Covid 19: Did preventive restrictions work?

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Abstract:

In the ongoing Covid-19 pandemic, if a preventive restriction (PR), intended to arrest the transmission of the virus, is effective we expect a decrease in the rate of transmission. If an effective PR is lifted or relaxed, the rate may show some increase. We test this expectation in the history of PR imposition and relaxation in all countries based on available public database. We found marginal or no negative correlation between standing stringency index of PR and change in slope of the local curve. A change in stringency index was significantly negatively correlated with change in slope, but change in stringency of PRs could explain only 6.1 percent of the variance in rates of transmission. The distribution of slope changes after imposing versus after relaxing PRs was highly overlapping with only a tail consisting of 4.5% PR impositions being clearly non-overlapping with PR relaxation. Non-parametrically, only 9.4% of PR impositions were associated with a reduction in the slope above the expectation of a null hypothesis. In brief, globally, preventive restrictions have played a very small role in the pandemic process over the one year period. This feedback needs to be considered in making policy for disease prevention in the further course of the pandemic as well as in any future threats of respiratory disease epidemics.

Keywords: Covid-19; lockdown; preventive restriction; rate of transmission; public health policy
In the ongoing pandemic of Covid-19, non-pharmaceutical interventions for prevention of transmission were implemented on an unprecedented global scale. They ranged from personal level safety measures such as use of masks to nation-wide lockdowns. The question whether and to what extent the preventive measures worked is difficult to answer. In the first phase of the epidemic many studies tried to estimate the effect of various non pharmaceutical interventions (NPIs), some of which found the interventions to be quite effective (Alfano and Ercolano 2020, Kharroubi and Saleh 2020, Brauner et al 2021) and others showed limited or disappointing effects (Krishnan et al 2020, Meo et al 2020). The constraints on data in the first phase posed many difficulties in making an unbiased estimate. In any of these studies, there was no control group to compare with, which was an inevitable limitation. Some studies are based on patterns in a single country (Vinceti et al 2020, Gupta et al 2020, Krishnan et al 2020, Kharroubi and Saleh 2020) while others compare across countries (Alfano and Ercolano 2020, Meo et al 2020, Pachetti 2020, Brauner et al 2021, ). A major hurdle in comparative analysis across countries is that a large number of other variables differ substantially between countries making a fair comparison difficult. Some studies take the reduction in an index such as prevalence or rate of transmission as the measure of effectiveness of the intervention (Meo et al 2020, Vinceti et al 2020, Brauner et al 2021). Such studies suffer from a lack of appropriate null model based on spontaneous changes in slope independent of the intervention. Given the multiple hurdles in estimating the efficiency of an intervention, a robust conclusion has been difficult. No study so far has looked at the global picture. Nevertheless, given the global importance of the infection and the possibility that such pandemics can arise again, it is necessary to evaluate the efficacy of the preventive measures using a sound and realistic approach minimizing biases and confounding.

We employed a novel approach to assess the effects of preventive restrictions (PR) on the time trend in incidence on a global scale using countries as units. We avoid any comparison between countries or groups of countries. Instead we look at the intrinsic rate of growth or decline in every country as the slope of the logarithm of daily new cases registered. If a PR measure is applied at a given point in time, after an expected lag, the slope should decrease if the PR were effective. On the other hand if PR were partially or fully lifted, the slope should show an increase over the slope prior to the action. We correlated the change in stringency index at a given time with the subsequent change in slope, for every country separately and then pool the global data. In the course of an epidemic the slope also changes naturally in the absence of any intervention. However, if the spontaneous changes are assumed to be independent of PR, they will not contribute to the correlation. This consideration appropriately incorporates the requirement of a null model of spontaneous change independent of PRs. By this approach, although it is difficult to state whether a given observed change in slope after a change in stringency is spontaneous or is in response to PR, pooling many such cases one can estimate whether and to what extent a change in stringency is correlated to a change in the intrinsic growth rate. If a change in the expected direction, i.e. decrease in slope after imposing PR and increase after relaxing or lifting PR is not observed with a frequency significantly greater than the possible spontaneous change, PR cannot be said to be effective. The significance can be checked parametrically as well as non-parametrically. We tested the population level effect of PRs using this principle, followed by a sensitivity analysis where the assumptions were challenged, the possible biases estimated and it was assessed whether the observed pattern was contributed by the possible biases.
Figure 1: The expected change in slope of the daily incidence trend by imposing or relaxing PR measures. Although in the course of an epidemic, the slope may change spontaneously, if PRs were important determinants of the slope, we expect significant correlation between a change in stringency level of PR and the change in slope associated with it.

