Available online at www.sciencedirect.com

ScienceDirect

Physics of Life Reviews ••• (••••) •••–•••

PHYSICS of LIFE reviews

www.elsevier.com/locate/plrev

Reply to comment

Early sub-exponential epidemic growth: Simple models, nonlinear incidence rates, and additional mechanisms
Reply to comments on "Mathematical models to characterize early epidemic growth: A review"

Gerardo Chowell [a,b,*], Lisa Sattenspiel [c], Shweta Bansal [d,b], Cécile Viboud [b]

[a] *School of Public Health, Georgia State University, Atlanta, GA, USA*
[b] *Division of International Epidemiology and Population Studies, Fogarty International Center, National Institutes of Health, Bethesda, MD, USA*
[c] *Department of Anthropology, University of Missouri, Columbia, MO, USA*
[d] *Department of Biology, Georgetown University, Washington DC, USA*

Received 29 August 2016; accepted 30 August 2016

Communicated by J. Fontanari

We would like to thank all of the commentators for their insightful and positive reactions to our review paper [1]. Their comments touch on both theoretical and applied aspects of sub-exponential growth dynamics and the mechanisms that generate them, and have greatly enhanced and broadened the discussion. Here we aim to further discuss key points raised by Brauer [2], Danon and Brooks-Pollock [3], Allen [4], Merler [5], Champredon and Earn [6], and House [7].

Brauer [2] underscores the flexibility of the generalized-growth model to capture the early transmission dynamics of infectious disease outbreaks, particularly in situations where retrospective investigations are not sufficient to elucidate the underlying mechanisms. We agree with this assessment. In real epidemic settings, gaining a complete understanding of the actual mechanisms that shape early epidemic growth could be particularly challenging in the absence of additional data to characterize contact patterns, population behavior changes, and transmission pathways (e.g., hospital vs. community transmission). This is further complicated when the epidemiology or transmission mechanisms of the infectious disease in question have not been fully elucidated. Related to this point, Danon and Brooks-Pollock [3] argue for the application of data science approaches to further our understanding of the processes that shape epidemic outbreaks, which, in turn could lead to improved predictive models. We could not agree more with this suggestion. Mathematical epidemiology has made important strides in recent years precisely because new and better data sources are becoming available. These data sources include electronic records containing information about the health of individuals such as primary care visits, hospitalizations, and deaths. In addition,

DOI of original article: http://dx.doi.org/10.1016/j.plrev.2016.07.005.
DOI of comments: http://dx.doi.org/10.1016/j.plrev.2016.08.004, http://dx.doi.org/10.1016/j.plrev.2016.08.006, http://dx.doi.org/10.1016/j.plrev.2016.08.012, http://dx.doi.org/10.1016/j.plrev.2016.08.007, http://dx.doi.org/10.1016/j.plrev.2016.08.011, http://dx.doi.org/10.1016/j.plrev.2016.08.005.

* Corresponding author at: School of Public Health, Georgia State University, Atlanta, GA, USA.
E-mail address: gchowell@gsu.edu (G. Chowell).

http://dx.doi.org/10.1016/j.plrev.2016.08.016

non-traditional data sources such as digital data streams (e.g., social media, internet news reports) can contribute both to the early identification of emerging pathogen outbreaks [8] and to early estimates of key transmission parameters [8,9].

Allen [4] expanded on our review of SIR models incorporating inhomogeneous mixing through power-law incidence rates. In particular, Allen underscores the earlier application of these models to measles [10,11]. We appreciate this comment as it further highlights the early application of these relatively simple models. It is also worth pointing out that these simple models have found relatively few applications, compared to classical SIR models assuming linear incidence rates. A likely issue with nonlinear incidence SIR models is that of parameter identifiability: multiple combinations of parameter values could yield similar epidemic curves, which complicates the interpretation of power-law scaling parameters. As a technical point, the scaling exponents affecting the incidence rate of SIR models have not been mapped to a particular polynomial degree when the scaling exponent is below 1.0. It is only when the scaling exponent acts on the total number of cases (rather than disease prevalence) that the generalized growth model yields a closed form solution. In this special case, there is direct mapping between the deceleration of growth parameter to specific polynomial degrees representing the growth of case incidence.

Merler [5] highlights the need to better understand the factors behind early sub-exponential growth dynamics. He suggests that the variation in epidemic growth profiles across outbreaks could be related to the epidemiological characteristics of infectious diseases. For instance, some infectious pathogens are airborne but generate relatively low case fatality rates (e.g., influenza) while others are only transmitted via close contacts but could generate high case fatality rates in the absence of early treatment (e.g., Ebola). These epidemiological features could influence individual behavior, including the number and type of contacts made by individuals for a perceived level of risk [12]. Another important factor here is the role of cultural practices on individual behavior.

Champredon and Earn [6] share Merler's interest in the potential mechanisms behind sub-exponential growth dynamics. Of particular note is their discussion on the role of demographic stochasticity and changes in case reporting, which may artificially generate sub-exponential growth dynamics in observed case data. We completely agree – these are important factors that should be given full consideration when characterizing and forecasting infectious disease outbreaks using early outbreak data. Indeed, stochasticity during the early epidemic phase could not only lead to early outbreak extinction (e.g., the index case does not generate secondary cases), but also generate variation in the early epidemic growth profile. We believe the generalized-growth model is particularly suited to capture this variation. Future work should examine the impact of stochasticity on shaping early epidemic growth and the extent to which the generalized-growth model is able to characterize this variation in different transmission contexts. Champredon and Earn also provide comments based on their own application of the generalized-growth model (GGM) to the epidemic curve of the spring wave of the 2009 A/H1N1 influenza epidemic in Mexico [13], and find evidence of "hyper-exponential growth" ($p > 1$). This is surprising but may be attributed to an abrupt shift in transmission regimes in this particular epidemic: an initial phase characterized by the occurrence of sporadic cases for least 10 disease generations, followed by a sustained epidemic growth period for several disease generations before the epidemic peaks. This shift in transmission patterns from low incidence to sustained epidemic growth could explain their estimates of p above 1.0. It is likely that the low incidence pattern covering the first 33 days of the epidemic curve could have been shaped by characteristics of the surveillance system and multiple importations of the disease possibly from a reservoir (Fig. 1). We also note that our application of the GGM has focused on the analysis of the ascending epidemic phase comprising 3–5 generations of the disease. For influenza, this observation window comprises 9–15 epidemic days if one considers a mean generation interval of 3 days. Accordingly, our fitting of the GGM to the sustained period of case growth of the epidemic which starts at day 33 of the time series yields $r = 0.96$ (95%CI: 0.73, 1.2) and $p = 0.81$ (95%CI: 0.81, 0.88), which is consistent with modest sub-exponential growth (Fig. 1). Whether hyper-exponential growth dynamics can be found in nature is an interesting area for future research.

Finally, House [7] offers some interesting theoretical arguments which could provide a general framework to characterize early epidemic growth patterns. We look forward to further developments of this framework and its application to empirical data. Perhaps a next step could involve the simulation of early epidemic growth patterns using the generalized growth model. These simulations could in turn be used for testing the ability of this and other frameworks to characterize differences in epidemic growth patterns, ranging from sub-exponential to exponential epidemic growth.

Please cite this article in press as: Chowell G, et al. Early sub-exponential epidemic growth: Simple models, nonlinear incidence rates, and additional mechanisms. Phys Life Rev (2016), http://dx.doi.org/10.1016/j.plrev.2016.08.016