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The temporal association of introducing and lifting non-pharmaceutical interventions with the time-varying reproduction number (R) of SARS-CoV-2: a modelling study across 131 countries

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Abstract

Background

Non-pharmaceutical interventions (NPIs) were implemented by many countries to reduce the transmission of SARS-CoV-2, the causal agent of COVID-19. A resurgence in COVID-19 cases has been reported in some countries that lifted some of these NPIs. We aimed to understand the association between introducing/lifting NPIs and the level of transmission of SARS-CoV-2 as measured by the time-varying reproduction number (R) from a broad perspective across 131 countries.

Methods

We linked data on daily country-level estimates of R from the London School of Hygiene and Tropical Medicine (LSHTM) with data on country-specific policies on NPIs from the Oxford COVID-19 Government Response Tracker (OxCGRT), available between 31-December-2019 and 20-Jul-2020. We defined a phase as a time period when all NPIs remained the same and we divided the timeline of each country into individual phases based on the status of NPIs. We calculated the R ratio as the ratio between daily R of each phase and the R from the last day of its previous phase (i.e. before the NPI status changed) as a measure of the association between NPI(s) status and transmission of SARS-CoV-2. We then modelled the R ratio using a log-linear regression with introduction and relaxation of each NPI as independent variables for each day of the first 28 days following the change in the corresponding NPI.

Findings

A total of 790 phases from 131 countries were included in the analysis. Individual NPIs, including school closure, workplace closure, public events ban, requirements to stay at home, and internal movement limits, were associated with a reduction in R of 7–24% on Day 28 following the introduction although the reduction was only statistically significant for public events ban. Re-opening school, lifting ban on public events, lifting ban on social gathering of >10 persons, and lifting internal movement limits were associated with an increase in R of 11–25% on Day 28 following the relaxation, although the increase was only stastically significant for re-opening school and lifting ban on social gathering of >10 persons. The effects of introducing and lifting NPIs were not immediate; it took 8 days (interquartile range, IQR: 6–9) following the introduction to observe 60% of their maximum reduction in R and even longer (17 days, IQR: 14–20) following the relaxation to observe 60% of the maximum increase in R. In response to a possible resurgence of COVID-19, a control strategy of banning public events and social gathering (of >10 persons) was estimated to reduce R, with an R ratio of 0·71 (95% CI: 0·55-0·93) on Day 28; and with an R ratio of 0·62 (95% CI: 0·47-0·82) on Day 28 if measures to close workplaces is added.

Interpretation

Individual NPIs, including school closure, workplace closure, public events ban, ban on gathering size of >10 persons, requirements to stay at home, and internal movement limits, are associated with reduced transmission of SARS-CoV-2 but the effect of introducing/lifting these NPIs is delayed by 1–3 weeks, with this delay being longer when lifting NPIs. These findings provide additional evidence that can inform policy-maker decisions on the timing of introducing and lifting different NPIs, although it should be noted that R needs to be interpreted in the context of its known limitations.

Funding

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Research in context

Evidence before this study

The time-varying reproduction number (R or R_t), defined by the expected number of secondary cases arising from a primary case infected at time t, is a metric that describes the viral transmission on population level. An R over one indicates a growing outbreak and an R below one indicates a shrinking outbreak. We searched PubMed, MedRxiv and BioRxiv for studies that reported the effects of introducing and lifting non-pharmaceutical interventions (NPIs) on R of SARS-CoV-2 between 1st Jan 2020 and 5th Aug 2020, using the keywords "COVID-19", "SARS-CoV-2", "intervention" and "transmission". Earlier studies in China (including Hong Kong), South Korea, Singapore and several European countries showed that major NPIs including school closure, social distancing and lockdown could reduce R substantially to near or below one. However, little was known about the effects on R following the relaxation of these NPIs.

Added value of this study

To the best of our knowledge, this is the first study that explicitly quantified the effects of both introducing and lifting individual NPIs on R over time from a broad perspective across 131 countries. By linking the global dataset of country-level daily R values with the global dataset of country-level policies on NPIs, we modelled the change in R values (as R ratio) from Day 1 to Day 28 following the introduction and relaxation of eight individual NPIs among 131 countries. We found that re-opening schools, lifting ban on public events, lifting ban on social gathering of >10 persons, and lifting internal movement limits were associated with an increase in R of 11–25% on Day 28 following the relaxation. However, the effects of introducing and lifting NPIs were not immediate; it took 8 days (IQR: 6–9) following the introduction of NPIs to observe 60% of their maximum reduction in R and even longer (17 days, IQR: 14–20) following the relaxation to observe 60% of the maximum increase in R. A similar delay in response to the introduction/relaxation of NPIs was also identified using Google mobility data. We compared four different candidates of composite NPIs that countries might consider in response to a possible resurgence of COVID-19.

Implications of all the available evidence

We quantified the change in the transmission of SARS-CoV-2 as measured by R following the introduction and relaxation of individual NPIs and highlighted the delay of 1–3 weeks in observing the effect of introducing and lifting these NPIs. These findings provide additional evidence that can inform policy-maker decisions on which NPIs to introduce or lift and when to expect a notable effect following the introduction or the relaxation.

Introduction

The novel coronavirus SARS-CoV-2 that originated in Wuhan, China in December 2019 has since spread worldwide and the resulting COVID-19 pandemic has caused over 18 million confirmed cases and over 690,000 deaths as on 3rd August 2020.[1] From early March 2020, population-level non-pharmaceutical interventions (NPIs) to reduce SARS-CoV-2 transmission were introduced in a number of countries affected by COVID-19, and have included school closures, public event bans, restrictions on gatherings, and requirements to stay at home. Since the beginning of May 2020, a number of countries started to lift some of these NPIs and some countries have witnessed a second surge in the number of reported COVID-19 cases. It is important to understand the impact of introducing and lifting these NPIs on the transmission of SARS-CoV-2.

The time-varying reproduction number, which is often referred to as "R" or "R_t", is defined by the expected number of secondary cases arising from a primary case infected at time t. R is an important metric for measuring time-specific transmissibility and could be used for assessing whether current interventions appear to be effective, or whether additional interventions are required. If R remains below one, then the epidemics will eventually die out; if R is above one, sustained epidemics are expected.

Earlier studies in China (including Hong Kong), South Korea, Singapore and several European countries showed that major NPIs including school closure, social distancing and lockdown could reduce R substantially to near or below one.[2-12] However, little was reported regarding the effects on R following the relaxation of these NPIs. In the present study, we aimed to assess the temporal association between introducing and lifting different NPIs and levels of SARS-CoV-2 transmission measured by R from a broad perspective across 131 countries.

Methods

Data sources

We included data on country-level estimates of R from the EpiForecasts project by London School of Hygiene and Tropical Medicine (LSHTM).[13] Briefly, the instantaneous reproduction number was estimated based on the daily counts of confirmed COVID-19 cases reported by the European Centre for Disease Prevention and Control. The instantaneous reproduction number represents the average number of secondary cases that would arise from a primary case infected at a given time if the conditions remained identical after that time; and thus measures the instantaneous transmissibility.[14] The modelling framework accounted for reporting delay between symptom onset and case notification, right truncation of notification dates, and the delay between onset and infection based on empirical data to ensure that temporal variations in R could be compared directly with the times at which NPIs were implemented.[13]

We included data on country-specific policies on NPIs from the Oxford COVID-19 Government Response Tracker (OxCGRT).[15] OxCGRT was established by a dedicated team of public policy and goverance experts, who collected publicly available information on indicators of government response. In OxCGRT, NPIs were grouped into the following eight categories: closure of schools, closure of workplaces, public event bans (e.g. sports, festive, religious, etc.), restrictions on (size of) gathering, closure of public transport, stay at home orders, restrictions on internal movement and restrictions on international travel. Country-specific information on each of the NPIs was available on a daily basis. We also included data on testing policy and contact tracing of each country from OxCGRT for sensitivity analyses.

Data processing

We linked the two above-mentioned datasets by country and date. This generated our working dataset that contained time series of daily R estimates and the status of the eight NPIs for 131 countries between 31-December-2019 and 20-Jul-2020. Details on the start and end date of our working dataset are available in **Table S1** (pp 2–4 in the appendix).

The original variables of NPIs in the OxCGRT dataset were ordinal, generally from "no intervention" (0 points), to "recommend intervention" (1 point), and then to "require intervention" (2 points). In the present study, we converted these NPI variables to a binary variable by merging the levels of "no intervention" and "recommend intervention", in order to increase the statistical power of the analysis. Details of the conversion of each NPI variable are available in **Table S2** (pp 5–6 in the appendix).

Data analysis

We defined a phase as a time period when all of the eight NPIs remained the same and we divided the timeline of each country into individual phases based on the status of NPIs. We first described the duration of phases, the frequency of introducing/lifting each NPI and the temporal order of introducing/lifting each NPI. For each phase, we defined $R_{day=i}$ as the R of the ith day of that phase (i.e. since the NPI status changed) and defined $R_{day=0}$ as the R of the last day of its previous phase (i.e. before the NPI status changed). As the effect of NPIs on transmission (measured as R) is expected to be relative to its original level, we calculated the R ratio between $R_{day=i}$ and $R_{day=0}$ as a measure of the degree of association between introducing/lifting NPI(s) with the transmission of SARS-CoV-2 (**Figure 1**). An R ratio of > 1 indicates an increase in transmission since the change in the

NPI(s) and an R ratio of < 1 indicates a decrease in transmission. Based on the change of NPIs between two neighbouring phases and the corresponding R ratio, we were able to assess the effect of ordering/lifting each of the NPIs.

In the main analysis, we modelled the R ratio using a log-linear regression, with the following equation, for each day of the first 28 days following the change in the corresponding NPI (i.e. a total of 28 separate models).

$$\log(Y^t) = \beta_0^t + \beta_1^t X_1^t + \beta_2^t X_2^t + \cdots + \beta_{16}^t X_{16}^t + \beta_{17}^t Z_1^t + \beta_{18}^t Z_2^t$$

where Y^t represents the R ratio on Day t ($t = 1, 2, \ldots, 28$); X_1^t to X_{16}^t are binary indicators of whether each of the eight NPIs are introduced and lifted, respectively; Z_1^t and Z_2^t are binary indicators of whether multiple NPIs are introduced and lifted simultaneously, respectively. Hence, β_0^t represents the baseline change in R on Day t in the absence of changes in NPI status; β_1^t to β_{16}^t represent the individual effects of introducing and lifting NPIs on Day t; β_{17}^t and β_{18}^t represent the interaction between introducing and lifting multiple NPIs are introduced and lifted simultaneously, respectively. No days beyond the first 28 days following the change were included due to limited data availability.

Based on the model estimates, for each NPI, we calculated the time length in days needed to reach 60% of its maximum effect (measured by R ratio) in the first 28 days as a measure of immediacy. Furthermore, we modelled the total visits to workplace and the total time of staying at residential areas using Google mobility data by applying the same regression model as main analysis among 101 countries (details in Appendix p 7). We compared the immediacy results of introducing/lifting workplace closure between using R ratio and using total visits to workplace. We also compared the immediacy results of introducing/lifting requirements to stay at home between using R ratio and using total time of staying at residential areas.

We conducted a series of sensitivity analyses. First, we replaced the NPI of ban on gathering size of >10 persons with ban on gathering size of >100 persons in the model; this is to understand how limiting social gatherings of different sizes could affect the transmission. Second, we presented the effect of individual NPI by only including phases in which only one NPI was changed. Third, we used a different comparator, the average R in the last 7 days (rather than R of Day 0), when calculating the R ratio. Fourth, we excluded early phases in which country's first NPI was introduced. Fifth, we excluded a list of countries that could have greater variability in NPI policies: Brazil, Canada, China, India, Russia and United States. Sixth, we conducted 20 sets of analyses, each of which randomly excluded 10 countries from the dataset, in order to understand how our estimates had been impacted by possible outliers. Seventh, we only included the phases with comprehensive testing (defined as requiring to test anyone with COVID-19 symptoms) in the analysis since testing practice could affect the estimate of R. Eighth, we only included the phases with comprehensive contact tracing (defined as requiring to conduct contact trancing for all COVID-19 cases) introduced to understand how contact tracing could modify the effect of NPIs in our model.

In addition, based on the modelled effect of individual NPIs from our main analysis, we conducted an ad-hoc analysis on estimating the effect of introducing multiple NPIs that could be considered for re-introduction to tackle the possible resurgence of SARS-CoV-2. We considered four candidate strategies for the re-introduction:

- Ban on public events and gathering (>10 persons) —Candidate 1
- Workplace closure, and ban on public events and gathering (>10 persons) —Candidate 2
- Workplace closure, ban on public events and gathering (>10 persons), and internal movement limits —Candidate 3
- School and workplace closure, ban on public events and gathering (>10 persons), internal movement limits, and requirements to stay at home —Candidate 4

All data analyses and data visualisation were conducted in the R software (version 3.6.1).[16] The R codes and the corresponding working dataset used for the analyses are available in GitHub (https://github.com/leoly2017/COVID_NPI_R).

Role of the funding source

The study received funding from Wellcome Trust Institutional Strategic Support Fund and Data-Driven Innovation initiative. The funders of the study had no role in study design, data collection, data analysis, data interpretation, writing of the manuscript, or the decision to submit for publication. All authors had full access to all the data in the study and were responsible for the decision to submit the manuscript for publication.

Results

Descriptive results of phases and NPIs

A total of 790 phases from 131 countries were included in the analysis (details on daily R estimates and NPI status for each country in **Figure S1**, Appendix pp 8–40). The median duration of phases was 11 days (interquartile range, IQR: 3–27), with shortest median duration observed in phases in which closure of schools (3 days [IQR: 1–8]) and public events ban (3·5 days [IQR: 2–7]) were introduced (**Figure S2**, Appendix p 41). Requirements to stay at home and restrictions on internal movements were the most common NPIs introduced and were most often introduced and lifted simultaneously (**Figure 2**). With regard to the temporal sequence of introducing and lifting NPIs, closure of schools and public events ban were the first two NPIs introduced and were lifted later than most NPIs. Requirements to stay at home and closure of public transport were the last two NPIs introduced and were lifted earlier than most NPIs (**Figure 2**).

Temporal associations between NPI status and transmission level as measured by R

According to the results from the main analysis, a decreasing trend over time in the R ratio was found in the first 14 days following the introduction of school closure, workplace closure, public events ban, requirements to stay at home and internal movement limits (**Figure 3**). The introduction of a public events ban was associated with the highest reduction in R; the corresponding R ratio on Day 7, Day 14 and Day 28 was 0·90 (95% CI: 0·82–0·99), 0·83 (95% CI: 0·68–1·00) and 0·76 (95% CI: 0·58–1·00), respectively (**Table 1**). An increasing trend over time in the R ratio was found following the relaxation of NPIs, especially after the first week after relaxation (**Figure 3**). The relaxation of a ban on gathering size of >10 persons was associated with the highest increase in R; the corresponding R ratio on Day 7, Day 14 and Day 28 was 0·99 (95% CI: 0·93–1·06), 1·07 (95% CI: 0·96–1·20) and 1·25 (95% CI: 1·03–1·51). Negative interaction, i.e. towards R ratio of 1, was identified when multiple NPIs were introduced or lifted simultaneously (**Figure S3**, Appendix p 42).

The immediacy of effect by introducing/lifting NPIs differed. The effects of introducing and lifting NPIs were not immediate; it took 8 days (interquartile range, IQR: 6–9) following the introduction to observe 60% of their maximum reduction in R and even longer (17 days, IQR: 14–20) following the relaxation to observe 60% of the maximum increase in R (**Figure S4**, Appendix p 43). Similar delays were noted for workplace closure and requirements to stay at home using Google mobility data (**Figure S5**, Appendix p 44): it took 6 days and 12 days (compared with 6 days and 9 days by using R) following the introduction and relaxation of workplace closure, respectively, to observe 60% of the maximum change in the total visits to workplace; it took 6 days and 17 days (compared with 6 days and 23 days by using R) following the introduction and relaxation of requirements to stay at home, respectively, to observe 60% of the maximum change in the total time of staying at residential areas.