Methods: We use public data base (https://ourworldindata.org/coronavirus-data) for the analysis. The stringency index of PRs as available in the database which is a composite measure based on Hale et al (2020) consisting of nine response indicators including school closures, levels of workplace closures, and travel bans, rescaled to a value from 0 to 100 (100 = strictest).

An increase in stringency index corresponds to imposition of a new PR measure and decrease corresponds to relaxing or lifting it. We took the regression slope of eight days prior to the change as the prior slope, then assumed n days’ lag for the effect of the PR change and calculated the regression slope of 8, 11 or 15 following days as the consequent slope. Since there is no clear estimate of the lag time, we used 5, 8, 11, 14 and 17 day’s lag for the analysis. The difference between consequent slope and prior slope was correlated with the standing level of stringency or with the change in stringency. A strong negative correlation was expected if PRs were effective in reducing transmission. We also used R^2 to estimate what proportion of the changes in slope was explained by imposing or lifting PRs.

We used two different sets of correlations based on different expectations. In one, the stringency level of PR on a given day was expected to affect the slope independent of when it was imposed and when relaxed. Here we correlated the stringency index of all days to the difference between consequent and
prior slopes. In another approach, we assume that only a change in stringency level is expected to bring about a change in slope. Here we take only the days on which PRs were imposed or relaxed/lifted and correlate the difference between consequent and prior slope with the change in stringency index.

Results and discussion:

The correlation of standing stringency index and change in stringency index was correlated with the slope change using 5,8,11,14 and 17 days’ lag. The correlation coefficients were seen to be affected by the lag to varying degree. We selected the lag time that gave strongest correlation.

Correlation with standing stringency index

<table>
<thead>
<tr>
<th>n</th>
<th>r</th>
<th>Sample size</th>
<th>p</th>
<th>Variance explained</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>-0.02</td>
<td>26962</td>
<td>=0.001</td>
<td>0.04 %</td>
</tr>
<tr>
<td>8</td>
<td>-0.0128</td>
<td>26382</td>
<td>=0.037</td>
<td>0.0165%</td>
</tr>
<tr>
<td>11</td>
<td>-0.0044</td>
<td>25971</td>
<td>NS</td>
<td>0.0019%</td>
</tr>
<tr>
<td>14</td>
<td>-0.001</td>
<td>25749</td>
<td>NS</td>
<td>9.86E-05 %</td>
</tr>
<tr>
<td>17</td>
<td>-0.0047</td>
<td>25158</td>
<td>NS</td>
<td>2.24E-03 %</td>
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</table>

Correlations with change in stringency

<table>
<thead>
<tr>
<th>n</th>
<th>r</th>
<th>Sample size</th>
<th>p</th>
<th>Variance explained</th>
</tr>
</thead>
<tbody>
<tr>
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<td>1542</td>
<td>&lt;0.0001</td>
<td>0.045 %</td>
</tr>
<tr>
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<tr>
<td>11</td>
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<td>&lt;0.0001</td>
<td>4.3%</td>
</tr>
<tr>
<td>14</td>
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<td>1490</td>
<td>&lt;0.0001</td>
<td>4.42%</td>
</tr>
<tr>
<td>17</td>
<td>-0.209</td>
<td>1457</td>
<td>&lt;0.0001</td>
<td>4.37%</td>
</tr>
</tbody>
</table>

It can be seen that the standing level of PR was poorly correlated with the change in slope (figure 2a). Comparatively the change in stringency, i.e. imposing and relaxing restrictions showed better negative correlations with change in slope (Figure 2b). Maximum effect of PR was seen after 14 days of lag. At this n, maximum correlation was obtained using 11 days for consequent slope. Therefore we did further analysis using this combination of parameters.

