiology and Biostatistics, Indiana University School of Public Health, Bloomington, IN, USA <https://orcid.org/0000-0003-1753-4749>

Research Article

Keywords: generation time, viral dynamics, multi-scale modeling

Posted Date: September 25th, 2026

DOI: <https://doi.org/10.21203/rs.3.rs-11154983/v1>

License: © ⓘ This work is licensed under a Creative Commons Attribution 4.0 International License.
[Read Full License](#)

Additional Declarations: The authors declare potential competing interests as follows: HY has received research funding from Sanofi Pasteur, Shenzhen Sanofi Pasteur Biological Products Co., Ltd, Shanghai Roche Pharmaceutical Company, and SINOVAC Biotech Ltd. None of the research funding is related to this work. All other authors declare no competing interests.

The impact of the distributions of the latent and infectious periods on epidemic dynamics

Paulo C. Ventura¹, Allisandra G. Kummer¹, Yong-Dam Jeong^{2,3}, Shreeya Mhade¹, Shingo Iwami³, Stefano Merler⁴, Hongjie Yu^{5,6}, Keisuke Ejima⁷, Maria Litvinova⁸, Marco Ajelli^{1,*}

¹ Laboratory for Computational Epidemiology and Public Health, Department of Epidemiology and Biostatistics, Indiana University School of Public Health, Bloomington, IN, USA

² Department of Applied Mathematics, Pukyong National University, Busan, Republic of Korea

³ interdisciplinary Biology Laboratory (iBLab), Division of Biological Science, Graduate School of Science, Nagoya University, Nagoya, Japan

⁴ Center for Health Emergencies, Bruno Kessler Foundation, Trento, Italy

⁵ Shanghai Institute of Infectious Disease and Biosecurity, Department of Epidemiology, School of Public Health, Fudan University, Shanghai, China

⁶ Department of Epidemiology, School of Public Health, Fudan University, Key Laboratory of Public Health Safety, Ministry of Education, Shanghai, China

⁷ Lee Kong Chian School of Medicine, Nanyang Technological University, Singapore, Singapore

⁸ Department of Epidemiology and Biostatistics, Indiana University School of Public Health, Bloomington, IN, USA

*Corresponding Author. marco.ajelli@gmail.com

Abstract

This study quantifies the impact of the distributions of the latent and infectious periods on epidemic dynamics. Using an individual-based modeling framework that incorporates transmission in social settings such as households, schools, and workplaces, we compare two model parameterizations of the latent and infectious periods: one based on the analysis of viral-load data (VLP) and a traditional one based on geometric distributions (GP). We analyze these through the lens of a “push-pull” mechanism, where competition for susceptible individuals favors earlier transmission events while longer infectiousness increases the opportunity for a transmission event to take place. Our findings show a clear decreasing trend in the latent period, infectious period, and generation time as the reproduction number increases, with more pronounced differences under GP compared to VLP. Moreover, timing and magnitude of the epidemic peak was highly dependent on the parameterization, varying more than 50% between the models. Our findings highlight that the average value and the shapes of the latent and infectious period distributions are fundamental drivers of epidemic spread. By providing insights into how these distributions shape epidemic spread, we provide a framework to refine model projections through data-driven parameterization.

Introduction

Understanding the mechanisms driving the transmission of respiratory pathogens is critical for knowing how to prepare and respond to epidemic outbreaks¹. Two key parameters that provide insights into how quickly an epidemic spreads and how many people will be affected are the reproduction number (the average number of secondary infections from a typical infector, a measure of transmissibility) and the generation time (the time interval between a primary infection and a secondary infection)^{2,3}. The generation time is highly dependent on the transmissibility of the pathogen⁴. For example, higher transmissibility increases “competition” between infectious individuals to infect the susceptible individuals within their same social network, thus shortening the generation time^{4,5}. This effect is stronger in small clusters, such as households, where the pool of susceptible individuals is limited and unchanged.

The generation time is intrinsically connected with biological mechanisms and social behaviors^{4,5}. Biology dictates when an individual is able to transmit the pathogen^{6–8}. In the first phase after infection, a pathogen starts to replicate within a host before transmission is possible (i.e., latent period); during a second phase, the pathogen reaches a stage that allows for between-host transmission (i.e., infectious period); during the last phase, the host clears the virus, thus they are no longer infectious. During the infectious period, although biology determines the transmissibility potential of a pathogen, transmission events need to take place as hosts need contact with (susceptible) hosts for transmission to take place.

Traditionally, modelers have relied on the knowledge of the latent and infectious periods to parameterize mechanistic models of pathogen transmission (e.g., SLIR – susceptible, latent, infectious, removed models)^{9,10}. However, the distributions of the latent and infectious periods are difficult to estimate from field studies as the exact time of infection between pairs is often hard to identify¹¹. Thus, a common approach is to calibrate them to match the distribution of the generation time estimated from contact tracing and/or household studies^{12,13}. An alternative to field studies, viral load data has increasingly been used to estimate the generation time as it provides insights into when an individual starts to be infectious (latent period) and for how long (infectious period)^{14–17}.

