**Pandemics in the digital age: Caution coupling explains Covid-19 curves simply**

John S. McCaskill1,2 and Norman H. Packard1,2

1. European Centre for Living Technology, Venice, Italy

2. Chemelion Inc., San Francisco, USA

The understanding of epidemics through modelling is gained both through highly simplified population models such as the early SIR model [1, 2] (distinguishing Susceptible, Infective, and Recovered individuals) and its extensions: both to more stage-differentiated models like SEIR [3-6] and SIDARTHE [7, 8] and age-differentiated social mixing models [9, 10], and to include stochastic effects [11, 12] and spatial [13-15] or other network structure [16-18]. Cause and effect can also be analysed in agent models [19, 20] making use of detailed population data (big data) [21, 22]. However, certain key features of the Covid-19 pandemic data affecting us all have not been explained simply. In particular, the remarkably common extended linear phase in countries’ cumulative confirmed cases is poorly understood. While small world network effects may account for non-exponential early growth [16], they do not explain the linear saturation effect well below levels required for “herd immunity”. In this letter, we show that central features of this societal response complexity can indeed be understood using the S(E)IR(D) family of models by means of a single additional deterministic coupling, one reflecting societal introspection: *caution*. As society reacts to and endeavours to contain the strong effects of the Covid-19 virus on health, social well-being and the economy, it may appear that explanation requires every aspect of society to be modelled in detail: from the use of public transport, religious practises and child play patterns to political decision making, the media and legislature[23]. However, the prolonged near linear response both in the cumulative number of Corona cases as well as those in individual populations can be understood as a generic human response to the epidemic in the age of information. This insight may in turn help us to focus societal measures and responses more effectively.

In March 2020, a study in Oxford [24] suggested, using an SIR model, that a much larger portion of society may be infected than normally inferred from the testing data, which was parsimoniously biased to symptom carriers. This was in-line with standard epidemiological modelling that relates the epidemic proliferation peak and its subsequent decline to the advent of a significant fraction of the population becoming immune to the disease. However, subsequent testing data has shown that the fraction of individuals infected, while significantly higher than that measured in the first wave of infection, is in all countries much lower than the level of infection required for herd immunity [??]. The proposed caution models will also account for the existence of these lower first peaks in daily infection rates quantitatively.

The data for different countries, shown in Figure 1, display dynamics strikingly different from standard epidemiological models. The cumulative case count curves shown in Figs 1A and 1C have long linear regions (shown with a simple three-segment piecewise linear fit superimposed on the data), which correspond to broadened peaks in the daily data shown in Figs 1B and 1C, uncharacteristic of the classical epidemiological models. The typical response is an early saturation peak followed by an extended period with nearly constant rates of daily infection, at varying levels depending on the individual countries, prior to a second wave of infection. In the USA, for example, the constant infection rate phase persisted without much attenuation from the initial peak level for 2.5 months from April to mid-June 2020. This high constant infection rate phase is also seen in the whole world data (not shown) and other large countries like Brazil and Russia. In many other countries, such as Italy, Spain, and Germany in Europe, but also Japan, South Korea, and Australia, the extended constant phase is also seen but at a significantly lower level than the initial peak. We shall see how the cautioned SIR family of models explain these phenomena, while capturing other features including the timing of second infection peaks.

Contemplating the early linear global data, see Fig. 1A and 1C, the authors were struck by the similarities with bacterial viral proliferation kinetics inside a single cell and in evolution experiments *in vitro*, which systematically show exponential growth giving way to linear growth in the absence of immunity [25, 26]. The fundamental reason for this is specific host resource limitation, for example of the Qß viral replicase enzymes responsible for copying the RNA viral genome [26]. This, like the nesting site limitation in bird populations, has a straightforward explanation: when most replicase enzymes are occupied in the copying process with a particular RNA genome, they are not available for proliferation of other RNA, and the throughput of copied RNA becomes a constant, limited by the throughput of such copying enzymes. The authors propose a similarly endogenous mechanism that can account for the observed linear growth phases for Covid-19 in societies shown in Fig. 1 A and C.

We add an endogenous informed human cautionary response to simple compartmentalized S(E)IR models in the following way. We split the population of susceptible individuals S into two classes S and Sc, the former acting unaffectedly and hence experiencing exposure to the virus at the initial rate, the latter exercising informed caution and hence reducing their exposure to the virus by a factor c0 < 1. We then identify the subpopulation C in the deterministic population model most indicative of the negative impact of the disease for the population, as the trigger for this response. For example, in the case of the simple SIR model, it is the class C=I of infected individuals, and more realistically in the SEI3R model, which adds an exposed class E of not yet infectious individuals and two additional classes I2 and I3 of infectious individuals (in hospital and in intensive care respectively), it is the class C=I3. Although one may expect that the number of deaths also dramatically influences the execution of caution, it is a cumulative category which does not reflect the current situation as does I or I3. In fact, the daily number of deaths would be an appropriate indicator, but this is simply proportional to C as chosen: I in the SIR and SEIR models and I3 in the SEI3R model.

To capture the response to this cautionary trigger, we employ a simple reaction mechanism: a reversible caution binding mechanism. Individuals observing the pandemic can be triggered to become cautious but after a while also shed this caution. So the model involves both a forward transition of unaffected susceptible individuals S to cautious individuals Sc, with a rate proportional to the product S\*C of their population fractions (as in the law of mass action for chemical interactions), as well as a reverse transition from cautious individuals to individuals acting unaffectedly, proportional to the fraction Sc of cautious individuals (resulting in a natural single exponential decay of caution in time). The mechanism and equations of two representative endogenous caution models are shown in Fig. 2. Note that in our first approach, we did not distinguish between cautious and non-cautious exposed or infected individuals E, I for simplicity, but for consistency this should be done, especially for the class E (individuals do not know that they are exposed). We have tested the impact of including cautioned classes for all non-hospitalized individuals in a second set of models, also shown in Fig. 2, which share the prediction of a linear phase, with a stronger impact of caution. Once in hospital, we assume naturally that all individuals are exercising (or having exercised for them by hospital staff) a significant degree of caution. Further model distinctions are analysed in the SI.

An alternative threshold trigger response replaces the product law by a threshold activation rate of the form where is the difference between the endogenous cautionary trigger signal introduced above and a threshold value (e.g. 25% of hospital ICUs being occupied) and describes the sharpness of the transition. While this may be required to fit accurately the sudden press-amplified responses to reports of rising death tolls, it is not essential to explain the observed long linear response phases. It is clear that human caution response is related to risk assessment and much more complex than our simple model [27]. We shall discuss this further below.

The generic linear phases of growth for the cumulative confirmed cases are surveyed in data taken from Johns Hopkins University database, using a rolling average over 7 days to remove prominent weekly variations in reporting and some fluctuations, in Fig 1A for 7 major European countries (Italy, Spain, Germany, France, UK, and for comparison Sweden and Turkey) as well as for the 7 countries (US, Brazil, India, Russia, South Africa, Mexico, Peru) with the most cases (on Aug 1 2020) in Fig 1B. Despite the differences in detail, all the comparatively mature responses in Europe demonstrate an extended linear phase of growth, which is markedly different from the herd immunity saturation common to the S(E)IR family of models. The saturation also takes place well before the percentage of infectives can cause any effective herd immunity. Although still in the pre-saturation phase for some (notably India), the other largest Covid-19 epidemic countries in Fig. 1B also demonstrate an extended linear saturation response (two such phases with differing levels are visible in the US data).