<table>
<thead>
<tr>
<th>Days for trend</th>
<th>r</th>
<th>Sample size</th>
<th>p</th>
<th>Variance explained</th>
</tr>
</thead>
<tbody>
<tr>
<td>8</td>
<td>-0.211</td>
<td>1520</td>
<td>&lt;0.0001</td>
<td>4.42%</td>
</tr>
<tr>
<td>11</td>
<td>-0.24</td>
<td>1456</td>
<td>&lt;0.0001</td>
<td>5.7%</td>
</tr>
<tr>
<td>15</td>
<td>-0.19</td>
<td>1441</td>
<td>&lt;0.0001</td>
<td>3.7%</td>
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</table>

At its best, imposition and relaxation of PRs explained only 6.1 % variance in the changes in slope (figure 2b). Thus over 93% of the course of the pandemic does not appear to be influenced by PRs.
Figure 2: Scatter plots of (A) standing stringency index and the associated change in slope. In this analysis we didn’t see the expected correlation between stringency and change in slope. (B) The change in stringency, i.e. imposing or relaxing restrictions was significantly negatively correlated with slope change, but the variance in slope explained was only 6.1%.

Pooling all impositions together and all relaxations together, we observed that the distribution of change in slopes after imposition of PR and relaxation of PR were highly overlapping with only a marginal shift leftwards by imposing restrictions. There was a longish left hand tail to this distribution clearly non-overlapping with the distribution of slopes following PR relaxation, presumably representing the exceptional cases in which PR gave an undoubted and spectacular success. Such clear effective demonstrations of the efficiency of PRs are only 33, i.e. 4.5 % of the total PRs imposed. Although an increase in stringency is expected to give a negative change in slope, 31% PR impositions resulted into a positive change. Similarly although lifting of PR was expected to increase the slope, 45.4 % times the slope actually decreased.
Figure 3: The frequency distribution of slope change in response to imposing PR (red bars) and lifting PRs (blue bars). The distribution is surprisingly overlapping, i.e. both imposing and lifting restriction is followed by positive and negative changes in slope. The modes of the distribution lie very close to each other. The main difference is in the longish left hand tail that the distribution after PR imposition has, which represents about 4.5% of all PR impositions.

The mean change in slope on imposing restrictions was -0.01636 and on relaxing PR was 0.001734 the absolute mean difference being -0.01809 corresponding to 0.41 standard deviation.

Non-parametric analysis: We see how frequently a positive change in PR is associated with a negative change in slope, taking a null hypothesis of independence. We see again that the effect of change in PR is statistically highly significant (Chi sq = 50.54, p < 0.0001), but only 9.4% of PRs lie above what is expected by the null hypothesis.
Figure 4: We expect that imposing PR should reduce the transmission and lifting PR should have the reverse effect. This effect is seen statistically significantly, but a surprisingly large proportion of changes appear to be independent of stringency change.

In brief standing levels of restrictions did not appear to affect the rate of transmission, whereas increase in stringency reduced the transmission with statistically significant frequency but using different statistical considerations only between 4.5 to 9.4 % of the changes could be accounted for by imposition or relaxation of PRs.

Limitations, Sensitivity to biases and confounding factors:

We relaxed our assumptions and checked for possible sources of biases to examine whether the low performance of PRs is a result of one or more sources of bias in the data. The data has certain limitations and some possible sources of bias can be identified.

