Do Interventions Matter in COVID-19?
PSTAT 120C Literature Review

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Abstract

COVID-19 has caused a huge amount of damage worldwide, in various perspective, including public health, economics, etc. It is a common sense that a strong intervention strategy can effectively control the disease transmission, but it also incurs a huge loss of economical benefits. It is urgent to quantify the impact of interventions to help governments make a wiser decision on defending the unexpected disaster. In this report, we review two papers talking about the impact of interventions, which take the case study of Wuhan city of China and BC province of Canada respectively. An age-structured susceptible-exposed-infected-removed (SEIR) model and a Bayesian epidemiological model are perceptively proposed to mathematically quantify the impact of interventions (physical distancing). The general conclusions both state that the interventions play an essential role, and especially a relatively relaxed strategy can still make the transmissions under control.

1 Introduction

In December 2019, the new coronavirus emerged in the City of Wuhan, Hubei Province, China. Indeed, the governments have taken unprecedented measures in response to the COVID-19 outbreak caused by SARS-CoV-2. Unfortunately, the disease has spread worldwide and have caused a huge global damage.

The world has witnessed the success of Chinese success in defending the unexpected disease, which is believed to strongly reply on the effective interventions from Chinese governments. However, the inventions have a huge damage towards economics and society. Hence, it is important and meaningful to quantify the impact of an interventions, which can guide the governments to a wiser decision in both controlling disease and balancing economics.

Although the inventions vary from regions to regions and from governments to governments, in a high-level summary, the control strategies can be categorized as Suppression and Mitigation [1]:

- Suppression: a strong intervention. The purpose of suppression is to lower the human-to-human reproduction number, which is the indicator to show the transmission rate, the ideal rate is below 1. For example, government announce stay-at-home policy.
- Mitigation: a weak intervention. The purpose of mitigation is reduce the health impact of an epidemic rather than interrupt the transmission. For example, adopt non-pharmaceutical interventions such as vaccines or drugs.

Our literature review aims to study the roles of the control strategies (referred to social distancing in some contexts). We review two papers about the impacts in epidemic transitions worldwide, including Wuhan city of China [2], British Columbia province of Canada [3]. These two regions can be seen as two representatives of two kinds of strategies: Wuhan is for suppression and BC province is for Mitigation, although the original papers do not give such a conclusion.

Two papers both study the transmission dynamics of the disease. The population in these two are both divided according to the infection status. But here is some main difference between them

- Population group. [2] divides the population into four groups based on infection status, and further divides it based on age to study the more detailed dynamics of population with different ages. [3] only considers the infection status, but divide the population into six groups, which is more detailed than the former one.

- The ways used to model the intervention impact. [2] reflects the impacts via the changing setting of lots dynamics parameters, while [3] links the impact to a specific parameter f in the system dynamics. It means that [2] is more adjustable for a detailed description of intervention strategy since each specific one can be reflected by a corresponding parameter. However, [3] tried to quantify the impact from a larger picture, combining all together as a simple parameter to investigate a more macro decision.
- The ways to model system uncertainty are different: [2] models the uncertainty via sampling a key parameter, reproduction number. While [3] adopts a Bayesian estimation framework to estimate the posterior of interested quantities.

The general conclusion of two paper both come to that Interventions do help in controlling disease transmission, which is an undoubted common sense, but the two papers quantify the impact under various assumptions and setting via mathematical models. Especially, a relatively relaxed strategy still works for defending the disease transmission. In particular, [2] stats that physical distancing were the most effective method if the staggered return to work was at the beginning of April in Wuhan. [3] shows that intermediate distancing measures (not as strong as suppression) could already control COVID-19 transmission in BC, Canada. However, a too relaxed intervention strategy could make the epidemic curve grow exponentially and out of control.

2 Research Goal

Relying on the data from the COVID-19 outbreak in Wuhan, China as a case study, [2] proposes a mathematical model to quantify the potential impact of a range of control measures that reduce social mixing.

Distancing measures have high economic, health, and social impacts. Hence, it is urgent to understand what level of contact rate and physical distancing measures are optimal to reduce transmission while at most keep the economical benefits. [3] assumes that the initial transmission has been under control, then try to answer that what relaxation in interventions could keep it under control.

3 Case study of Wuhan [2]

3.1 Data set

Due to the publication timeline, data used here is from the COVID-19 outbreak in Wuhan, China from late-2019 to the date of mid February, 2020.

3.2 Susceptible-exposed-infected-removed (SEIR) model

The infection population is divided into four status:susceptible (S), exposed (E), infected (I) and removed (R). Besides, the age-structure is considered in the model: population is divided into 5-year as a bin until 70 years and for people who over 70 will be considered as one group.

For each age group i, at time slot t, the transmission model is described as follows:

$$S_{i,t+1} = S_{i,t} - \beta S_{i,t} \sum_{j=1}^{n} C_{i,j} I^c_{j,t} - \alpha\beta S_{i,t} \sum_{j=1}^{n} C_{i,j} I^{SC}_{j,t}. \tag{1}$$

$$E_{i,t+1} = (1-\kappa)E_{i,t} + \beta S_{i,t} \sum_{j=1}^{n} C_{i,j} I^c_{i,j} + \alpha\beta S_{i,t} \sum_{j=1}^{n} C_{i,j} I^{SC}_{j,t}. \tag{2}$$

$$I_{j,t+1} = \rho_i \kappa E_{i,t} + (1-\gamma) I^c_{j,t}. \tag{3}$$

$$I_{j,t+1} = (1-\rho_i)\kappa E_{i,t} + (1-\gamma) I^{sc}_{j,t}. \tag{4}$$

$$R_{i,t+1} = R_{i,t} + \gamma I^c_{j,t+1} + \gamma I^{sc}_{j,t+1}. \tag{5}$$

According to [2], "β is the transmission rate which is scaled to the right value of R_0, $C_{i,j}$ describes the contacts of ago group j made by ago i, $\kappa = 1 - \exp(-1/d_L)$ is the daily probability of an exposed individual becoming infectious (with d_L being the average incubation period), and

$\gamma = 1 - \exp(-1/d_I)$ is the daily probability that an infected individual recovers when the average duration of infection is d_I."

Overall speaking, the above statistical parameters represent the transmission relations among groups. In this paper, the parameters are estimated by other literature. After setting down the parameters, with certain reasonable initialization, the transmission model can be simulated to see the outbreak.

One of the key parameters is R_0. It is the basic reproduction number, which indicates how fast COVID-19 can spread in the early stages. While, R_0 is hard to measure since it is hard to know how many people get infected in a given time. That is to say, reported cases are likely to be just a small fraction of true cases, while the probability of people get infected is different over time due to the change of population behaviour in response to the epidemic. Thus, the authors adopt an existing method from [4] which fitted a stochastic transmission model to multiple datasets on the timing of cases in Wuhan and timing of international exported cases from Wuhan, and verified the estimation on a period of data which is not used for inference, shown in Figure 1. The R_0 is

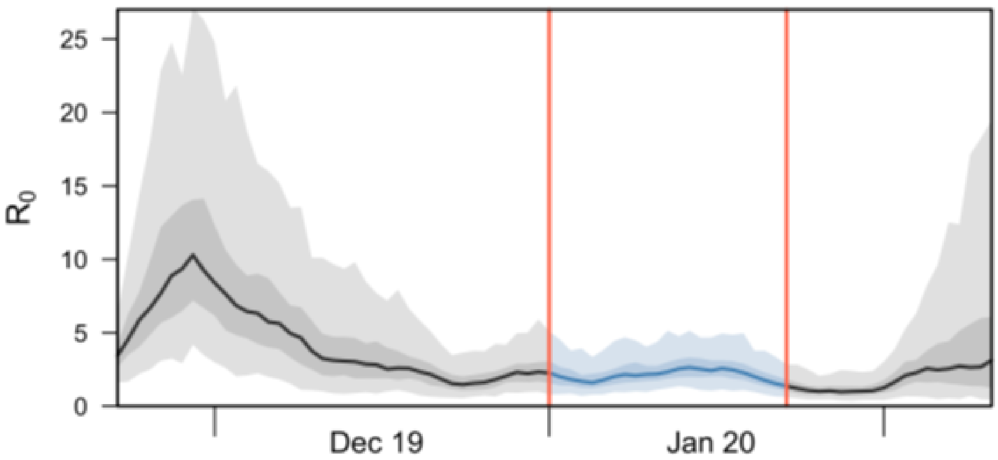

Figure 1: The estimated R_0 from a stochastic transmission model: R_0 models the uncertainty in the proposed SEIR scheme [2].

uniformly sampled from 95% confidence interval to explore the uncertainty of the proposed SEIR model.