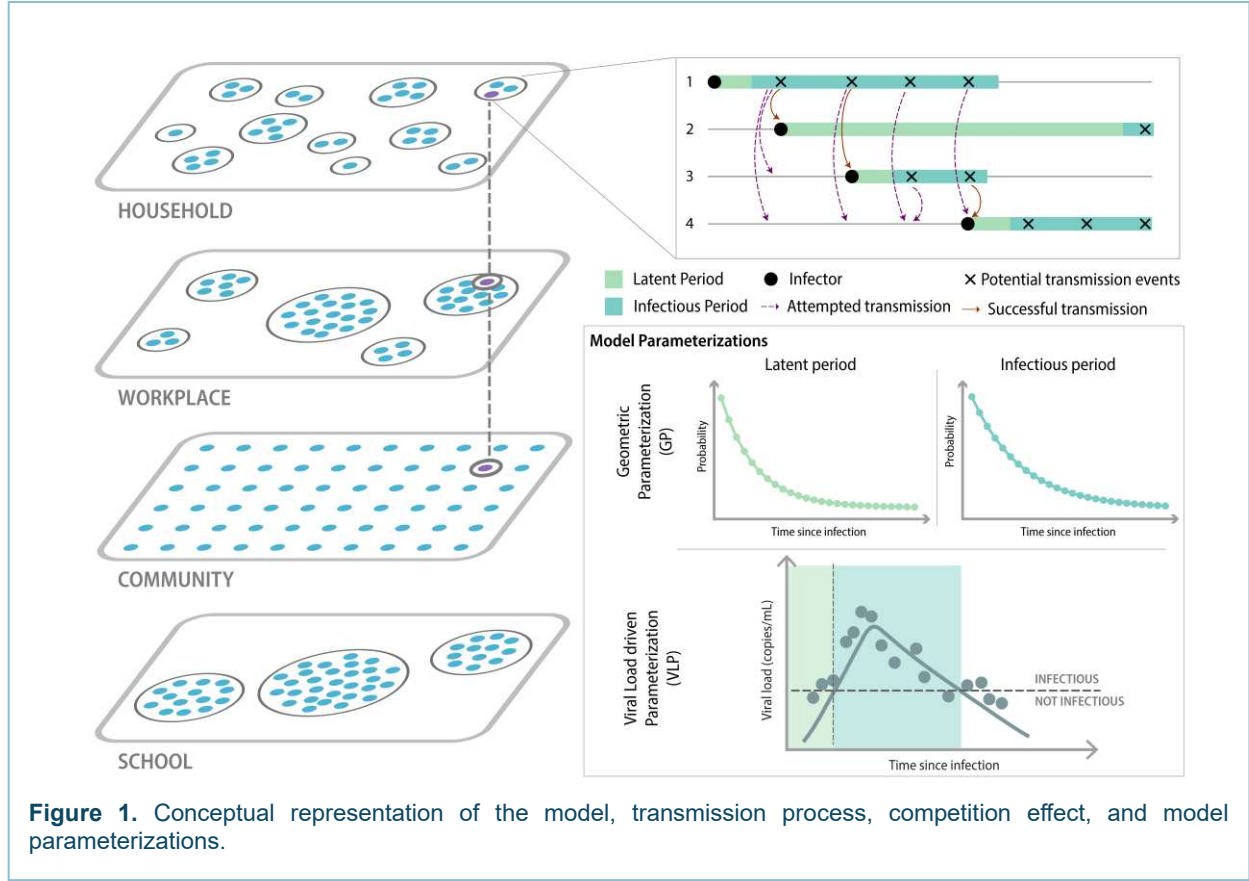
In this study, we aim to quantify the impact of the distributions of the latent and infectious periods on epidemic dynamics. To this aim, we developed an agent-based model that simulates SARS-CoV-2 transmission in the US population according to two different parameterizations of the latent and infectious periods: one as traditionally done assuming geometrically distributed periods and another one based on viral load data.

Methods

Modeling framework

In this study, we use the VIBES (Viral Dynamics Individual-Based Epidemic Simulator) framework¹⁷ to simulate SARS-CoV-2 transmission through a synthetic population of agents that interact in four settings: household, school, workplace, and the community. We used a synthetic population taken from our previous work that is statistically representative of the Indiana, USA, population¹⁸. Each agent in the synthetic population is assigned to a household and the general community while their workplace and/or school (if applicable) is based on age-dependent employment and school enrollment rates. The size of each household, school, and workplace matches those reported in the census data. More detail on the synthetic population can be found in our previous study¹⁸.

At each time step of the simulation, individuals are classified as: susceptible, latent, infectious pre-symptomatic, infectious symptomatic, infectious asymptomatic and removed. Susceptible individuals can acquire an infection from infectious individuals within their same social cluster.



The probability $p_{j \rightarrow i}(t)$ that individual j infects individual i that is in contact with j in setting $l \in \{\text{household, workplace, school, community}\}$ at time t is defined as:

$$p_{j \rightarrow i}(t) = \alpha \cdot \frac{\beta_l}{N_{j,l}} \cdot g_j \cdot \psi_j \cdot u_j(t - \tau_j) \cdot \Delta t,$$

where

- α is the overall transmission rate;
- β_l is the layer-specific relative transmission risk¹³;
- $N_{j,l}$ is the number of individuals in the given cluster of layer l where individual j belongs to; thus homogeneous mixing is assumed within each setting;
- $u_j(t - \tau_j)$ is the normalized infectiousness of individual i at step $t - \tau_j$, where τ_j represents the time of infection of individual j ;
- g_j is a gamma-distributed random variable determining the overall infectiousness of individual j , with shape 0.235 and scale 4.26 to obtain the distribution of the number of secondary infections reported in Sun et al¹⁹.
- ψ_j is the infectiousness of symptomatic individuals relative to asymptomatic individuals; namely, $\psi_j = 1$ if i is asymptomatic and $\psi_j = \psi$ if i is symptomatic.
- $\Delta t = 0.25$ days is the duration of a single time step in the simulation.

Details are included in the Supplementary Material, and a full description of the VIBES framework can be found in Ventura et al.¹⁷.

Model parameterizations

Viral load driven parameterization

For the viral load driven parameterization (VLP), we use VIBES in its original implementation¹⁷. We define infectiousness as the per contact probability of transmission where an individual is considered infectious if their viral load is above a given threshold (i.e., $10^{5.0}$ copies/ml)^{6,7} and non-infectious otherwise. Here, we considered the infectiousness and viral load to be logarithmically proportional during the infectious period and estimated the normalized infectiousness using the following equation:

$$u_i(t) = \begin{cases} A_i \cdot \log(V_i(t)), & t \in [t_{i,1}, t_{i,2}], \\ 0, & \text{otherwise,} \end{cases}$$

where

- $t_{i,1}$ is the time when the viral load for individual i crosses the infectiousness threshold and they become infectious;
- $t_{i,2}$ is the time when the viral load for individual i falls below the infectiousness threshold and they become non-infectious;
- and A_i is a normalizing factor, defined as $A_i = 1/\sum_{t=t_{i,1}}^{t_{i,2}} \log V_i(t)$.

Geometric parameterization

For the geometric parameterization (GP), the epidemiological statuses, synthetic population and symptom-development probabilities are the same as those used in the VLP parameterization. However, instead of using viral dynamics to determine infectiousness, we use a simpler algorithm that assumes memory-free (Markovian) transitions.

For each infected individual, we sampled the length of the latent period from a geometric distribution with success probability η , resulting in an average latent period of $\Delta t + 1/\eta$, where a simulation step length Δt is added due to the model constraint of preventing the individual to become infectious on the same time step of infection. Similarly, we sampled the length of the infectious period from a geometric distribution with success probability γ , resulting in an average duration of $\Delta t + 1/\gamma$. We allowed the overall infectiousness to be determined by the length of the infectious period by setting $g_i = 1$ for all individuals i .

Once the durations of the latent and infectious periods are determined, the infectiousness profile for individual i is defined as:

$$u_i(T) = \begin{cases} 1, & T \in [T_{L_i}, T_{I_i}], \\ 0, & \text{otherwise,} \end{cases}$$

where T is the time since infection, T_{L_i} is the time from infection to the start of the infectious period (i.e., latent period), and T_{I_i} is the time from infection to the end of the infectious period. Essentially, in the traditional formulation of the SLIR model, the longer an individual is infectious and the higher their infectiousness is²⁰.

Model calibration

When using VLP, the latent and infectious period, and thus the generation time, emerge naturally as a feature of the model¹⁷. For GP, we need to set the values of latent and infectious period to obtain a set generation time. To compare the two parameterizations, we set the average latent and infectious period for GP at 4 days and 3.75 days, respectively. This leads to a realized generation time of 5.7 days for $R = 2.5$, which exactly matches the value of the realized generation time emerging from VLP for the same reproduction number.