(i) Limitations of stringency index: Our analysis is based on a stringency index defined by Hale et al 2021 and made available by (https://ourworldindata.org/coronavirus-data). The allocation of importance to the different components of PR is rather subjective and all components are not expected to contribute equally to the effect. Nevertheless, as long as some components were effective, they should have been reflected at least in the non-parametric analysis. It is also possible that the stringency index is based on the official declaration of the respective governments, but the on ground implementation does not closely follow the one declared. It is important to examine in what direction this limitation can bias the analysis. In this analysis we are not comparing countries with each other. So the stringency index of one country need not be identical to the same index of another. As long as a positive change in stringency brings about a negative change in transmission, our analysis can detect it. For countries where implementation was weak, we can make a limiting assumption that the changes in slope were independent of the stringency index in
that country. This will certainly create more noise in the correlation, but as long as a sizable number of countries implement the PRs efficiently, a good correlation is expected if PRs worked. The poor R² implies that either very few countries implemented the PRs efficiently or they worked poorly throughout the globe.

(ii) Prior slope and implementation bias: Throughout the data, independent of PRs, we observe a negative correlation of prior slope and slope difference. This is expected by any typical epidemiological model as well. When an epidemic spreads, the rate of transmission reduces gradually. In the global data there is a strong negative correlation between prior slope and change in slope (r= -0.81, p < 0.0001). Furthermore PR implementation is more likely when slope is positive and PR relaxation more likely when prior slope is negative. This negative correlation is also evident in the data (r=0.097, p < 0.0001) although somewhat weak. Therefore even if PRs are assumed to have no effect, a negative correlation is expected owing to the combined effect of these two biases. This bias is likely to have contributed to the observed negative correlation between change in stringency and change in slope. Any attempt to correct for this bias would weaken the negative correlations further.

(iii) Since this approach to test the efficiency of PR is based on collective data, it cannot be applied to individual countries. In individual cases it is not possible to segregate spontaneous changes in slope from PR induced changes. Our analysis therefore does not state in which countries PRs were effective and in which countries they were not. This is a limitation of our approach.

Conclusions: Although we see a statistically significant negative correlation between a change in stringency of PR and change in the slope indicating rate of transmission, the variance in the rate of transmission explained by preventive restrictions is very small. Interestingly, standing level of stringency does not show significant correlation with change in rate of transmission, only a change in stringency does. It is likely that in dynamics of transmission, the rate reaches a steady state with a given level of stringency and does not drop further. It is also likely that immediately after imposing PR the implementation is tight but slowly the rigor of implementation declines. Further, given the possibility of bias, the apparent magnitude of effect is questionable, and the true magnitude might be even lower. Thus globally the preventive restrictions appear to have very marginal effects on the transmission of the virus. Our conclusion contrasts many of the early studies that claimed substantial success of the lockdown in many countries (Alfano and Ercolano 2020, Kharroubi and Saleh 2020, Brauner et al 2021). This contradiction is likely to be because of multiple factors. First, most of these studies did not consider the spontaneous changes in slope as a null model. All the studies were conducted during the first phase of the epidemic. For any statistical test, a necessary assumption is the independence of data points from each other. In the first phase there was substantial synchrony in the epidemic curves and the imposition of lockdown measures, which may have violated this assumption. Subsequently different countries accumulated differences in the ups and downs of the epidemic as well as the history of imposing and relaxing PRs. Therefore statistics at the current stage is less likely to violate the assumption of independence. An epidemic is a complex process and the relationship between contact behaviors and viral transmission is likely to be highly non-linear. Therefore the simple assumptions behind the PRs may work in reality only in certain contexts but not in others. Furthermore in the first phase, when PRs were
implemented, the number of infective foci and the proportion of asymptomatic cases was smaller. At this stage PRs are more likely to be effective. As the infectious foci increased and the number of undetected and asymptomatic cases increased, it would have been more difficult to arrest the transmission by preventive restrictions (Nisar et al 2020, Gao et al 2020, Wavte et al 2020). Therefore although the PRs might have helped in the early phase of the pandemic, they might have lost their efficiency subsequently.

This was the first time in the history of preventive medicine that PRs were applied on a global scale with the intension of reducing the viral transmission. The PRs have a large social and economic cost, which some communities can tolerate but others cannot (Ghosh 2020). Therefore the policy of applying stringent measures for arresting the spread of respiratory infections needs rethinking and evaluating vis-a-vis their social costs in the context of every community separately.

References: