Supplementary Information

Country-specific optimization strategy for testing through contact tracing can help maintain a low reproduction number (R_0) during unlock

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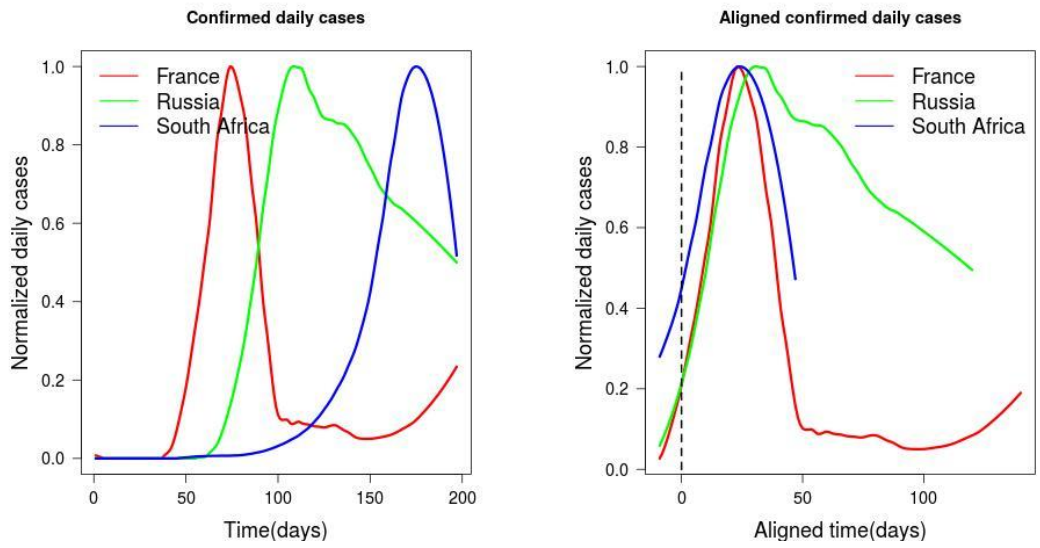
Content

I. Alignment of the time courses

From the calculation of the doubling rate time courses (Figure 1B), we identified the maximum doubling rate time point for each country and superimposed the time points with each other to align them. To demonstrate this, take three countries and show how these three countries are aligned based on the doubling rate with time. In the figure below, the normalized daily cases are shown and then these three time traces are aligned at the maximum doubling rate. The dashed vertical line at zero in the doubling rate aligned figure corresponds to the maximum doubling rate time point for each country.



II. Model for optimizing the quarantine rate

The basic reproduction ratio for the SEIQR model discussed above is given by

$R_0 = \frac{\beta}{\alpha_2}\frac{\rho}{\rho_{max}}$ where $\frac{\rho}{\rho_{max}}$ represents the extent of unlock. So this equation can be transformed as

$$\alpha_2 = \beta\frac{\rho}{\rho_{max}}\frac{1}{R_0}$$

The value of quarantine rate α_2' to keep R_0 equal to one would be

$$\alpha_2' = \beta\frac{\rho}{\rho_{max}}$$

Thus,

$$F_\alpha = \frac{\alpha_2'}{\alpha_2} = \frac{\left[\beta\frac{\rho}{\rho_{max}}\right]}{\alpha_2}$$

This equation shows that the required fold change to the keep R_0 value lower than one is higher as the extent of lockdown is more. Thus, we argue that the higher F_α has a benefit of unlocking the economy but it comes with a cost in spending financial as well as medical resources in testing. The benefit can be simply written as

benefit=$\frac{F_\alpha}{F_0+F_\alpha}$ takes into account the fact that above certain high quarantine rate F_0 the benefit would saturate. The cost, on the other hand, would also increase with higher quarantine rate as

cost=$\frac{F_\alpha}{F_c-F_\alpha}$ where F_c depicts the maximum capacity of the quarantine rate possible for a particular country on the basis of it's financial and medical resource limitations. The overall balance between the cost and benefit can now be written as

$B = \frac{F_\alpha}{F_0+F_\alpha} - \lambda F_c \frac{F_\alpha}{F_c-F_\alpha}$where λ represents the resource utilization price per unit of maximum testing rate.

At the optimal F_α value, the derivative of the balance equation must be zero. Hence,

$$\frac{\partial B}{\partial F_\alpha} = \frac{F_0}{\left(F_0+F_\alpha\right)^2} - \lambda F_c \frac{F_c}{\left(F_c-F_\alpha\right)^2} = 0$$

$$F_\alpha^{opt} = F_c \frac{\left(\lambda\frac{F_c^2}{F_0}\right)^{\frac{3}{2}}+1}{\left(\lambda\frac{F_c^2}{F_0}\right)^{\frac{1}{2}}+1}$$

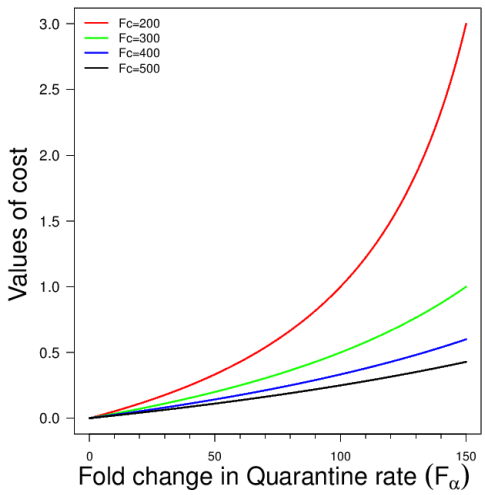
Thus the optimal unlock would be

$$\frac{\beta}{\alpha_2}\frac{\rho_{opt}}{\rho_{max}} = F_c \frac{\left(\lambda\frac{F_c^2}{F_0}\right)^{\frac{3}{2}}+1}{\left(\lambda\frac{F_c^2}{F_0}\right)^{\frac{1}{2}}+1}$$

According to the R0 value from the analytical calculation, it is in general demonstrable that the increased transmission rate can be compensated by increasing the quarantine rate. However, the

quarantine rate can be accentuated by increasing the testing rate incurring extra cost. On the other hand increased transmission rate by partially unlocking the system would benefit the economic transaction. This can be understood quite intuitively. However, each country has different maximum testing capacity. The maximum testing capacity is defined as the maximum number of tests a country can perform per day. Thus, it is not possible to perform more tests than the maximum due to complete exhaustion of resources. Therefore, the relative cost for tests greater than the maximum would be infinite. At test rate zero, the cost would be zero. The cost would approach infinity at the maximum quarantine rate. The simplest possible function which can achieve both the assumptions that it should be zero at zero quarantine rate ($F_\alpha = 0$)and infinite at a maximum quranatine rate ($F_\alpha = F_c$) is $\frac{F_\alpha}{F_c - F_\alpha}$ which is a convex function. From this simple principle, we can argue that the cost curve must be convex as we assumed in the paper based on the assumption that it should monotonically increase with quarantine rate.

So, the main aim of the cost-benefit model is to quantitatively demonstrate that if the maximum quarantine rate is high, then the relative increase in cost for increasing the quarantine rate by some amount is less compared to the case of increasing the quarantine rate by the same amount when maximum quarantine capacity is low. To demonstrate this we plotted the cost curve for different maximum quarantine rate capacities for a particular country and show that the cost is higher for lower maximum capacity for the same increase in quarantine rate.



This can also be illustrated by taking derivative of the cost with respect to F_α

$$C = \frac{F_\alpha}{F_c - F_\alpha} \Rightarrow \frac{dC}{dF_\alpha} = \frac{F_c}{(F_c - F_\alpha)^2} \Rightarrow \frac{1}{C}\frac{dC}{dF_\alpha} = \frac{1}{F_\alpha}\frac{F_c}{F_c - F_\alpha}$$

This equation shows that for a constant value of F_α, both the absolute ($\frac{dC}{dF_\alpha}$) and relative changes in cost ($\frac{1}{C}\frac{dC}{dF_\alpha}$) reduce as the maximum capacity F_c increases (since $F_c > F_\alpha$). This further demonstrates that the relative change in cost becomes very high when quarantine rate change F_α approaches the maximum capacity F_c ($F_c \approx F_\alpha$) owing to exhaustion of resources. This conclusion would remain the same irrespective of the existence of optimum.

As long as the benefit is monotonically increasing with the lockdown opening, at least one maximum would always exist in the cost-benefit trade-off. However, if benefit is so low that the benefit curve never intersects the cost curve, there will be no optimum giving rise to a hopeless situation where no amount of testing is sufficient to open the lockdown.

III. Calculation of of R_0 from the ODE based model

If we assume quarantine by testing following the agent based model described in the previous section, the exposed asymptomatic population would also be quarantined with a rate in addition to the symptomatic infected patients. The equations for this case would be

$$\frac{dS(t)}{dt} = \delta - \delta S(t) - \beta S(t)I(t) - \beta_0 S(t)E(t)$$

$$\frac{dE(t)}{dt} = \beta_0 S(t)E(t) + \beta S(t)I(t) - \alpha_1 E(t) - \alpha_3 E(t) - \delta E(t)$$

$$\frac{dI(t)}{dt} = \alpha_1 E(t) - \alpha_2 I(t) - \delta I(t)$$

$$\frac{dQ(t)}{dt} = \alpha_2 I(t) + \alpha_3 E(t) - \gamma\, Q(t) - \delta Q(t)$$

$$\frac{dR(t)}{dt} = \gamma Q(t) - \delta R(t)$$

Where, we assumed a birth/death rate δ and an extra quarantine rate α_3 in order to accommodate

quarantine by testing which can also identify asymptomatic exposed individuals. In this calculation, we incorporated both the recovered and death by one equation for R(t).

The jacobian at the infection free equilibrium (I=0,E=0) is given by

$$\begin{bmatrix} -\delta & -\beta_0 & -\beta & 0 \\ 0 & \beta_0-(\alpha_1+\alpha_3+\delta) & \beta & 0 \\ 0 & \alpha_1 & -(\alpha_2+\delta) & 0 \\ 0 & \alpha_3 & \alpha_2 & -(\gamma+\delta) \end{bmatrix}$$

The eigenvalues are

$\lambda_1 = -\ \delta, \lambda_2 = -\ \gamma\ -\ \delta$

$$\lambda_{3,4} = \frac{1}{2}\left(\beta_0 - \alpha_1 - \alpha_3 - 2\delta - \alpha_2\right) \pm \frac{1}{2}\sqrt{\left(\beta_0 - \alpha_1 - \alpha_3 - 2\delta - \alpha_2\right)^2 - 4\left[\left(\beta_0 - \alpha_1 - \alpha_3 - \delta\right)\left(\delta + \alpha_2\right) + \alpha\right.}$$

For the infection free equilibrium to be stable

$$\left(\beta_0 - \alpha_1 - \alpha_3 - \delta\right)\left(\delta + \alpha_2\right) + \alpha_1\beta < 0$$

$$R_0 = \frac{\alpha_1\beta}{(\alpha_2+\delta)(\alpha_1+\alpha_3+\delta-\beta_0)} < 1$$

This shows that the reproduction ratio R_0 would reduce if quarantine rate is increased by increasing the test rate through α_3. In the original model for fitting, we assumed that α_3 is small and additionally, the natural death rate/birth rate δis also small in the time scale of the pandemic infection progression so that the total population characteristics remain the same over the timescale. The equation further demonstrates that R_0 would also reduce if the incubation rate $\alpha_1$is high indicating the fact that if the asymptomatic exposed population exhibits symptoms at a higher rate, the spread of infection would be less. However, this will only happen when an asymptomatic carrier is capable of exposing a susceptible person. In fact, if $\beta_0$is negligibly small ($\beta_0 \ll \alpha_3$) in the equation above, the R_0 value would no longer reduce with increasing α_1. This result further illustrates that the effect of asymptomatic spread of infection can be largely mitigated by facilitating more testing and quarantine of the asymptomatic individuals.

According to our calculation shown above, the values of R0 is given by

$$R_0 = \frac{\alpha_1\beta}{(\alpha_2+\delta)(\alpha_1+\alpha_3+\delta-\beta_0)}$$

For the special case we used to fit the data, we assumed that asymptomatic population is not spreading much infection, i.e. $\beta_0 \approx 0$. Additionally, the asymptomatic cases are not quarantined, i.e $\alpha_3 \approx 0$. The δ represents the natural death rate of the population. So the term **δ-δS(t)** corresponds to a birth rate δ and death rate δ for the population where the total population size is normalized to one. Thus at steady state when there is no infection S(t)=1. Now, if we make the final assumption that the natural death rate is small compared to the time scale of infection spread, we can set $\delta = 0$ in the calculation of R0. Consideration of these three assumptions finally produce the R0 as

$$R_0 = \frac{\beta}{\alpha_2}$$

With the introduction of lock down parameter the transmission rate β is replaced as $\beta\frac{\rho}{\rho_{max}}$, finally producing the R0 used in the main text $R_0 = \frac{\beta}{\alpha_2}\frac{\rho}{\rho_{max}}$. Here , $\frac{\rho}{\rho_{max}}$ is the lockdown degree, $\rho = 1$ being the full lockdown case whereas $\rho = \rho_{max}$ being the full unlock scenario. Thus β is the value of transmission rate at full unlock situation.

IV. A case for the periodic lockdown

In a previous study, it was suggested that a periodic lockdown may be a good strategy to optimize unlock and economic activity [1]. Thus, if after every T_1time of full unlock, a lockdown period is imposed for a period of T_2 over a total time N and this cycle continues. Hene, over a cycle of period T, for the interval T_1 , the $\frac{\rho}{\rho_{max}} = 1$and followed by an interval T_2 where $\rho = 1$. The average R_0 over this period is given by

$$\langle R_0 \rangle = \frac{\alpha_1\beta}{\alpha_2(\alpha_1+\alpha_3)}\frac{\left[T_1+\frac{1}{\rho_{max}}(T-T_1)\right]}{T}$$

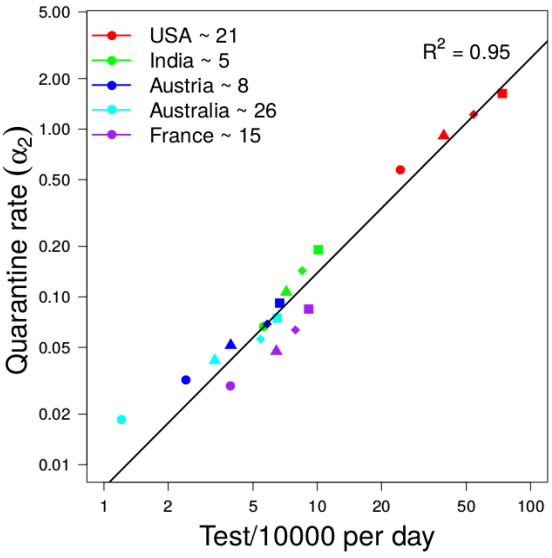
To keep the average equal to 1,

$\frac{T_1}{T} = \frac{\frac{\alpha_2(\alpha_1+\alpha_3)}{\alpha_1\beta}-\frac{1}{\rho_{max}}}{1-\frac{1}{\rho_{max}}}$ which represents allowed unlock number of days over a period time N to keep the average R_0 at equal to 1. This shows that as the effect of lockdown ρ is high the allowed unlock period would also be high. The allowed period can further be stretched by increasing the quarantine rate

involved with testing and quarantining the exposed subjects at a rate α_3 where as small value of α_3 corresponds to the case when testing rate is low which is used in fitting the data.

V. Scaling relation between agent based model and analytical model

In order to investigate the scaling between ODE based and agent based models, we calculated the quarantine rate required to maintain R0 at a value of 1 from the analytical calculation and the corresponding R0 value required to maintain R0 at 1 from the agent based model. We then performed the calculation for all the countries at different unlock degrees and plotted them. So, the x-axis displays the testing rate required to keep R0<1 determined by the ABM whereas the y-axis represents the quarantine rate required to keep R0<1 determined from the analytical calculation. For example, the four red points correspond to four unlock degrees for the USA (square : Full unlock, diamond: 75 % unlock, triangle: 57% unlock and circle: 37% unlock). Similar procedure was followed for other countries as indicated in the figure. Indeed, we found that all points fall on a straight line displaying a high correlation. This result suggests that ODE-based model and agent-based model scale in a linear fashion with each other if we use the same parameter values for both cases and keep the population size the same for all the countries. Thus, one can convert fold change in quarantine rate to fold change in testing rate with a linear scaling.



VI. References

1. Omer Karin *et al.* (2020) Adaptive cyclic exit strategies from lockdown to suppress COVID-19 and allow economic activity. ***medRxiv*** doi: https://doi.org/10.1101/2020.04.04.2005357

VII. Supplementary Figure legends

Figure S1: (A) The regions highlighted in figure 1B are expanded to display the country names (B) The correlation between test rate and doubling rate at two different time points is shown using scatter plot (t=6 and 30 corresponds to the time after alignment as described in the previous section) (C) The scatter plot between test rate and daily confirmed cases for generating the Figure 1C and 1D is shown at two different time points, as an example.

Figure S2: The SEIQR models fit the data for 50 countries, as indicated, for the cumulative confirmed cases. The figures indicate the cumulative data and the corresponding fit is based on the SEIQR model

explained the study.The number of days in X axis corresponds to the time course data available in JHU CSSE [40] where 0 coroposponts to 22nd January, 2020 and the end time point corresponds to 15th August, 2020. It can be noted that keeping the fitted parameters constant but varying extent of lockdown the future increase or decrease in the infection spread trajectory for a given country can be estimated.

Figure S3: (A)The scatter plot showing the relationship between the R_0 and different demographic and medical facility factors as indicated in the figures and in their legend. (B) The scatter plot shows the relationship between the frequencies of seven clades in different countries and corresponding R_0 values.

Figure S4: (A-D) The relationship between the R_0 values and the testing rates for different extents of unlock is shown, as indicated, for different countries. (E) The total number of confirmed cases evolving with time is shown for different percentages of superspreaders, shown here for testing rate of 9/10000

Figure S5: The dynamics of the spread of the infection starting from the initial one infected agent at the centre is shown as a representative output of the agent based stochastic simulation. This example is the result of a simulation for parameter values of the USA with full unlock condition at the testing rate 2.4/10000. The blue, red, green and cyan respectively represent susceptible, undetected infected(asymptomatic+symptomatic), quarantined and recovered agents respectively. The quarantine is performed by testing individuals through contact tracing of the already quarantined patients

Figure S1A

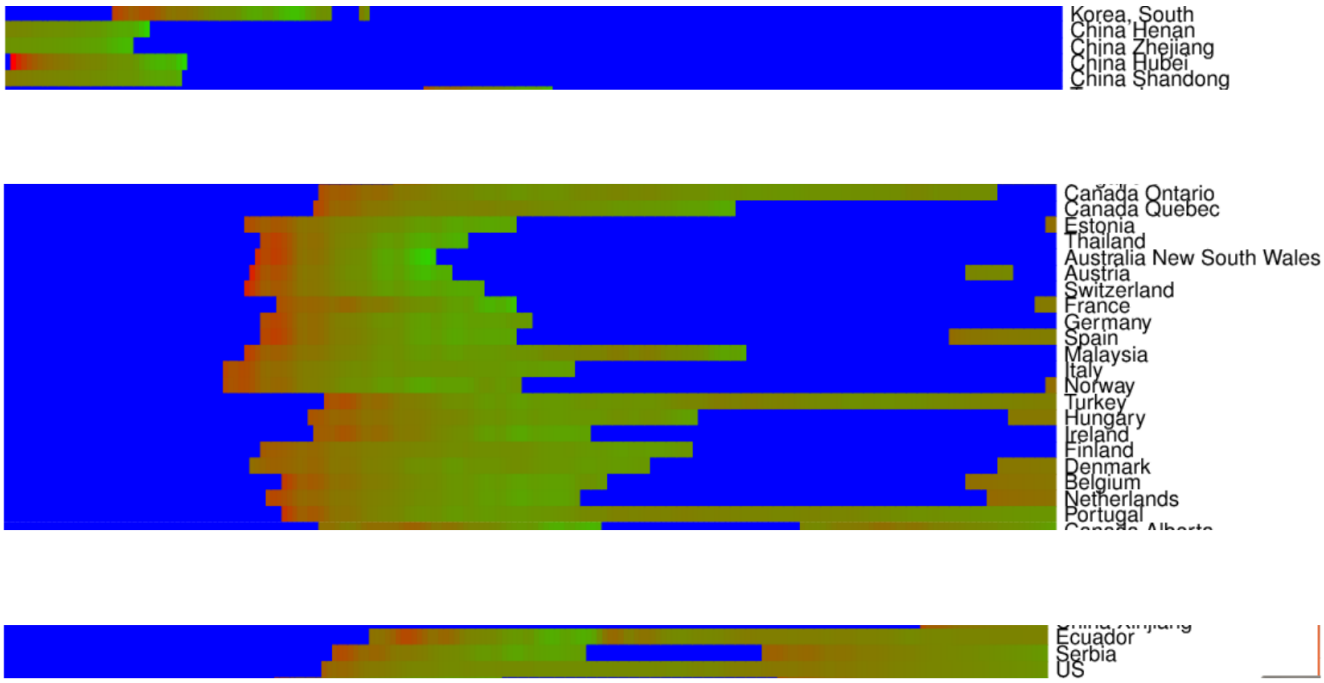

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Figure S1B and S1C

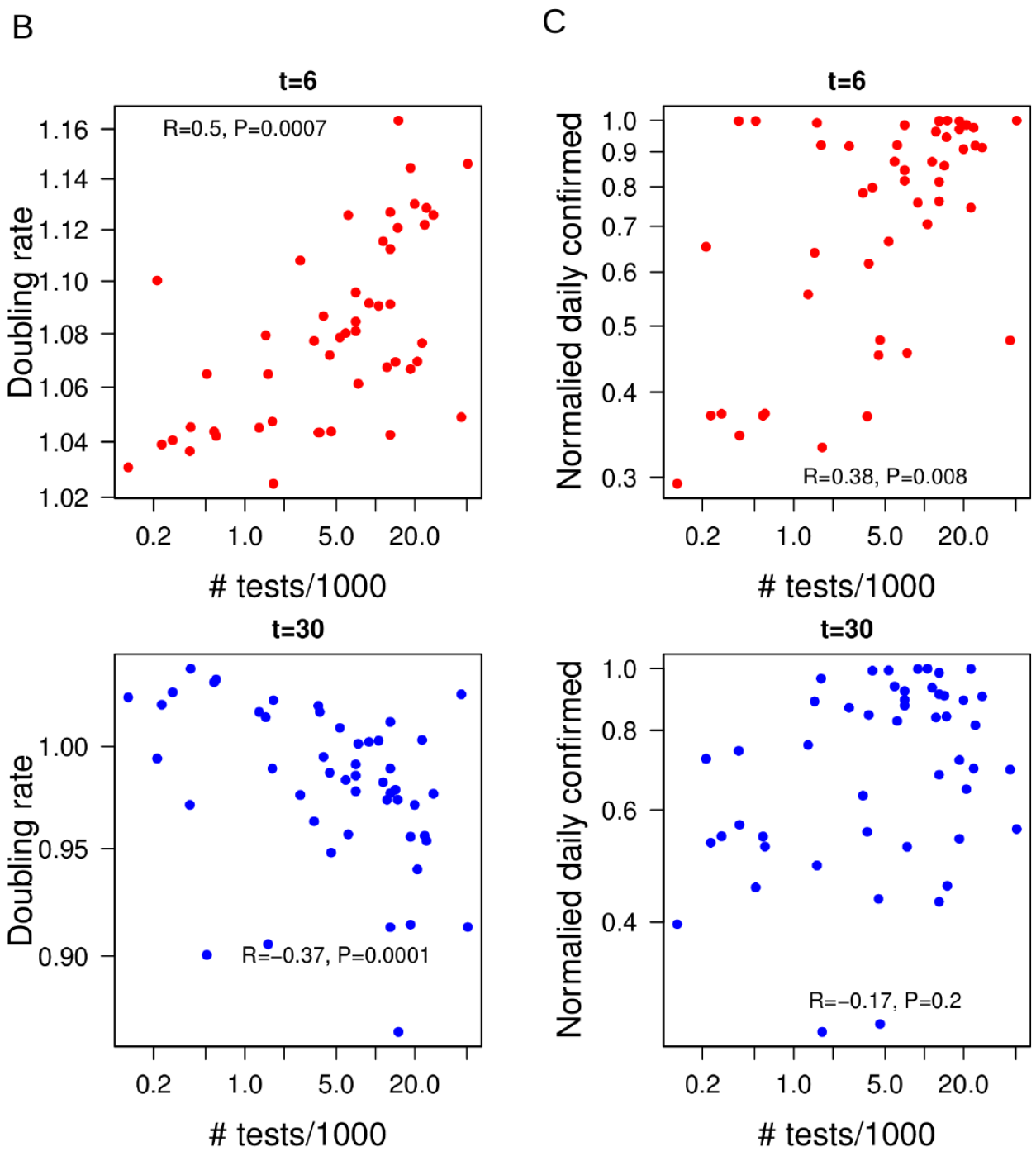

Figure S2

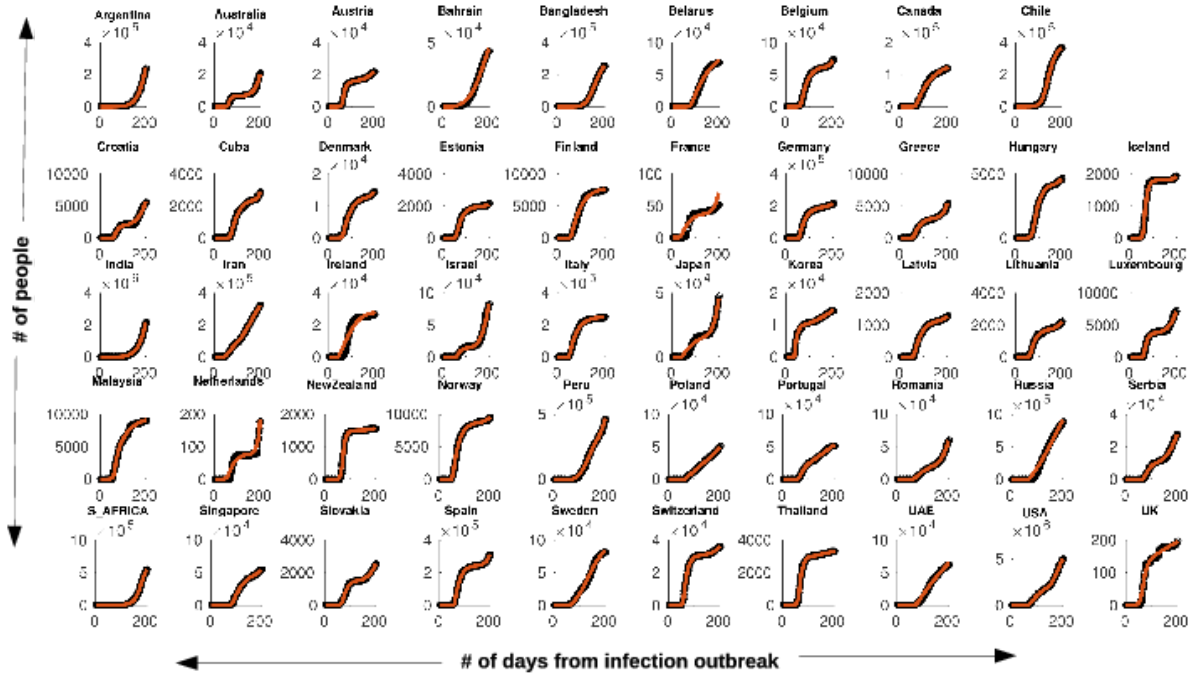
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Figure S3A

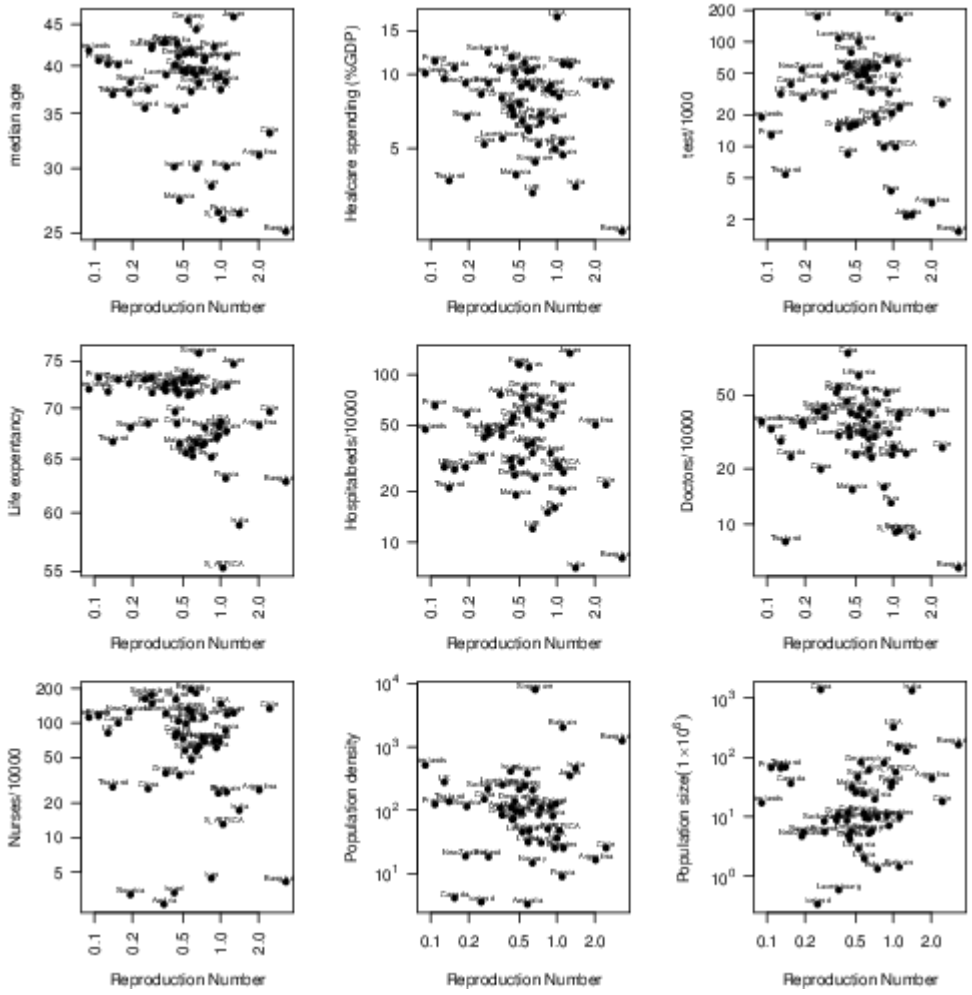
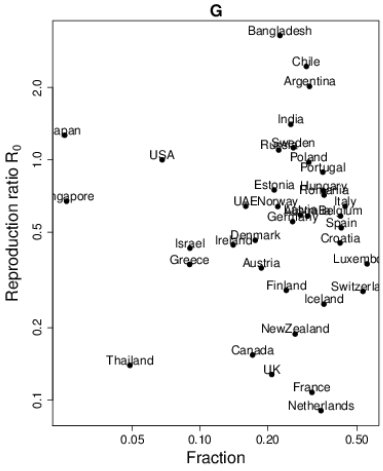


Figure S3B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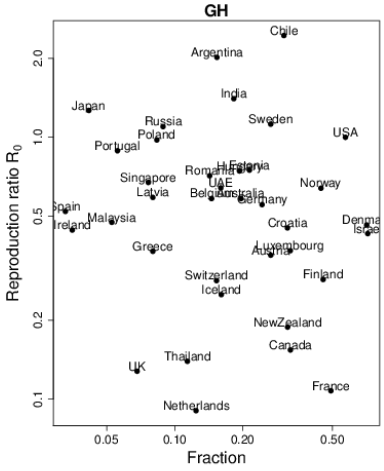
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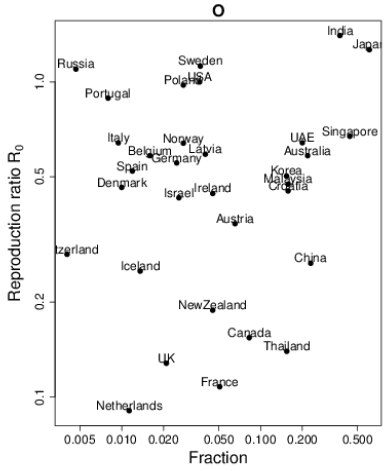
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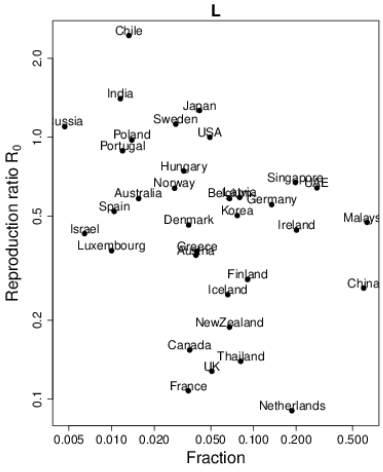
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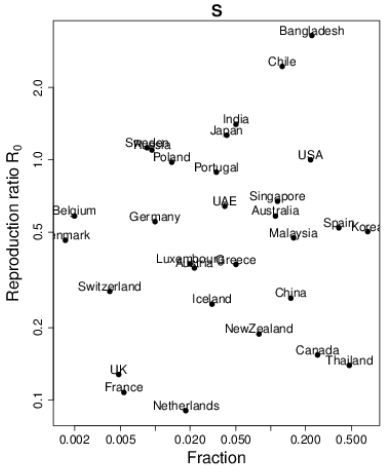
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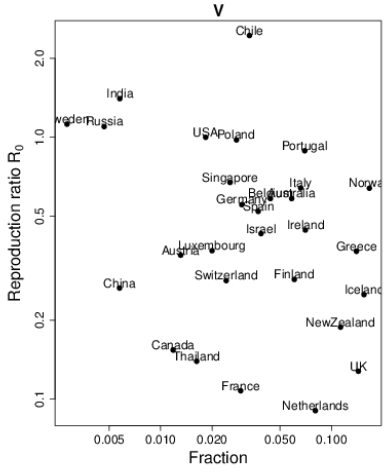
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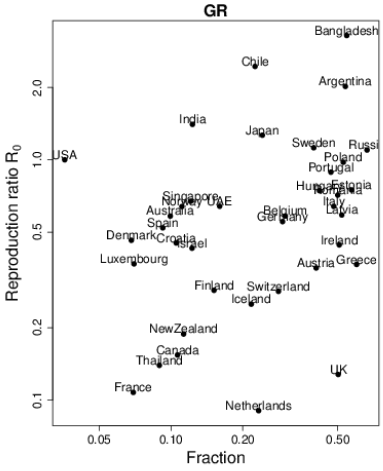
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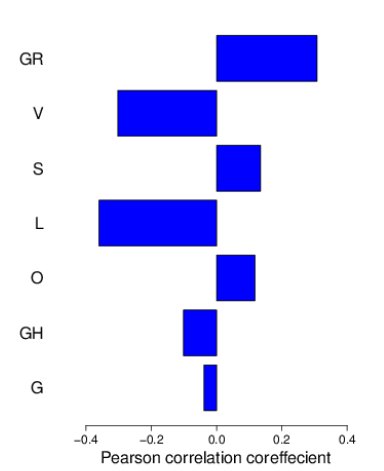
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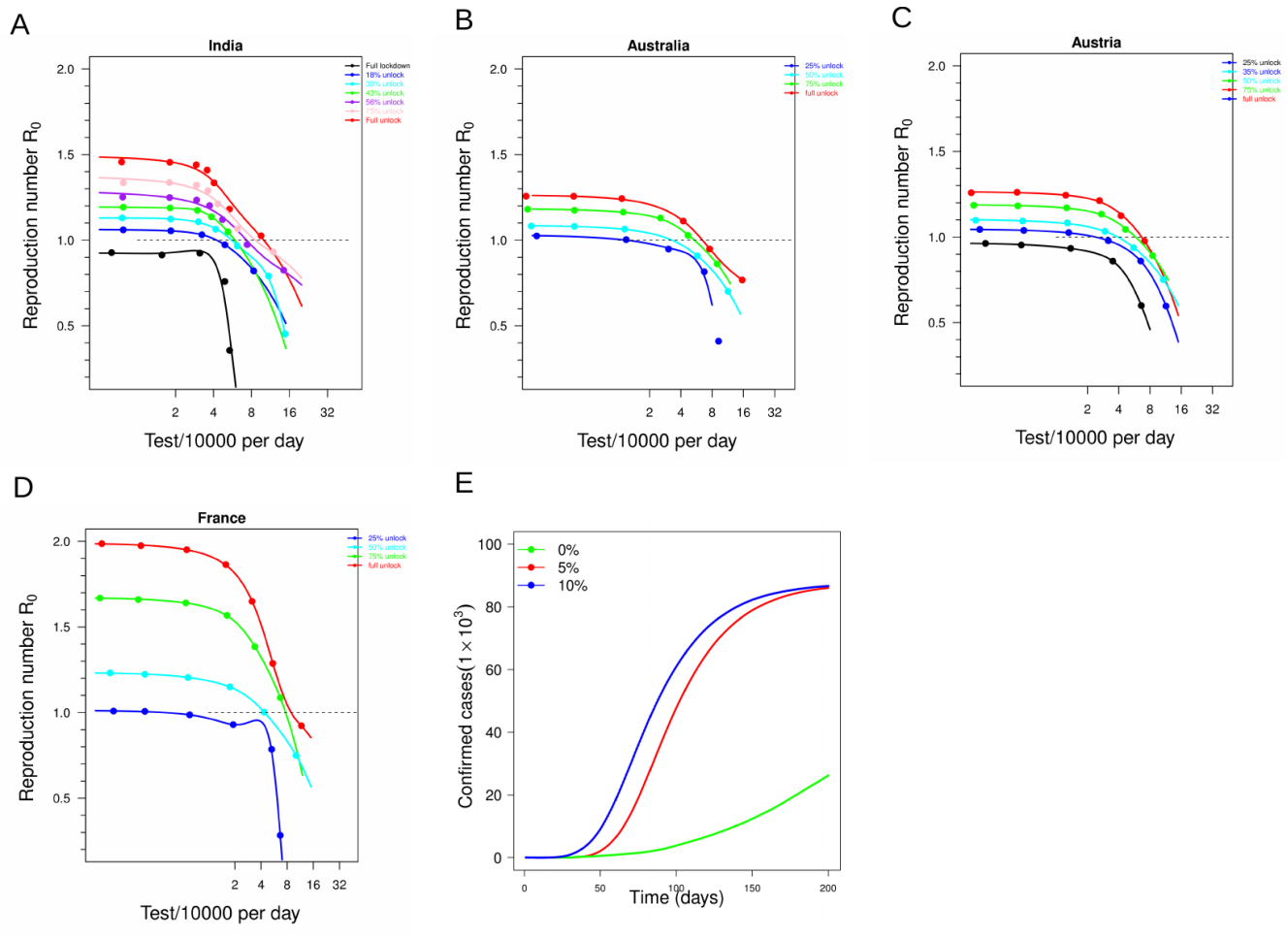
Pearson correlation coreffecient

Figure S4


A
India
Reproduction number R_0
Test/10000 per day
B
Australia
Reproduction number R_0
Test/10000 per day
C
Austria
Reproduction number R_0
Test/10000 per day
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Reproduction number R_0
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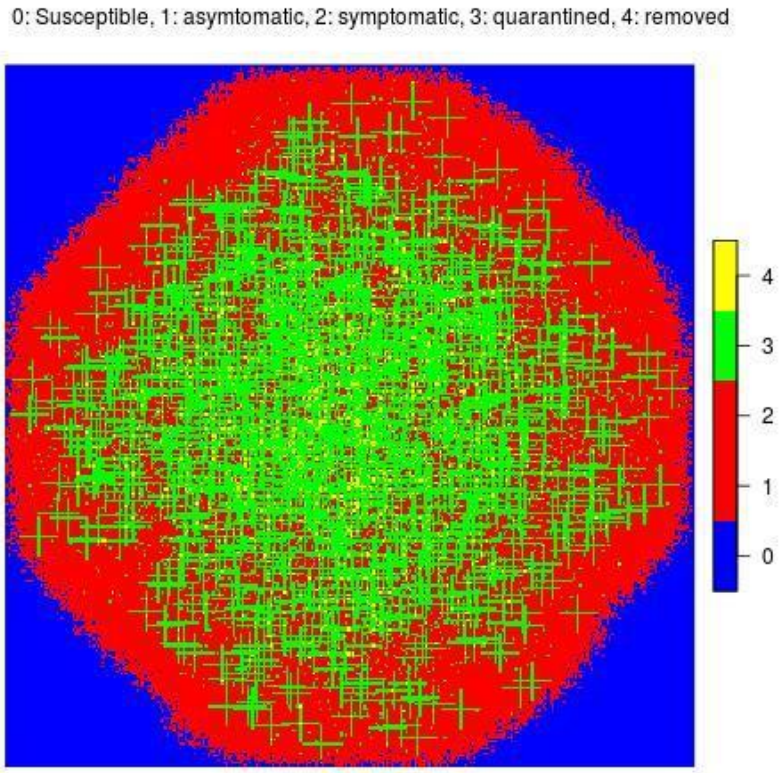
E
0%
5%
10%
Confirmed cases(1×10^3)
Time (days)

Figure S5


0: Susceptible, 1: asymtomatic, 2: symptomatic, 3: quarantined, 4: removed
4
3
2
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