Time-to-event metrics

The intrinsic latent period, infectious period, and generation time refer to the theoretical time interval that would be observed in an infinitely large, susceptible population^{4,21,22}. The realized periods refer to those that are observed while an epidemic unfolds and are thus affected by factors such as depletion of susceptible individuals in different social settings and pathogen transmissibility. VIBES tracks the entire transmission chain of infection, allowing us to estimate realized time-to-event metrics directly. Specifically, for any infector-infectee pair ($B|A$, where B is the infectee and A is the infector), we estimate the realized latent period, $T_{Lr}(B|A)$, the realized infectious period, $T_{Ir}(B|A)$, and the realized generation time, $T_{Gr}(B|A)$, as:

- Realized latent period: $T_{Lr}(B|A) = t_{A,1} - t_{A,0}$
- Realized infectious period: $T_{Ir}(B|A) = t_{B,0} - t_{A,1}$
- Realized generation time: $T_{Gr}(B|A) = T_{Lr}(B|A) + T_{Ir}(B|A) = t_{B,0} - t_{A,0}$

Where,

- $t_{i,0}$ is the time of infection of individual i ;
- $t_{i,1}$ is the time when individual i becomes infectious.

We compute mean time-to-event metrics by averaging across all infector–infectee pairs observed during a simulation. In addition to the three time-to-event metrics, we estimate the: (i) infection attack rate (i.e., the proportion of the population that has been infected by the end of an epidemic); (ii) peak day; and (iii) peak incidence of new daily infections. To compare the results of these metrics between the two parameterizations, we estimate the mean reduction with respect to VLP as:

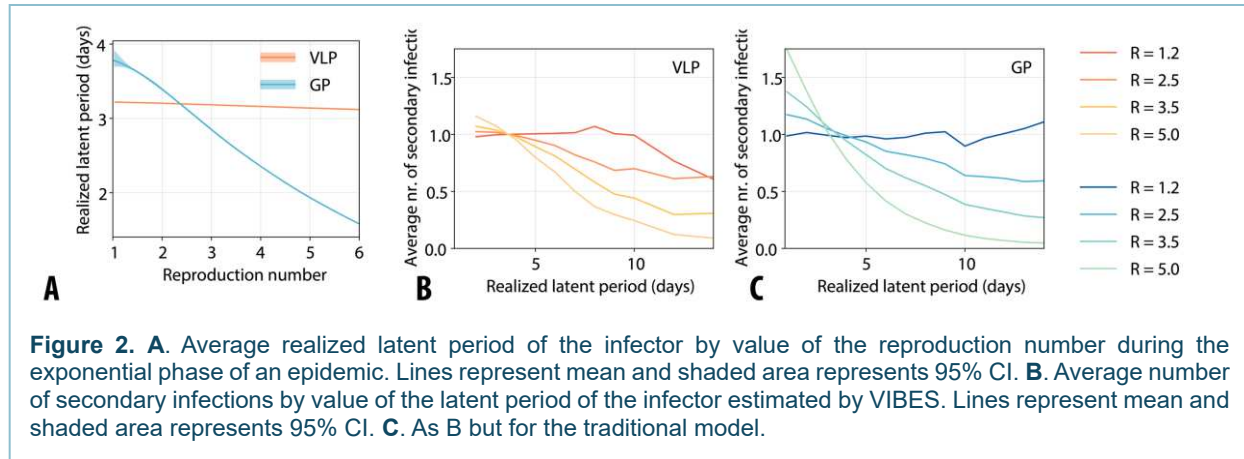
$$Y = \frac{X_{GP} - X_{VLP}}{X_{VLP}} \cdot 100$$

where Y is the percent reduction of the estimated metric (i.e., infection attack rate, peak day, and peak incidence of infection) between the two parameterizations relative to VLP, X_{GP} is the estimate of the metric using GP, and X_{VLP} is the estimate of the metric using VLP.

Results

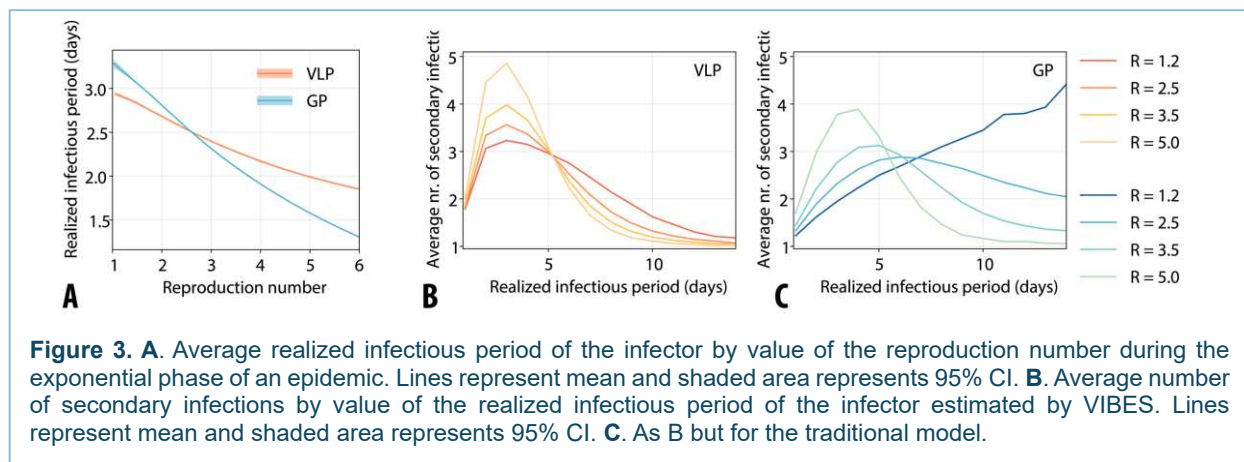
Realized latent period

The intrinsic latent period is entirely driven by biological mechanisms. Instead, the realized latent period, depends on the chance for infectors to infect individuals, which indeed depend on their social contacts and the co-presence of other infectors and susceptible individuals. Potential transmission events that take place early are more likely to be successful (as the pool of susceptible individuals is larger). This mechanism has the effect of shortening the realized latent period. In fact, for both model parameterizations (i.e., VLP and GP), we found as the competition effect increases with R , the realized latent period shortens (Fig. 2A). In fact, if we fix R , we observe that the number of secondary infections is higher for infectors with shorter latent periods (Fig. 2 B,C). However, the decrease in the length of the realized latent period is much more marked for GP than VLP: from 3.73 (95%CI: 3.68-3.81) days at $R = 1.2$ to 1.58 (95%CI: 1.53-1.63) days at $R = 6$ for GP vs. from 3.22 (95%CI: 3.21-3.23) days at $R = 1.2$ to 3.12 (95%CI: 3.11-3.13) days at $R = 6$ for VLP (Fig. 2A). For low values of R (e.g., $R = 1.2$), the competition effect is mild, and infectors infect about the same number of susceptible individuals regardless of their latent period for both model parameterizations (Fig. 2 B,C).



Realized infectious period

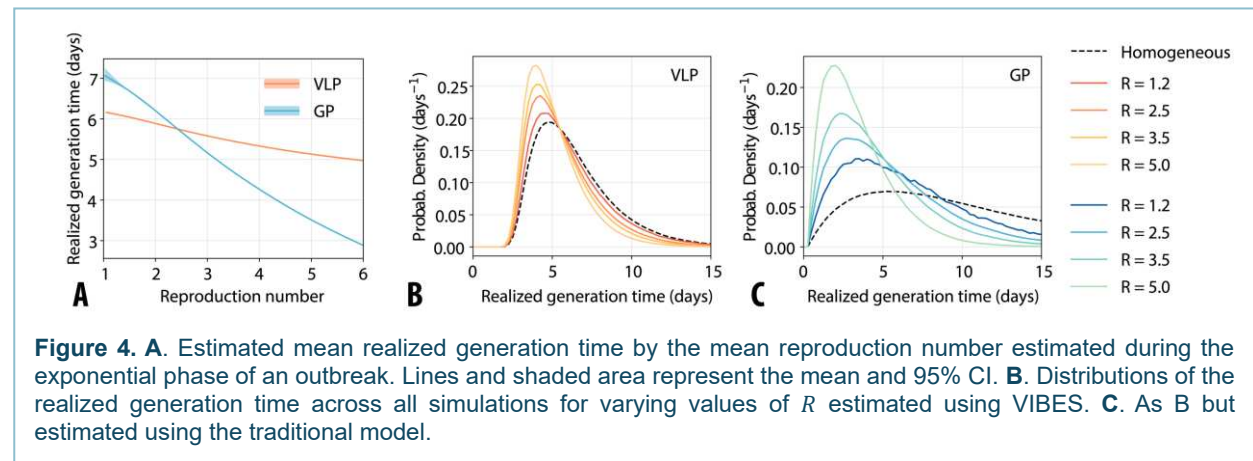
The realized infectious period is driven by both biological and social factors. Similar to the latent period, competition for susceptible individuals has the effect of shortening the realized infectious period for both model parameterizations (Fig. 3A). From a quantitative perspective, the decrease in the length of the realized infectious period is larger for GP than VLP: from 3.20 (95%CI: 3.16-3.24) days at $R = 1.2$ to 1.30 (95%CI: 1.27-1.34) days at $R = 6$ for GP vs. from 2.91 (95%CI: 2.88-2.93) days at $R = 1.2$ to 1.85 (95%CI: 1.81-1.89) days at $R = 6$ for VLP (Fig. 3A). Such a difference is not as marked as the one we observed for the latent period. This is because, for the realized infectious period, there is an interplay between the shortening effect (potential transmission events that take place early are more likely to be successful) and the fact that the longer the infectious period of an infector, the more chances to infect. Therefore, the first mechanism pulls towards a shorter realized infectious period, while the second mechanism pulls towards a longer one. When we look at the average number of secondary infections for varying lengths of the realized infectious period, we can see this push-pull effect (Fig. 3B,C). For VLP, the result is a mix of these two mechanisms for any R (Fig. 3B); although, secondary infections were consistently highest for individuals with an infectious period of 3 days. For GP, we see a mix of the two effects but only for relatively high values of R (e.g., $R = 2.5$ or higher), while for low values (e.g., $R = 1.2$), the mechanism (ii) appears to dominate (Fig. 3C).



Realized generation time

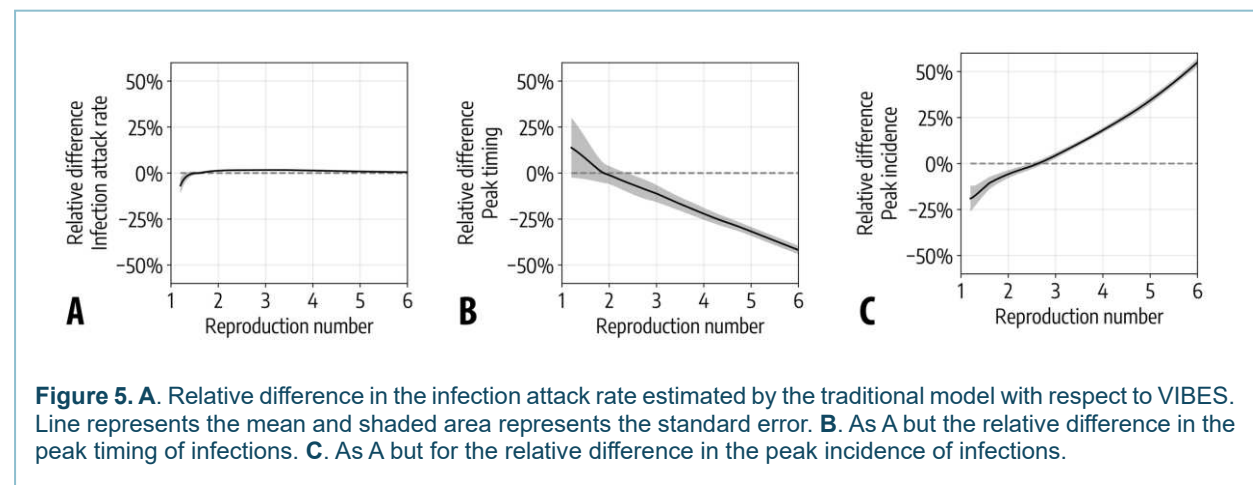
The realized generation time is a convolution of the realized latent and realized infectious periods. Therefore, it follows the same general decreasing trend as transmissibility increases (Fig. 4A). Note that the curves for the two model parameterizations intersect at $R = 2.5$ because the generation times were fixed to be identical at this value as part of the calibration process. Similar to the previous metrics, the decline of the realized generation time is more marked for GP than VLP: from 6.93 (95%CI: 6.86-7.05) days at $R = 1.2$ to 2.88 (95%CI: 2.80-2.96) days at $R = 6$ for GP vs. from 6.12 (95%CI: 6.10-6.16) days at $R = 1.2$ to 4.97 (95%CI: 4.92-5.02) days at $R = 6$ for VLP.

Regarding the distribution of the generation time (rather than its average value), for the VLP, we observe an initial phase where infectors are not able to transmit as a minimum length of the latent period appears of about 2 days to be intrinsic to the data used to calibrate the model (Fig. 4B). On the other hand, for GP, the distribution of the generation time follows a gamma distribution (Fig. 4C), allowing for shorter latent periods where shorter realized latent periods are more likely to be observed (Fig. 2C).



Impact on epidemic spread

Mathematical epidemiology theory shows that the infection attack rate depends on the reproduction number, while it does not depend on the generation time²⁰. Our results confirm that for both model parameterizations, once R is fixed, the infection attack rate is the same (Fig. 5A). In terms of peak timing, however, we estimate remarkable differences between the two model



parameterizations (Fig. 5B). This difference spans from the epidemic spreading 13% (SE: 16%) slower for GP at $R = 1.2$ to 42% (SE: 2%) faster for GP at $R = 6$ as compared to VLP (Fig. 5B). Even larger differences are estimated for the peak daily incidence, which span from the epidemic spreading 19% (SE: 7%) lower for GP at $R = 1.2$ to 55% (SE: 2%) higher for GP at $R = 6$ as compared to VLP (Fig. 5C).

Discussion

In this study, we quantified the impact of the infectiousness profile distribution, which in turn determines the shape of the latent and infectious period distributions, on epidemic dynamics. Our findings highlight that the shape of these distributions is a fundamental driver of epidemic spread. The realized metrics estimated in this work (i.e., latent period, infectious period, and generation time) are driven by a distinct “push and pull” effect between the biological potential of the pathogen and the social structure of the population. While biology dictates the window during which an individual is capable of transmission, social factors, specifically the availability of susceptible contacts, determine when transmission actually occurs. As transmissibility increases, competition for susceptible individuals forces transmission events to occur earlier in the infector's window, especially in small clusters, such as households. Consequently, an individual may remain biologically infectious for an extended period, but the diminishing pool of susceptible contacts effectively “pulls” the realized generation time toward the time of infection. At the same time, a longer duration of infectiousness would provide the infector more chances to infect susceptible individuals, thus “pushing” the realized generation time towards longer durations.

While this competition effect is a fundamental mechanism present in both parameterizations, we found that its magnitude varies significantly depending on the shape of the latent and infectious period distributions. From a quantitative perspective, the traditional geometric parameterization (GP) shows a much more pronounced reduction in realized latent period, infectious period, and generation time as the reproduction number increases compared to the viral-load-driven parameterization (VLP). The sharp decline of the generation time for the GP parameterization appears to be larger than the evidence reported in empirical epidemiological studies. On the other hand, the VLP parameterization, which captures a biological lower bound for the latent period, yields results that are more consistent with these studies²³. This suggests that when using traditional geometric distributions to define disease states, the latent and infectious periods may need to be recalibrated for different values of R to ensure the realized generation time remains consistent with the observed data. This is underscored by the fact that at the specific reproduction number ($R = 2.5$) where we set the realized generation time to match between the two model parameterizations, the choice of parameterization had only a moderate effect on epidemic dynamics, confirming that the proposed recalibration effectively bridges the gap between these two approaches.

Our results confirm a key result of mathematical epidemiology: the final infection attack rate is invariant to the latent and infectious periods once R is fixed. However, we estimated remarkable differences in peak timing and peak daily incidence between the two parameterizations. Depending on the value of the reproduction number, the choice of the distributions can lead to projections of an epidemic spreading remarkably faster or slower, with peak incidences that vary by more than 50% between models. These differences have profound implications for public health preparedness and response, as the epidemic timing dictates the timeline of deployment of interventions, while the peak incidence is a major determinant of the stress for the healthcare system.

This study is subject to several limitations. First, the viral load data used for the VLP parameterization serves as a proxy for infectiousness rather than a direct measurement. Consequently, the estimated distributions derived from this approach should not be interpreted as

“ground truth”. However, the distributions of key time-to-event metrics, including the generation time, serial interval, and incubation period, resulting from the VLP parameterization were validated in our previous work¹⁷, suggesting that this approach provides good approximations of the real distributions. Second, our analysis focuses on the ancestral lineage of SARS-CoV-2 and uses the population structure of Indiana, USA, as a primary case study. While our specific quantitative estimates may not be directly generalizable to other respiratory pathogens or geographical settings, the fundamental effects identified here, such as the competition for susceptible individuals, the “push-pull” dynamics between biology and social clusters, and the dependence of the epidemic spread on the distribution of the generation time, represent general epidemiological phenomena. Third, the model was neither calibrated nor validated against empirical incidence data. The transmission dynamics during the early phase of the COVID-19 pandemic, the period during which the viral load data used here was collected, were significantly shaped by the deployment of non-pharmaceutical interventions. Comparing model outcomes to observed incidence under these conditions would be challenging. However, a retrospective explanation of the dynamics of a specific outbreak is beyond the scope of this work.

It is important to emphasize that the aim of this work is not to identify the best method for parameterizing the distributions of the latent and infectious periods, but rather to quantify how different parameterization choices fundamentally impact epidemic dynamics. To this end, we compared a viral-load-driven parameterization (VLP) with a commonly adopted approach of using geometric distributions (GP). While these two methods served as our primary focus, other approaches could be utilized, ranging from the implementation of different mathematical distributions (e.g., gamma distributions) to the use of empirical estimates obtained directly from the primary analysis of epidemiological field data (e.g., from contact tracing or household studies). However, it must be stressed that just as viral-load-informed methods are subject to limitations, epidemiological field studies also possess inherent limitations such as recall bias, difficulty in identifying the exact date of infection between pairs, limited sample size, and the fact that such studies often consider only specific settings (e.g., households)²⁴.

In conclusion, this work shows that the mathematical distributions of latent and infectious periods are major drivers of epidemic dynamics. By providing insights into how these distributions shape epidemic spread, we provide a framework to refine model projections through data-driven parameterization or parameter recalibration.

Funding

Sh.M., M.L., and M.A. authors acknowledge support from the CDC-RFA-FT-23-0069 cooperative agreement from the CDC's Center for Forecasting and Outbreak Analytics. The findings and conclusions in this study are those of the authors and do not necessarily represent the official position of the funding agencies. Any use of trade, firm, or product names is for descriptive purposes only and does not imply endorsement by the U.S. Government. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Competing interests

HY has received research funding from Sanofi Pasteur, Shenzhen Sanofi Pasteur Biological Products Co., Ltd, Shanghai Roche Pharmaceutical Company, and SINOVAC Biotech Ltd. None of the research funding is related to this work. All other authors declare no competing interests.

Code and data availability

The data and code used in this study is available on GitHub at <https://github.com/paulocv/vibes-model-project>.

References

1. World Health Organization. *Managing Epidemics: Key Facts about Major Deadly Diseases*. (World Health Organization, 2023).
2. Griffin, J. T., Garske, T., Ghani, A. C. & Clarke, P. S. Joint estimation of the basic reproduction number and generation time parameters for infectious disease outbreaks. *Biostatistics* **12**, 303–312 (2011).
3. Wallinga, J. & Lipsitch, M. How generation intervals shape the relationship between growth rates and reproductive numbers. *Proc. R. Soc. B Biol. Sci.* **274**, 599–604 (2007).
4. Liu, Q.-H. *et al.* Measurability of the epidemic reproduction number in data-driven contact networks. *Proc. Natl. Acad. Sci.* **115**, 12680–12685 (2018).
5. Park, S. W. *et al.* Inferring the differences in incubation-period and generation-interval distributions of the Delta and Omicron variants of SARS-CoV-2. *Proc. Natl. Acad. Sci.* **120**, e2221887120 (2023).
6. Wölfel, R. *et al.* Virological assessment of hospitalized patients with COVID-2019. *Nature* **581**, 465–469 (2020).
7. van Kampen, J. J. A. *et al.* Duration and key determinants of infectious virus shedding in hospitalized patients with coronavirus disease-2019 (COVID-19). *Nat. Commun.* **12**, 267 (2021).
8. Jeong, Y. D. *et al.* Designing isolation guidelines for COVID-19 patients with rapid antigen tests. *Nat. Commun.* **13**, 4910 (2022).
9. Miller, J. C., Davoudi, B., Meza, R., Slim, A. C. & Pourbohloul, B. Epidemics with general generation interval distributions. *J. Theor. Biol.* **262**, 107–115 (2010).
10. Svensson, Å. A note on generation times in epidemic models. *Math. Biosci.* **208**, 300–311 (2007).
11. Britton, T. & Scalia Tomba, G. Estimation in emerging epidemics: biases and remedies. *J. R. Soc. Interface* **16**, 20180670 (2019).
12. Aleta, A. *et al.* Quantifying the importance and location of SARS-CoV-2 transmission events in large metropolitan areas. *Proc. Natl. Acad. Sci.* **119**, e2112182119 (2022).
13. Liu, Q.-H. *et al.* Model-based evaluation of alternative reactive class closure strategies against COVID-19. *Nat. Commun.* **13**, 322 (2022).
14. Goyal, A., Reeves, D. B., Cardozo-Ojeda, E. F., Schiffer, J. T. & Mayer, B. T. Viral load and contact heterogeneity predict SARS-CoV-2 transmission and super-spreading events. *eLife* **10**, e63537 (2021).
15. Marc, A. *et al.* Quantifying the relationship between SARS-CoV-2 viral load and infectiousness. *eLife* **10**, e69302 (2021).
16. Ferguson, N. M. *et al.* Strategies for mitigating an influenza pandemic. *Nature* **442**, 448–452 (2006).
17. Ventura, P. C. *et al.* VIBES: A multiscale modeling approach integrating within-host and between-hosts dynamics in epidemics. *Proc. Natl. Acad. Sci.* **123**, e2523055123 (2026).
18. Mistry, D. *et al.* Inferring high-resolution human mixing patterns for disease modeling. *Nat. Commun.* **12**, 323 (2021).

19. Sun, K. *et al.* Transmission heterogeneities, kinetics, and controllability of SARS-CoV-2. *Science* **371**, eabe2424 (2021).
20. Diekmann, O. & Heesterbeek, J. A. P. *Mathematical Epidemiology of Infectious Diseases: Model Building, Analysis and Interpretation*. vol. 5 (John Wiley & Sons, 2000).
21. Champredon, D. & Dushoff, J. Intrinsic and realized generation intervals in infectious-disease transmission. *Proc. R. Soc. B Biol. Sci.* **282**, 20152026 (2015).
22. Manica, M. *et al.* Intrinsic generation time of the SARS-CoV-2 Omicron variant: An observational study of household transmission. *Lancet Reg. Health - Eur.* **19**, 100446 (2022).
23. Xu, X. *et al.* Assessing changes in incubation period, serial interval, and generation time of SARS-CoV-2 variants of concern: a systematic review and meta-analysis. *BMC Med.* **21**, 374 (2023).
24. Scalia Tomba, G., Svensson, Å., Asikainen, T. & Giesecke, J. Some model based considerations on observing generation times for communicable diseases. *Math. Biosci.* **223**, 24–31 (2010).

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [suppmat.pdf](#)