Three scenarios of interventions are considered as follows:

- Theoretical: assume no change to social mixing patterns at all location types. (Even no school term break and Lunar New Year holidays.
- No interventions: the usual case. No particular social distance control but with school term break and Lunar New Year holidays.
- Interventions: the effect of intense control measures end at the beginning of March or April, and a staggered return to work is allowed while school remained closed.

The scenarios will be reflected to the parameters of the SEIR transmission model (Eq. 1 - 5).

The main limitation of the model is the large uncertainties around estimates of R_0 and the duration of infectiousness.

4 Case study of British Columbia Province [3]

4.1 Data set

The used data set is the case count data from British Columbia from March 1, 2020 (when a total of eight cases had been detected in the province) to April 11, 2020 at which time 1445 cases had been confirmed.

4.2 Bayesian epidemiological model

4.2.1 Epidemiological dynamics

Similar to the above mentioned SEIR model, with a more detailed categorization, the populations are divided into six groups based on the infection status: susceptible (S); exposed to the virus (E_1); exposed, pre-symptomatic, and infectious (E_2); symptomatic and infectious (I); quarantined (Q); and recovered or deceased (R) over time.

The non-physical-distancing (no intervention) differential equations are as follows:

$$\frac{\mathrm{d}S}{\mathrm{d}t} = -\beta[I + E_2 + f(I_d + E_{2d})]\frac{S}{N} - u_d S + u_r S_d \tag{6}$$

$$\frac{\mathrm{d}E_1}{\mathrm{d}t} = \beta[I + E_2 + f(I_d + E_{2d})]\frac{S}{N} - k_1 E_1 - u_d E_1 + u_r E_{1d} \tag{7}$$

$$\frac{\mathrm{d}E_2}{\mathrm{d}t} = k_1 E_1 - k_2 E_2 - u_d E_2 + u_r E_{2d} \tag{8}$$

$$\frac{\mathrm{d}I}{\mathrm{d}t} = k_2 E_2 - qI - \frac{I}{D} - u_d I + u_r I_d \tag{9}$$

$$\frac{\mathrm{d}Q}{\mathrm{d}t} = qI - \frac{Q}{D} - u_d Q + u_r Q_d \tag{10}$$

$$\frac{\mathrm{d}R}{\mathrm{d}t} = \frac{I}{D} + \frac{Q}{D} - u_d R + u_r R_d. \tag{11}$$

"Where β is the transmission parameter, D is the mean duration of the infectious period, f represents physical distancing, u_d and u_r are the rates of movement to and from the physical distancing compartments, k_1 is the rate of movement from the E_1 to E_2 compartment, k_2 is the rate of movement from the E_2 to I compartment, and q is the quarantine rate for movement from the I to Q compartment." The parameters and initial conditions are determined based on reality data and other literature. For short, these parameters describe the transmission dynamics. In particular, physical distancing is reflected by f in the dynamics: when $f = 1$, it means that no physical distancing (or no intervention).

To study the impact of intervention, the authors assume f as a time-dependent variable: f is closer to 1 means weaker physical distancing and vice verse.

$$f(t) = \begin{cases} 1 & t < t_1 \\ f_2 + \frac{t_2 - t}{t_2 - t_1}(1 - f_2) & t_1 \le t \le t_2 \\ f_2 & t \ge t_2 \end{cases} \tag{12}$$

Then the dynamics with physical distancing is described as below (the variables are denoted with a subscript d) and is visualized in Figure 2:

$$\frac{\mathrm{d}S_d}{\mathrm{d}t} = -f\beta[I + E_2 + f(I_d + E_{2d})]\frac{S}{N} - u_d S + u_r S_d \tag{13}$$

$$\frac{\mathrm{d}E_{1d}}{\mathrm{d}t} = f\beta[I + E_2 + f(I_d + E_{2d})]\frac{S}{N} - k_1 E_1 + u_d E_1 - u_r E_{1d} \tag{14}$$

$$\frac{\mathrm{d}E_{2d}}{\mathrm{d}t} = k_1 E_{1d} - k_2 E_{2d} + u_d E_2 - u_r E_{2d} \tag{15}$$

$$\frac{\mathrm{d}I_d}{\mathrm{d}t} = k_2 E_{2d} - qI_d - \frac{I_d}{D} - u_d I + u_r I_d \tag{16}$$

$$\frac{\mathrm{d}Q_d}{\mathrm{d}t} = qI_d - \frac{Q_d}{D} + u_d Q + u_r Q_d \tag{17}$$

$$\frac{\mathrm{d}R_d}{\mathrm{d}t} = \frac{I_d}{D} + \frac{Q_d}{D} + u_d R - u_r R_d. \tag{18}$$

4.2.2 Bayesian modeling

The interested quantities in this case study are as below:

- R_{0b}: the basic reproductive number. It can be calculated with an analytical form of the dynamics parameters.