We solved the ordinary differential equations of each model, using the python modelling package PyGom [28] (with its interface to SciPy) for convenience. We modelled the impact of endogenous caution on three successively more realistic models from the SIR family: SIR, SEIR and SEI3R. The first two are the classic early epidemic models, the second including delays associated with incubation of the disease in exposed non-infectious individuals, while the third involves the important progression of infected individuals to two severely infected groups with different responses, hospitalized and in critical care [29]. We do not here distinguish age groups or geographic diversity, both of which extensions would be straightforward but introduce additional complexity. Fig. 3 shows the range of epidemic responses in the number of daily cases for the caution extensions to the simple (SEIR → SCEIR & SC3EIR) and hospital differentiated (SEI3R → SCEI3R & SC3EI3R) models for representative variation of the three caution parameters about typical values. Note that the complete caution models (SC3EIR & SC3EI3R), which includes caution for susceptible, exposed and infected individuals, strengthen the caution response and predict strong second wave phenomena for some parameter values. The range of response forms appears to cover the majority of forms seen for 194 countries in the JHU data. Note that in Fig. 3, showing daily not cumulative cases, the linear phase of growth corresponds to constant daily cases.

An example of fitting the caution model to the data for Germany (confirmed, recovered and deaths) by varying the three parameters affecting the cautionary response (as well as the starting point of the infection) is shown in Fig. 4. [We plan to extend this figure to include three other countries with different shaped responses.] Note that this fit was achieved with simple manual adjustment, without considering various complications in the data: the increase in testing which leads to an increasing percentage of cases being confirmed, delays in registration of statistics, geographic and age structuring of infection etc. It is not the purpose of this paper to generate more accurate fitted models taking all these complications into account. Rather, we wish the reader to share the insight that the seeming complexity of the societal response to the Covid-19 pandemic can actually be better understood as belonging to a single simple phenomenon that distinguishes the Covid-19 pandemic from earlier epidemics: the ubiquitous internet mediated feedback of daily data collection inspiring a social distancing cautionary response in the population. A preliminary scan of the cumulative deaths in all monitored countries (JHU data) is shown in the supplementary material (together with simple fits from the cautionary model). Note that while the deaths data is deemed more reliable, since it is less dependent on incomplete Covid-19 testing, fitting just one quantity is less stringent than the example shown in Fig. 4, involving all three curves (confirmed, recovered and deaths).

This phenomenom is not restricted to European, US and Russian responses. Whereas some countries, with geographic advantages in isolation, by executing radical containment policies, have managed to reduce the daily new infection rate of the Covid-19 virus to a rather constant low level, which as predicted by our model is non-zero, another common growth response is a transition from an exponential (or possibly power law [16]) phase to a higher but also relatively constant rate of growth, often with 100s or 1000s of cases per day, in some cases after an initial overshoot. The explanatory power of our models is apparent in routinely replacing the generic feature of the SIR family of models – a daily infection peak following an exponential growth phase as limited by herd immunity – by a daily infection peak at orders of magnitude lower infection numbers, not related to herd immunity, and one having a long often flat tail which does not involve exponential decay of the number of infections, matching the typical responses observed for Covid-19. It is important to stress that while the cautionary response can predict an extended linear growth phase in the cumulative response (constant in the daily response), which was observed accurately over two months for example in the USA response, and longer in the Russian response, it does not do so for all parameters as seen clearly in Fig. 3. The shape of departures from constant daily responses seem also to correspond to those of real data. Further work is required to tease out these relations, exploiting the arsenal of world modelling techniques and data corrections required to deal with all the special cases of geographic, political and social circumstance.

We briefly address a potential critique of our result arising from limitations in the testing procedure. If the number of available tests is limited in a country, then this could result in a saturation in the number of confirmed cases per day, resulting in an apparent linear growth. Although such limitations have occurred and are visible for example in the data from Italy, we argue that our overall conclusions are independent of this effect. Firstly, overall testing levels in a significant number of countries have exceeded by a large factor the number of positive cases. Secondly, the linear trend also occurs in the number of deaths. Thirdly, the numbers of tests have been increasing in most countries and the linear trend persists.

The implications of these results are instructive. Firstly, it is no longer herd immunity but cautionary measures that is the primary limiter of spread of the disease: the latter have effect at much lower disease frequencies than herd immunity which would only be achieved much later after an enormous societal cost. Secondly, the strongly asymmetric peak responses to the daily case statistics and the linear population responses in cumulative case indicators (and in deaths) result from an active regulation of the degree of caution exercised in the population. As evidenced by the case of Sweden this is not entirely dependent on government legislation, which itself is in response to fears of repercussions based on severity indicators like the number of deaths, but also occurs naturally in the population, for example through the ubiquitous distribution of statistics concerning ICU cases. Depending on the timescale of relaxation of caution, the response can also involve second waves and longer-term oscillation. Thirdly, the natural human response, and as we have seen also government mediation of this apart from in a few nations, is not to maintain strict caution measures up until disease eradication. The successive relaxation of measures, even close to disease eradication results in very long periods of nearly constant case frequencies, consistent with the cautionary regulation process that we describe in this paper. Examples of this include Germany, Australia, South Korea, Switzerland and many other states. This response is no guarantee for containment with both model and recent data show second waves of infection.

Our model can be extended and integrated with existing extensions in various ways. Since its major feature of complete endogeny distinguishes it from conventional approaches such as external societal changes to the parameters (e.g. government decision influences on the R number), we outline one further simple endogenous extension in this work to show how a coupling of the cautionary response with economic impact can be introduced. Cautioned individuals have a vital positive effect on containing the epidemic, as we have seen, but the economic repercussions of this caution are often severe, resulting in significant reduction in economic capacity, by a factor . We model the economy simplistically as a single state variable with logistic dynamics with relaxation rate in the form (with a steady state carrying capacity normalized to one in the absence of the pandemic and linearly depressed by caution). While there may well be direct effects of the pandemic on the economy, we capture here the main effect of the economic response being mediated by caution.

To complete the economic coupling model, we also consider the economic influence on the cautionary response, by introducing a further dynamic class of heedless (“uncautionable”) individuals that become, through economic repercussions, “immune” to cautionary warnings. The economic trigger for this caution insensitivity is assumed simply proportional to the economic depression , and is absent in the absence of the pandemic when . Thus, the rate of transition to the uncautionable state from either cautioned or uncautioned susceptibles is modelled as times their fractions in the population, or . As with the cautioned class , we also allow for exponential decay of economic uncautionability with time, here at rate . We explore the impact of these four economic coupling parameters in SI fig. S5, revealing that the key parameter is . Fixing for simplicity the magnitude of the economic impact factor , and the timescale of the economic response to a quarter (three months) *i.e.* per day, we show in Fig. 5 how economic coupling reduces but does not eliminate the cautionary response and can explain the occurrence of higher second wave peaks in the pandemic.

Perhaps it will be possible for the human population to modulate its cautionary response using widespread information about the negative repercussions of the relaxation of caution. It is the authors’ view however that until a proven viable vaccine is available, additional work needs to be undertaken to enable the population to maintain the same benefits of high levels of caution but transferred to socially acceptable habits and routines that can have a longer lifetime than permitted by the media-supported awareness and focus generated by calamitous deaths in the population.

*Acknowledgements:*

The authors wish to acknowledge the support of the European Centre for Living Technology, and the access to Covid-19 data compiled by Johns Hopkins University. The authors wish to thank those who made their modelling software examples available on GitHub, in particular, Dr. Alison Hill (https://github.com/alsnhll/SEIR\_COVID19) and the authors of the PyGom package (https://github.com/PublicHealthEngland/pygom).

**Figures**



**Fig.1 Common linear phases of growth in individual countries.** **A)** The cumulative numbers of confirmed cases of Covid-19 in the larger European countries, including Turkey (similar size, 82 million) and Sweden (minimal government control, 10 million) as interesting cases for comparison having strong and weak central intervention. Superimposed with the data is a three-segment linear fit (using the python pwlf module). **B)** The weekly averages of daily confirmed cases for the same European countries. **C)** Cumulative confirmed cases for the world and seven countries with largest population epidemics in the world for Covid-19 as of Aug 1 2020, with the same three-segment linear fit superimposed. **D)** The weekly averages of daily confirmed cases for the same countries. Note that the long regions of linear growth in the cumulative graphs in (A) and (C) correspond to broadened peaks in the daily case counts; these broadened peaks are not produced by traditional SIR or SEIR models. For reference, infection rate and daily infection rate of a standard SIR model is shown in pink dashed lines, in (A) and (B), respectively. Data for Fig. 1 is taken from John Hopkins University compilation and averaged over 7 days to remove weekly oscillations in reporting.

|  |  |  |
| --- | --- | --- |
| SIR |  |  |
| SCIR |  |  |
| SEIR |  |  |
| SCEIR |  |  |

**Fig.2 The mechanism and equations of the two simplest endogenous caution models.** The two standard epidemic models SIR and SEIR are extended in the simplest way to self-regulating models with caution SCIR and SCEIR, by distinguishing two classes of susceptibles *S* and *Sc* with the switch to caution prompted by high observed number of infections and with caution decaying exponentially with time. Cautioned susceptibles have a reduced rate of infection. In the full models employed in Fig. 3 and below, the exposed *E* and infected individuals *I* are also distinguished by caution (see SI Fig S1), with cautioned infectives causing less infections of susceptibles, resulting in the SC2IR and SC3EIR models. Likewise, more differentiated standard models like the SEI3R model, with three stages of infected individuals (*I1* non-hospitalized, *I2* hospitalized and *I3* critical care) can be extended to cautionary feedback via *I3* as in SI Fig S1 to the models SCEI3R and SC3EI3R.



**Fig. 3 Effect of caution feedback for representative variation of the caution parameters**. The three underlying standard models SIR (left), SEIR (center) and SEI3R (right, with distinguished hospitalization and ICU treatment of infected individuals) shown in the blue curves in the first row (c0=1) are extended with caution, distinguishing the cautioned susceptible class as well as cautioned infected class (for or in the case of SEI3R for assuming hospitalized cases are always cautioned) and for cases with *E* the cautioned exposed class . The four rows show the separate variations of the response with each of three caution parameters about reference values (0.2, 21, 0.3): CautionFrac=c0: infectivity reduction factor; CautionRetention: caution retention time = 1/c1; CautionICUFrac: fraction of intensive care units (ICUs) occupied which result in a cautioning rate c2\*I3 of 1 per day, i.e. c2=1/(ICUFrac\*CautionICUFrac, fixing ICUFrac=0.002 for the plots, the fraction of ICUs per individual, assumed constant. This interpretation of c2 is adjusted by the fraction of critical cases amongst infectives in the first two columns to make the differentiated model commensurate with the first two. The vertical axis in all plots is the daily confirmed cases as a fraction of the population (allowing application to different regions or nations).

A close up of a map

Description automatically generated

**Fig. 4 Fit to country data (Germany) for caution arising from critical societal burden in SC3EI3R model**. The data for the registered fraction of population with Covid-19 infection (green), recovered (blue) and deaths x10 (red) is shown with points (daily JHU data) and curves from simulation of ODEs according to the model SC3EI3R (see Fig. S1 for mechanism and equations). The second wave in Germany is predicted correctly for a ca. 2-month caution retention time. The fit was produced manually by varying the caution parameter c\_1 as well as the fraction of infected individuals (at start date Jan 25). The parameters of the fit are {c0: 0.1, c1: 0.015, c2: 104, I0: 10-6.73} and the fixed parameters assumed were { β1: 0.4, β2: 0, β3: 0,α: 0.2, γ1: 0.07, γ2: 0.167, γ3: 0.1, p1: 0.03, p2: 0.083,μ: 0.1} based on the standard parameters Exposure=0.4, IncubPeriod=5, DurMildInf=10, FracMild=0.7, FracSevere=0.20, FracCritical=0.1, CFR=0.05, TimeICUDeath=5, DurHosp=4, FracConfirmedDet=0.125, FracDeathsDet=1.0, ICUFrac= 0.001.

Comments: This figure needs to be replaced by a panel of 4 countries with fits. Choose:

**Fig. 5 Economic coupling with caution in SC3UEI3R model**. The influence of economic stringencies on the cautionary response is shown, in **A** for typical variation of the coupling strength and **B** and **C** as a fit to the data for the USA and Spain. Note that the strength of the cautionary response on the pandemic is weakened by economic considerations as expected.

# Supplementary Material

|  |  |  |
| --- | --- | --- |
| SIR |  |  |
| SCIR |  |  |
| SC2IR |  |  |
| SEIR |  |  |
| SCEIR |  |  |
| SC3EIR |  |  |
| SEI3R |  |  |
| SCEI3R |  |  |
| SC3EI3R |  |  |

**Fig. S1 Mechanism of all models analysed in this work.** The three standard models SIR, SEIR and SEI3R are each extended with cautionary feedback in two ways: (i) firstly just distinguishing cautioned susceptibles and then (ii) distinguishing also cautioned exposed and/or infected individuals (non-hospitalized ones to be more precise). In each case the reference class employed to gauge the cautionary feedback is the class of most severely affected infected individuals. We assume for simplicity that the transition to caution is independent of exposure in the differentiated models.

Fig not yet available

**Fig. S2 Piecewise linear fits to all country data for cumulative deaths.** The piecewise linear analysis is extended to include all countries (up to Aug 1) for their cumulative deaths (deemed more reliable than the cumulative infections which depend more strongly on testing rates).

A close up of a map

Description automatically generated

**Fig. S3 Effect of caution feedback for representative variation of the caution parameters**. The three underlying models SIR (left third), SEIR (middle third) and the more realistic SEI3R (right third) with distinguished hospitalization and ICU treatment of infected individuals are extended with caution in two ways: (i) (1st and 3rd column) only adding cautioned susceptibles as in fig. 2, and (ii) (columns 2 and 4) adding cautioned susceptibles, exposed and infected S,E,I for all non-hospitalized classes, (assuming hospitalized cases are always cautioned). The three rows show the variations of the response with each of the three caution parameters (c0,c1,c2) about reference values (0.2,21,0.3) corresponding to (infectivity reduction factor, caution retention time in days, and sensitivity to ICU occupation fraction or equivalently to death rate, more precisely the fraction of ICUs occupied leading to transition to caution @ 1/day). The ICU fraction relative to population is a known country dependent parameter, set to a typical western value of 0.002 in this case. The vertical axis in all plots is the daily confirmed cases as a fraction of the population (allowing application to different regions or nations).

**References**

1. Kermack, W.O., McKendrick, A.G., Walker, G.T.: A contribution to the mathematical theory of epidemics. Proceedings of the Royal Society of London. Series A, Containing Papers of a Mathematical and Physical Character 115, 700-721 (1927) doi:10.1098/rspa.1927.0118

2. R.M., A., B., A., R.M., M.: Infectious Diseases of Humans: Dynamics and Control. Oxford University Press, Oxford, UK (1992) 9780198540403

3. Anderson, R., May, R.: Directly transmitted infections diseases: control by vaccination. Science 215, 1053-1060 (1982) 10.1126/science.7063839

4. Hethcote, H.W.: The Mathematics of Infectious Diseases. SIAM Rev. 42, 599–653 (2000) 10.1137/s0036144500371907

5. Wu, Z., McGoogan, J.M.: Characteristics of and Important Lessons from the Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of 72 314 Cases from the Chinese Center for Disease Control and Prevention. . JAMA 323, 1239–1242 (2020) <https://doi.org/10.1001/jama.2020.2648>

6. Lin, Q., Zhao, S., Gao, D., Lou, Y., Yang, S., Musa, S.S., Wang, M.H., Cai, Y., Wang, W., Yang, L., He, D.: A conceptual model for the coronavirus disease 2019 (COVID-19) outbreak in Wuhan, China with individual reaction and governmental action. Int. J. Infect. Dis. 93, 211-216 (2020) <https://doi.org/10.1016/j.ijid.2020.02.058>

7. Giordano, G., Blanchini, F., Bruno, R., Colaneri, P., Di Filippo, A., Di Matteo, A., Colaneri, M.: Modelling the COVID-19 epidemic and implementation of population-wide interventions in Italy. Nature Medicine (2020) <https://doi.org/10.1038/s41591-020-0883-7>

8. Gumel, A.B., Ruan, S., Day, T., Watmough, J., Brauer, F., van den Driessche, P., Gabrielson, D., Bowman, C., Alexander, M.E., Ardal, S., Wu, J., Sahai, B.M.: Modelling strategies for controlling SARS outbreaks. Proc Biol Sci 271, 2223-2232 (2004) 10.1098/rspb.2004.2800

9. Klepac, P., Kucharski, A.J., Conlan, A.J., Kissler, S., Tang, M., Fry, H., Gog, J.R.: Contacts in context: large-scale setting-specific social mixing matrices from the BBC Pandemic project. medRxiv (2020)

10. Prem, K., Liu, Y., Russell, T.W., Kucharski, A.J., Eggo, R.M., Davies, N., Flasche, S., Clifford, S., Pearson, C.A.B., Munday, J.D., Abbott, S., Gibbs, H., Rosello, A., Quilty, B.J., Jombart, T., Sun, F., Diamond, C., Gimma, A., van Zandvoort, K., Funk, S., Jarvis, C.I., Edmunds, W.J., Bosse, N.I., Hellewell, J., Jit, M., Klepac, P.: The effect of control strategies to reduce social mixing on outcomes of the COVID-19 epidemic in Wuhan, China: a modelling study. The Lancet Public Health 5, e261-e270 (2020) 10.1016/S2468-2667(20)30073-6

11. Hellewell, J., Abbott, S., Gimma, A., Bosse, N.I., Jarvis, C.I., Russell, T.W., Munday, J.D., Kucharski, A.J., Edmunds, W.J., Sun, F., Flasche, S., Quilty, B.J., Davies, N., Liu, Y., Clifford, S., Klepac, P., Jit, M., Diamond, C., Gibbs, H., van Zandvoort, K., Funk, S., Eggo, R.M.: Feasibility of controlling COVID-19 outbreaks by isolation of cases and contacts. The Lancet Global Health 8, e488-e496 (2020) <https://doi.org/10.1016/S2214-109X(20)30074-7>

12. Kucharski, A.J., Russell, T.W., Diamond, C., Liu, Y., Edmunds, J., Funk, S., Eggo, R.M., Sun, F., Jit, M., Munday, J.D., Davies, N., Gimma, A., van Zandvoort, K., Gibbs, H., Hellewell, J., Jarvis, C.I., Clifford, S., Quilty, B.J., Bosse, N.I., Abbott, S., Klepac, P., Flasche, S.: Early dynamics of transmission and control of COVID-19: a mathematical modelling study. The Lancet Infectious Diseases 20, 553-558 (2020) 10.1016/S1473-3099(20)30144-4

13. Angulo, J., Yu, H.-L., Langousis, A., Kolovos, A., Wang, J., Madrid, A.E., Christakos, G.: Spatiotemporal Infectious Disease Modeling: A BME-SIR Approach. PLOS ONE 8, e72168 (2013) 10.1371/journal.pone.0072168

14. Keeling, M.J.: The effects of local spatial structure on epidemiological invasions. Proc Biol Sci 266, 859-867 (1999) 10.1098/rspb.1999.0716

15. Danon, L., Brooks-Pollock, E., Bailey, M., Keeling, M.J.: A spatial model of CoVID-19 transmission in England and Wales: early spread and peak timing. medRxiv 2020.2002.2012.20022566 (2020) 10.1101/2020.02.12.20022566

16. Ziff, A.L., Ziff, R.M.: Fractal kinetics of COVID-19 pandemic. medRxiv (2020)

17. Simoes, J.M.: Spatial Epidemic Modelling in Social Networks. AIP Conference Proceedings 776, 287-297 (2005) 10.1063/1.1985395

18. Manchein, C., Brugnago, E.L., da Silva, R.M., Mendes, C.F.O., Beims, M.W.: Strong correlations between power-law growth of COVID-19 in four continents and the inefficiency of soft quarantine strategies. Chaos: An Interdisciplinary Journal of Nonlinear Science 30, 041102 (2020) 10.1063/5.0009454

19. Hunter, E., Mac Namee, B., Kelleher, J.D.: A Taxonomy for Agent-Based Models in Human Infectious Disease Epidemiology. Journal of Artificial Societies and Social Simulation 20, 2 (2017) 10.18564/jasss.3414

20. Chinazzi, M., Davis, J.T., Ajelli, M., Gioannini, C., Litvinova, M., Merler, S., Pastore y Piontti, A., Mu, K., Rossi, L., Sun, K., Viboud, C., Xiong, X., Yu, H., Halloran, M.E., Longini, I.M., Vespignani, A.: The effect of travel restrictions on the spread of the 2019 novel coronavirus (COVID-19) outbreak. Science 368, 395 (2020) 10.1126/science.aba9757

21. Wang, C.J., Ng, C.Y., Brook, R.H.: Response to COVID-19 in Taiwan: Big Data Analytics, New Technology, and Proactive Testing. JAMA 323, 1341-1342 (2020) 10.1001/jama.2020.3151

22. Zhou, C., Su, F., Pei, T., Zhang, A., Du, Y., Luo, B., Cao, Z., Wang, J., Yuan, W., Zhu, Y., Song, C., Chen, J., Xu, J., Li, F., Ma, T., Jiang, L., Yan, F., Yi, J., Hu, Y., Liao, Y., Xiao, H.: COVID-19: Challenges to GIS with Big Data. Geography and Sustainability 1, 77-87 (2020) <https://doi.org/10.1016/j.geosus.2020.03.005>

23. Bruinen de Bruin, Y., Lequarre, A.-S., McCourt, J., Clevestig, P., Pigazzani, F., Zare Jeddi, M., Colosio, C., Goulart, M.: Initial impacts of global risk mitigation measures taken during the combatting of the COVID-19 pandemic. Safety Science 128, 104773 (2020) <https://doi.org/10.1016/j.ssci.2020.104773>

24. Lourenco, J., Paton, R., Ghafari, M., Kraemer, M., Thompson, C., Simmonds, P., Klenerman, P., Gupta, S.: Fundamental principles of epidemic spread highlight the immediate need for large-scale serological surveys to assess the stage of the SARS-CoV-2 epidemic. medRxiv (2020) <https://doi.org/10.1101/2020.03.24.20042291>

25. Yin, J., Redovich, J.: Kinetic Modeling of Virus Growth in Cells. Microbiology and Molecular Biology Reviews 82, e00066-00017 (2018) 10.1128/MMBR.00066-17

26. Biebricher, C.K., Eigen, M., Gardiner, W.C.: Kinetics of ribonucleic acid replication. Biochemistry 22, 2544-2559 (1983) 10.1021/bi00279a036

27. Richard Eiser, J., Bostrom, A., Burton, I., Johnston, D.M., McClure, J., Paton, D., van der Pligt, J., White, M.P.: Risk interpretation and action: A conceptual framework for responses to natural hazards. International Journal of Disaster Risk Reduction 1, 5-16 (2012) <https://doi.org/10.1016/j.ijdrr.2012.05.002>

28. Tye, E., Finnie, T.J.R., Hall, I., Leach, S.: PyGOM - A Python Package for Simplifying Modelling with Systems of Ordinary Differential Equations. ArXiv abs/1803.06934, (2018)

29. Hill, A., Levy, M., Xie, S., Sheen, S., Shinnick, J., Gheorghe, A., Rehmann, C.: Modeling COVID-19 spread vs healthcare capacity, 2020., Planning as Inference in Epidemiological Models. Available from: <https://www.researchgate.net/publication/340295625_Planning_as_Inference_in_Epidemiological_Models>. (2020)