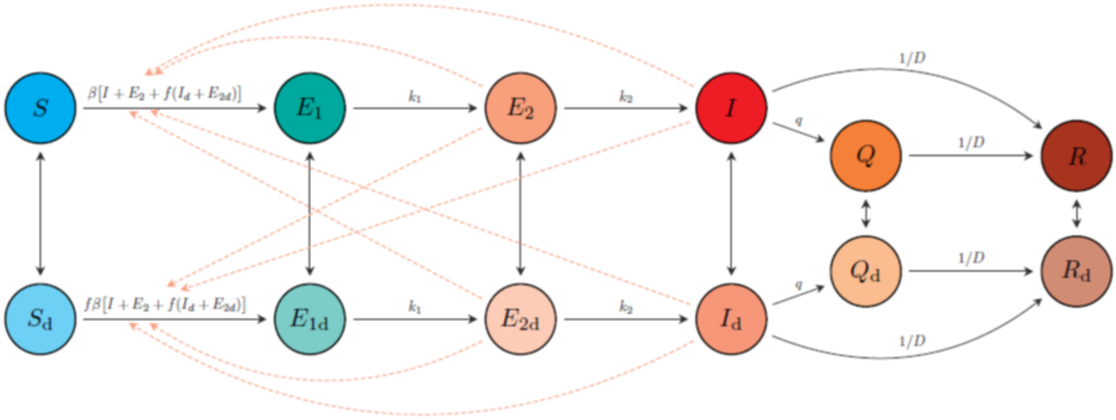

Figure 2: Schematic of used transmission dynamics [3].

- μ_r: model's predicted number of reported cases. It can also be calculated via dynamics variables and parameters.
- f_2: physical distancing impact parameter for describing a time-dependent f.

We denote C_r as the number of reported cases each day, where r is the discrete time of date. Then Bayesian model aims to infer the posterior of R_{0b}, μ_r and f_2 conditional on the reported case C_r.

The observation model relates the expected number of cases to the observations through a negative binomial observation model $NB2(C_r|\mu_r, \phi)$, where ϕ is the dispersion parameter. It is used to reflect the relationship between case counts and incident infections and to account for underestimation of the time between symptom onset and case reporting.

Then the joint posterior distribution can be written as

$$\mathbb{P}[R_{0b}, f_2, \phi|C] \propto \mathbb{P}[C|R_{0b}, f_2, \phi]\mathbb{P}[R_{0b}]\mathbb{P}[f_2]\mathbb{P}[\phi]$$

To perform the Bayesian inference, the prior of R_{0b}, ϕ and f_2 are set as three weakly informative distributions: $R_{0b} \propto$ Lognormal, $f_2 \propto$ Beta, $\frac{1}{\sqrt{\phi}} \propto$ Normal.

The Bayesian inference is implemented via a No-U-Turn Hamiltonian Markov Chain algorithm.

The main limitation of the modeling is that the age and contact structure are not considered. Also, the data of BC province may not be sufficient enough to draw a observation model.

5 Numerical Analysis

5.1 Wuhan case: SEIR model [2]

Firstly, we investigate the influence of R_0 on the transmission simulations as shown in Figure 3. From this figure, we can clearly see that each simulations scenario varies in a relatively large range, which means that the R_0 has a significant impact on the transmission dynamics. Besides, clearly, different intervention strategies will lead to very different dynamics, which will be further discussed later.

The simulations for different age groups are shown in Figure 4. The interested quantity of impact is the new cases per day. We can find that the age matters for the simulation: different age groups leads to different peaks and different peak time points, but the general trends under different intervention scenarios are similar for all age groups. The lower peak and delayed peak time point are incurred by a more stronger strategies, ordered by theoretical scenario (purple), No interventions (blue), intervention relaxed in March (red) and intervention relaxed in April (yellow). The results coincides with our common sense, but the key contribution here is to quantify the impact mathematically.

To quantitatively describe the impact under different scenarios, the authors show a more detailed figure focusing on the proportion of number of infections averted by end-2020 by age for different physical distancing measures. The additional proportions of cases averted (compared

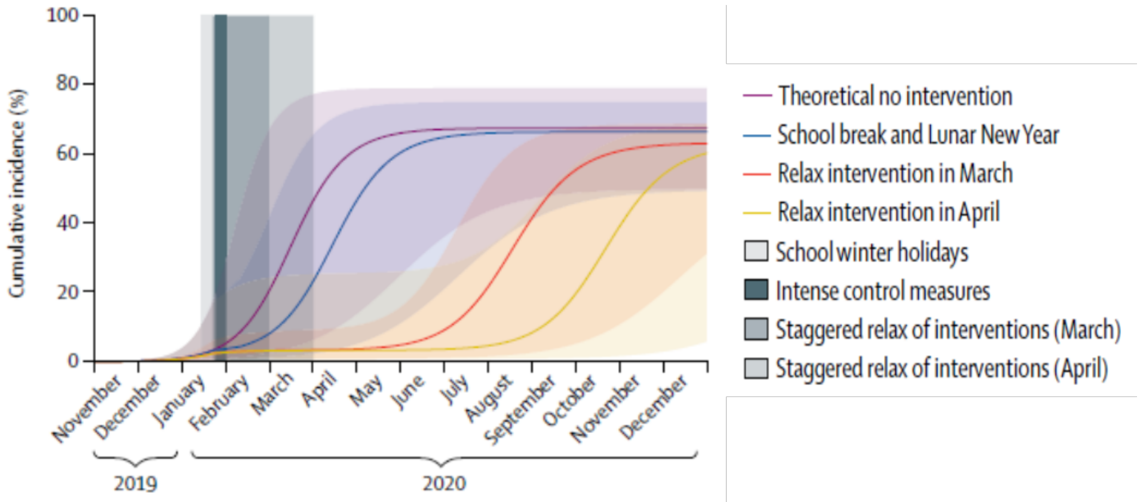

Figure 3: Effects of different physical distancing measures on cumulative incidence: the shadow represents the simulation results with uncertainty which is induced by sampled R_0 [2].

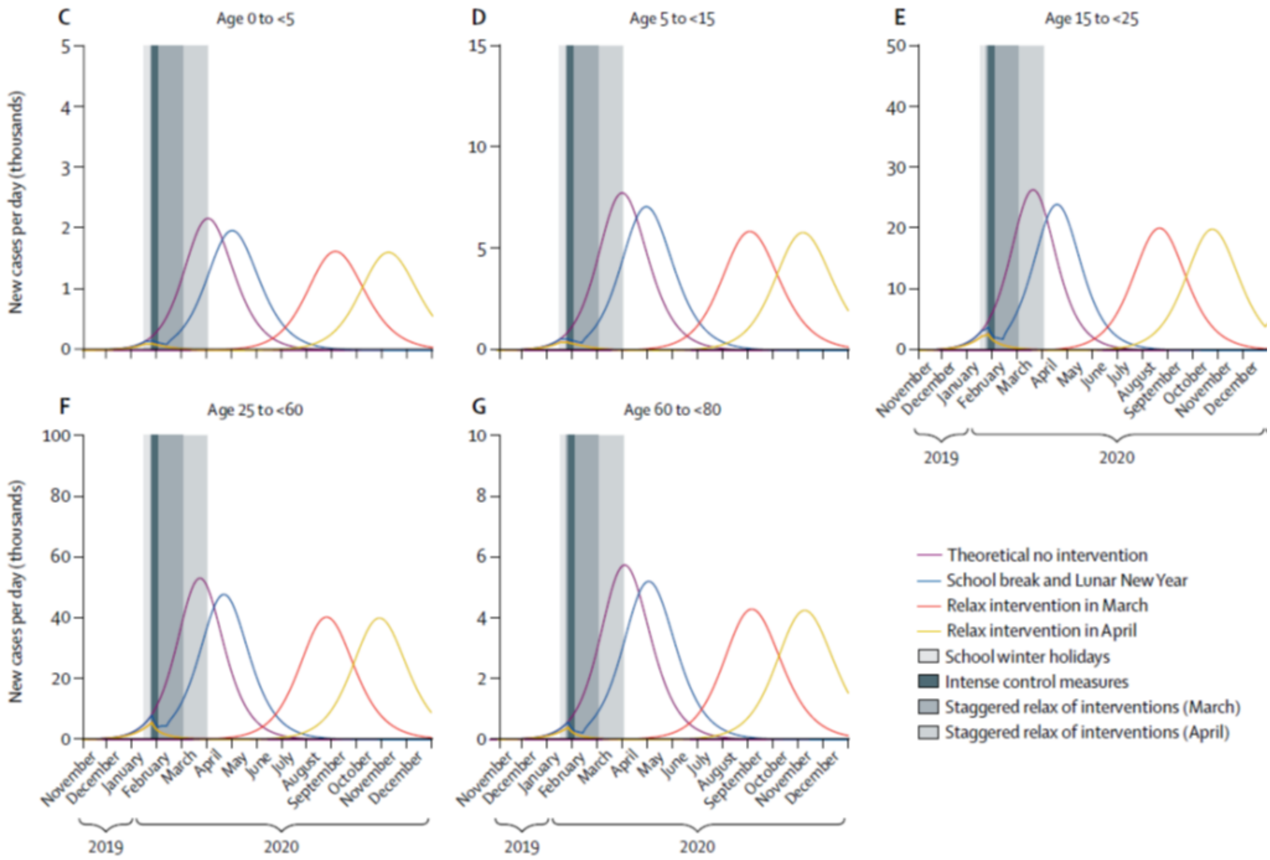

Figure 4: Age-specific incidence per day from late 2019 to end-2020 [2].

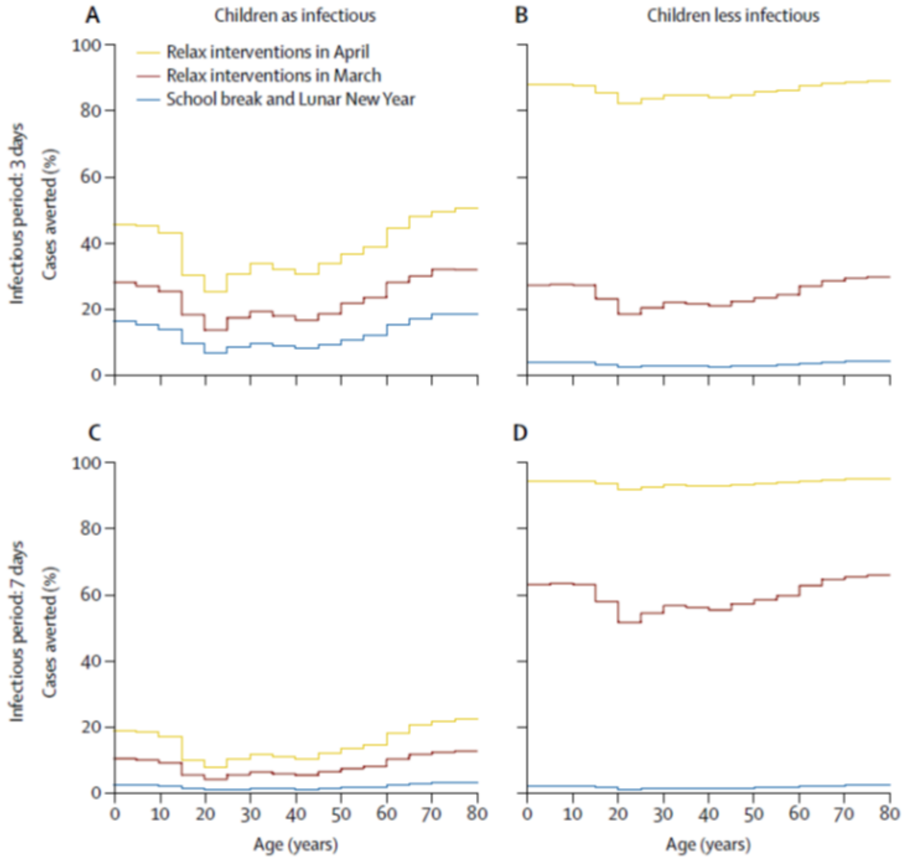

Figure 5: Modelled proportion of number of infections averted by end-2020 by age for different physical distancing measures, assuming the duration of infectiousness to be 3 days (A, B) or 7 days (C, D) [2].

with no intervention) are presented across age and by the different physical distancing measures as shown in Figure 5. See from the figure, we can easily find that if we have a stronger intervention strategy, more and more cases can be averted. In detail, if the disease had a short infectious period (3 days) and children are assumed as infectious, then our model suggests that relaxing physical distancing interventions in April could avert around 40 of cases averagely over age groups, while above 92% cases can be averted if the disease had a long infectious period (7 days) and children are assumed as less infectious.

Overall, the model simulations are performed under different parameter settings, including: the basic reproduction number, the average duration of infections, the initial proportion of cases infected, the susceptibility of children, and the role of younger individuals in transmission dynamics of COVID-19.

5.2 BC case: Bayesian epidemiological model [3]

Firstly, we show the inferred results of estimated case counts (A), estimated prevalence (C), posterior estimation for (B) R_{0b} and (D) fraction of (1-f_2) in Figure 6. Figures A and C show that the model describes the count data well, with reported cases showing a peak in late March, approximately two weeks after the initiation of distancing measures. Figures B and D show that the data are informative with respect to both main parameters: the posteriors are distinctly different and are more peaked than the their priors .

Next we will show how will the transmission related to the different level of interventions (reflected by different f_2) in Figure 7. The figures A and D tell that distancing measures are relaxed but prevalence and reported cases continue to decline, with slower decline and more variance in the number of reported cases in coming week. It means that it is possible to have some relaxation of current distancing measures without losing control of the epidemiological transmission. However, figures (B-F) show that if the interventions are relaxed too much, the prevalence and cases counts

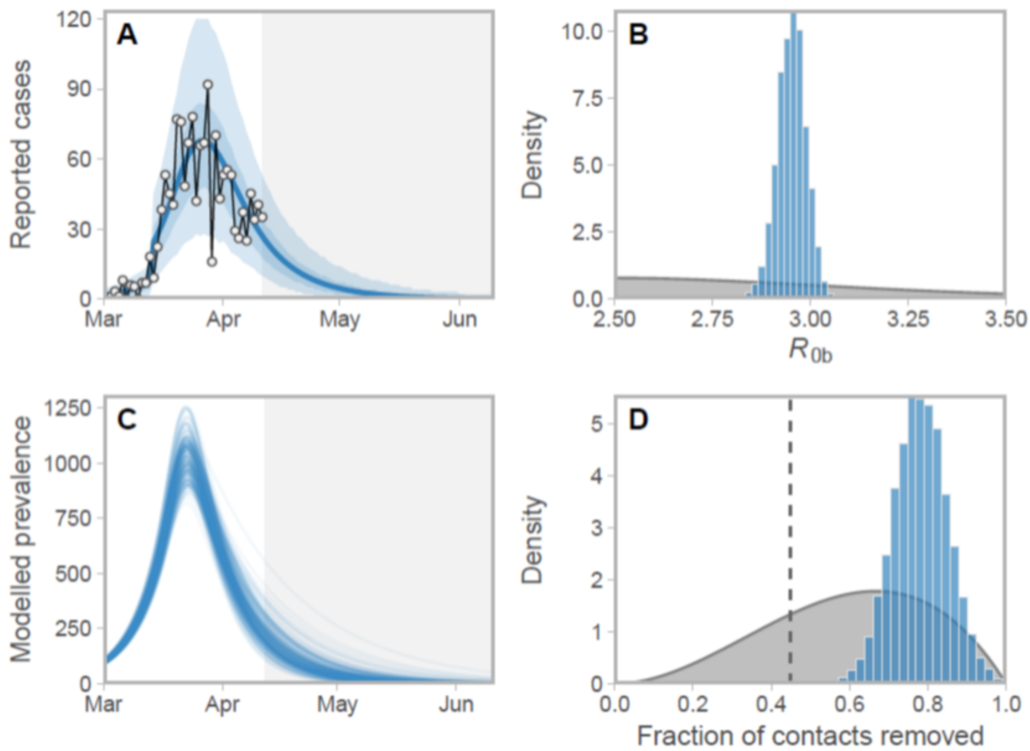

Figure 6: Bayesian estimation of estimated case counts (A), estimated prevalence (C), posterior estimation for (B) R_{0b} and (D) fraction of (1-f_2) [3].

begin to increase exponentially, which is definitely unacceptable.

6 Conclusion

In this literature review, we study two papers to quantify the impact of interventions on virus transmission. [2] studies the case of Wuhan, whose intervention strategy is relatively strong. The paper uses an age-structured susceptible-exposed-infected-removed (SEIR) model for several distancing measures. [3] studies the case of BC, Canada, whose control strategy is relatively relaxed but the severity of the disease is also milder. Except to epidemiological dynamics, a Bayesian framework is used to infer the posterior of interested quantities which quantifies the intervention impact. The conclusion from both papers is that interventions help a lot, and a relaxation on the physical distancing can still make the disease under control. In particular, [2] suggests a staggered return to work at the beginning of April while [3] concludes that a too relaxed strategy will lead to an exponential increasing on infections.

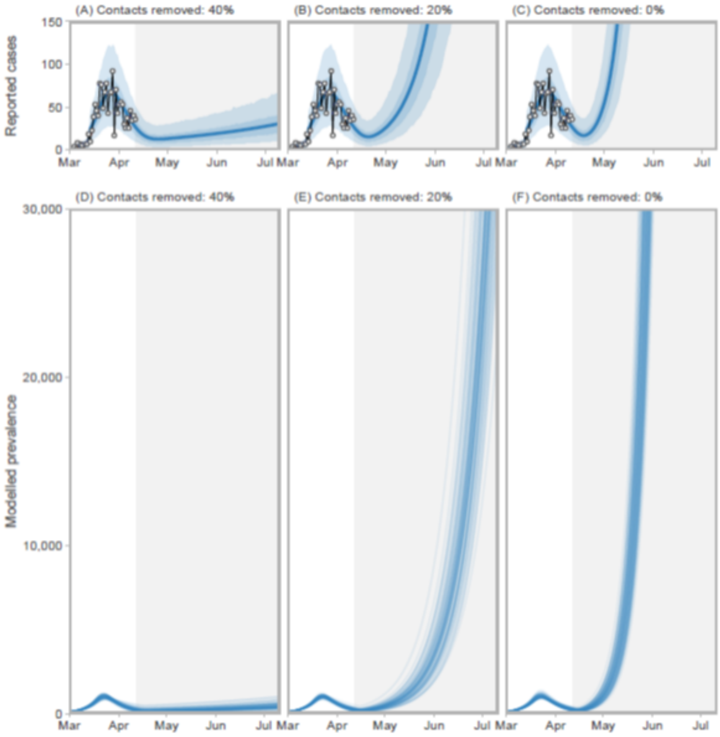

Figure 7: Three scenarios for relaxing distancing measures beginning on April 12 2020 [3].

References

[1] N. Ferguson, D. Laydon, G. Nedjati Gilani, N. Imai, K. Ainslie, M. Baguelin, S. Bhatia, A. Boonyasiri, Z. Cucunuba Perez, G. Cuomo-Dannenburg, *et al.*, "Report 9: Impact of non-pharmaceutical interventions (npis) to reduce covid19 mortality and healthcare demand," 2020.

[2] K. Prem, Y. Liu, T. W. Russell, A. J. Kucharski, R. M. Eggo, N. Davies, S. Flasche, S. Clifford, C. A. B. Pearson, J. D. Munday, S. Abbott, H. Gibbs, A. Rosello, B. J. Quilty, T. Jombart, F. Sun, C. Diamond, A. Gimma, K. [van Zandvoort], S. Funk, C. I. Jarvis, W. J. Edmunds, N. I. Bosse, J. Hellewell, M. Jit, and P. Klepac, "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*, vol. 5, no. 5, pp. e261 – e270, 2020.

[3] S. C. Anderson, A. M. Edwards, M. Yerlanov, N. Mulberry, J. Stockdale, S. A. Iyaniwura, R. C. Falcao, M. C. Otterstatter, M. A. Irvine, N. Z. Janjua, *et al.*, "Estimating the impact of covid-19 control measures using a bayesian model of physical distancing," *medRxiv*, 2020.

[4] A. J. Kucharski, T. W. Russell, C. Diamond, Y. Liu, J. Edmunds, S. Funk, R. M. Eggo, F. Sun, M. Jit, J. D. Munday, *et al.*, "Early dynamics of transmission and control of covid-19: a mathematical modelling study," *The lancet infectious diseases*, 2020.