When comparing the effect by the ban on gathering size of >10 persons and the ban on gathering size of >100 persons, we found that both bans showed a decrease of R ratio in the first week, followed by an increase of R ratio starting from the second week but the increase was more pronounced for the ban on gathering size of >100 persons, with R ratios of over 1 after Day 14 (**Figure 4**). When lifting these two bans, we observed a delayed increase of R for the ban on gathering size of >10 persons (**Figure S6**, Appendix p 45); the R ratio was 1·07 (95%: 0·96–1·20) for lifting the ban on gathering size of >10 persons on Day 14 and was 1·23 (95%: 1·07–1·42) for lifting the ban on gathering size of >100 persons on Day 14 (**Figure 4**).

Similar results were observed from sensitivity analyses that only included phases during which only one NPI was changed (**Figure S7**, Appendix p 45); used the average R of last 7 days (rather than the last day) in the previous phase for calculating R ratio (**Figure S8**, Appendix p 47); excluded early phases when country's first NPI was introduced (**Figure S9**, Appendix p 48); excluded countries that could have greater variability in NPI policies (**Figure S10**, Appendix p 49); excluded 10 countries randomly (**Figure S11**, Appendix p 50); included only phases with comprehensive testing (**Figure S12**, Appendix p 51); and included only phases with comprehensive contact tracing (**Figure S13**, Appendix p 52), although with wider confidence intervals due to data scarcity.

Effects of candidate composite NPIs over time

Based on the results from the main analysis, we estimated the effects of four candidates of composite NPIs (**Table 2** and **Figure S14**, Appendix p 53). A ban on both public events and on gathering size of >10 persons (i.e. Candidate 1) was associated with a reduction in R of 6% on Day 7, 13% on Day 14, and 29% on Day 28. If this was extended to include workplace closures (i.e. Candidate 2), the overall reduction in R would be 16% on Day 7, 22% on Day 14, and 38% on Day 28. If this was further extended to include internal movement limits (i.e. Candidate 3), the overall reduction in R would be 19% on Day 7, 24% on Day 14, and 42% on Day 28. Additionally, a more extreme intervention that included school closure and required people to stay at home in addition to interventions in Candidate 2 (i.e. Candidate 4) was associated with a reduction in R by 35% on Day 7, 42% on Day 14, and 52% on Day 28.

Discussion

To the best of our knowledge, this is the first study that assesses the temporal association between changing the status of a range of NPIs and the transmission of SARS-CoV-2 as measured by R for all countries for which there are data. Based on the empirical data from 131 countries, our findings suggest that individual NPIs, including school closures, workplace closures, public events ban, requirements to stay at home, and internal movement limits, are associated with a reduction in R of 7–24% on Day 28 following the introduction, compared with the last day of pre-introduction. Re-opening school, lifting ban on public events, lifting ban on social gathering of >10 persons, and lifting internal movement limits are associated with an increase in R of 11–25%, individually, on Day 28 following the relaxation. The effects of introducing and lifting NPIs were not immediate; it took 8 days (IQR: 6–9) following the introduction to observe 60% of their maximum reduction in R and even longer (17 days, IQR: 14–20) following the relaxation to observe 60% of the maximum increase in R. Our analysis suggests that, in the context of a resurgence of SARS-CoV-2, a control strategy of banning public events and social gathering (of >10 persons) would be associated with a reduction in R by 10% on Day 7, 16% on Day 14, and 30% on Day 28; and if this also included closing workplaces, the overall reduction in R would be 17% on Day 7, 24% on Day 14, and 41% on Day 28. These findings provide additional evidence that can inform policy-makers' decisions on the timing of introducing and lifting different NPIs.

Our findings on the effects of introducing NPIs were broadly in line with the earlier large-scale multi-country study by Flaxman and colleagues that assessed the impact of different NPIs among 11 European countries.[5] Flaxman reported that major NPIs (e.g. school closure, public events ban, etc.) and lockdown in particular had a large effect (81%) on reducing transmission.[5] However, Flaxman did not assess the change over time in the effect of lockdown and assumed that the effect was immediate. In the present study, we estimated that an extreme intervention similar to lockdown, consisting of school and workplace closure, ban on public events and gathering, requirements to stay at home, and limits on internal movement, could reduce R by 35% on Day 7, 42% on Day 14, and 52% on Day 28. Our findings on the effects of introducing NPIs were also qualitatively similar to the recent study by Islam and colleagues that modelled the incidence rate ratio of COVID-19 with OxCGRT NPI data,[17] although that study did not assess the effects of lifting NPIs.

Our analysis demonstrates that the effect of introducing/lifting NPIs was not immediate and the time required to reach certain levels of effect differed by NPI. This provides important evidence to policy-makers on when to expect a notable effect of introducing/lifting an NPI. The observed delay of introducing/lifting NPIs could be explained by behavioural inertia, which is supported by the results from our additional analysis using Google mobility data. We found that the delay (measured by the time length needed to achieve 60% of the maximum effect) for introducing/lifting workplace closure was 6 days/12 days using the total visits to workplace, similar to 6 days/9 days using the R value; the delay for introducing/lifting requirements to stay at home was 6 days/17 days using the total time of staying at residential areas, similar to 6 days/23 days using the R value.

School closure was widely adopted previously to control influenza outbreaks and pandemics and was shown to reduce and delay peaks of epidemics.[18,19] For SARS-CoV-2, the role of children in its transmission is still unclear. A modelling study from China showed that school closure alone could not interrupt transmission but it could potentially reduce peak incidence by 40–60% and delay the epidemic of COVID-19.[20] In the present study, we showed that closing school alone could decrease the transmission by 15% (R ratio of 0·85, 95% CI: 0·66–1·10) on Day 28 and re-opening school could increase the transmission by 24% (R ratio of 1·24, 95% CI: 1·00–1·52) on day 28. It should be acknowledged that in our analysis, we were unable to account for different precautions regarding school re-opening adopted by some countries, such as social distancing within classrooms (e.g. limiting class size and placing transparent dividers for individual students) and outside classrooms (e.g. distancing during mealtime, recreation and transportation), enhanced hygiene (e.g. routine deep-cleaning and personal handwashing and face-masks), and others (e.g. thermal temperature checks on arrival).[21,22] Such precautions are imperative for a safer school re-opening. A COVID-19 outbreak was reported in a high school of Israel 10 days after its re-opening; students were in crowded classrooms and were not instructed to wear facemasks due to high temperature.[23] In addition, it should be noted that we did not consider the normal school holidays in some countries. We were also unable to assess the effect of re-opening different levels of school (e.g. elementary *vs* middle schools) since the effect might differ by age within school-age children and adolescents.[23,24] A recent report found that young children (<5 years) with mild to moderate COVID-19 had high viral loads in their nasopharynx compared with older children and adults, and thus could potentially be important drivers of transmission in the general population.[25]

Our findings suggest that as a single NPI, banning public events resulted in the highest reduction in R, with the corresponding R ratio on Day 28 being 0·76 (0·58–1·00). This is expected because a ban on crowded activities could prevent super-spreading events that were commonly reported at the beginning of the COVID-19 pandemic.[26] Another explanation for the high reduction is that a ban on public events was often the first introduced NPI in countries; our sensitivity analysis that excluded firstly introduced NPIs showed a slightly lower reduction with an R ratio of 0·80 (0·57–1·11) on Day 28. Our findings also suggest that lifting public events ban and ban on gathering size could increase transmission by 21% and 25%, respectively, highest among all NPIs. However, we did not observe a substantial reduction in transmission following introducing ban on gathering size of >10 or >100, especially for >100 that even showed an increase of transmission after Day 14; possible explanations include low adherence and, for the ban on gathering size of >100, an increase of smaller-scale gatherings. In addition, it should be noted that for bans on physical gatherings, we were unable to further stratify our analysis by indoor/outdoor settings due to the scarcity of data.

Interestingly, we did not observe a substantial difference in our results when only including phases with comprehensive contact tracing in place as a sensitivity analysis. This could be due to the lack of representativeness as only 18% of our data were included in this sensitivity analysis. Nevertheless, a recent modelling study, which might explain our results, suggested that a contact tracing strategy will only contribute to containment of COVID-19 if it could be organised in a timely manner that minimises testing and tracing delays.[27] However, our data lacked the necessary granularity to further explore timeliness of testing and tracing. Additioinally, similar to the findings by Islam and colleagues,[17] we did not observe substantial effects of public transport closure on R ratio.

There are some advantages in our study. First, both the method for the R calculation and the method for recording NPIs remained consistent over time among different countries; this ensured comparability between different phases in different countries in our analysis. Second, by dividing timeline into different phases according to the changes in NPIs, we were able to assess the effect of individual NPIs. Third, we were able to estimate the change in the effect of NPIs over time.

We acknowledge several challenges and limitations regarding our analysis. First, our analysis was based on the data on control policy rather than actual population behaviour. In particular, we were unable to account for the growing awareness of personal hygiene (including wearing face-coverings) among the public in response to the pandemic. These behavioural changes lead to a further reduction of transmission and are likely to vary over time. We were also unable to examine the compliance with these NPIs due to the lack of suitable data which were reliable across countries over time. Second, some NPIs (e.g. school closure and public events ban) were often introduced earlier than other NPIs (e.g. requirements to stay at home); therefore, we were unable to assess the effect of different rank orders of changes in NPI status. NPIs which were introduced earlier might have had a longer-term effect on R and thus might bias the estimate of later NPIs. Third, our data on R and NPIs were at national level whereas both R and NPIs could vary among different parts of a country. An increase in national-level R could be due to a clustered outbreak in some areas or due to several scattered cases nationwide. Fourth, we acknowledged the potentially high heterogeneity across different countries in terms of both NPIs and COVID-19 case ascertainment. Our findings should be regarded as a broad summary across the full dataset and we did not intend to draw any separate conclusions for specific countries individually. Our sensitivity analyses indicated that our main findings were not sensitive to the removals of different lists of countries. Fifth, the effect of NPIs in R was from historical data that occurred under certain conditions that could change over time (e.g. wearing facemasks was uncommon before COVID-19 pandemic); therefore, the impact on R by future re-introduction/re-relaxation of NPIs might be substantially different. Sixth, we did not consider the role of underlying seasonality or meteorological factors (e.g. temperature and humidity) in SARS-CoV-2 transmission. A recent modelling study found that introduction of NPIs was strongly associated with growth of COVID-19 cases and, by comparison, humidity was only weakly associated with the growth; no association was found for latitude or temperature.[28] Seventh, we only assessed the effect of introducing/lifting NPIs for the first 28 days post-introduction/relaxation and the findings (including the trend) should not be generalised to beyond 28 days. Finally, although our study could essentially be regarded as a natural experiment study,[17] our findings did not necessarily imply causation.

We acknowledge several limitations of the methodology for the R estimate used in our analysis. First, the adjustment for reporting delays was only conducted globally and not specific to each country, due to the lack of available data on reporting delays. This could lead to temporal inaccuracy of R, which could bias our findings on the immediacy of changes in R associated with NPIs. Nonetheless, our findings on the immediacy of changes associated with NPIs were consistent with the results of the additional analysis using Google mobility data, indicating that the possible temporal inaccuracy of R may have a limited impact on the overall findings. Second, the R estimate was subject to the specification of parameters (e.g. incubation period and generation time of COVID-19) in the model and could be biased upwards or downwards. However, we believe this bias was unlikely to affect the main findings of our study since we used the R ratio as the output metric (which cancels out all time-invariant elements related to the R estimate). Third, the modelling framework for R was unable to account for the change over time in eligibility for testing, method of testing or case definition in different countries. This could bias both the R estimate and the R ratio in our analysis for the dates during which the changes were ongoing. For example, we are likely to observe an artificial increase in R if a country increases the testing capacity within a short period. Lastly, the uncertainty range of the national R estimate was based on the number of national reported cases and therefore did not reflect any variations in R within the country.

We also acknowledge the innate limitations of R as a measure of transmission of SARS-CoV-2. First, although R is often assumed to have straightforward interpretations in practice, estimating R from during an ongoing outbreak is complicated and associated with substantial uncertainty. Second, the estimates of R become unreliable with wider uncertainty range if the number of cases is low, which limits its application to very local level or when the number of cases in a large region is low. Third, R can be sensitive to a surge in the number of cases in certain settings (e.g. care homes, schools, factories and hospitals) and does not fully represent the transmission in the general population. Fourth, R is an average population-level measure of transmission and does not reflect the individual-level transmission of SARS-CoV-2. The potential of SARS-CoV-2 transmission varies among individuals and is reflected by the reported “super-spreading” events.[26,29]

In summary, our findings provide additional evidence that can inform policy-makers’ decisions on the timing of introducing and lifting different NPIs. The decisions to re-introduce / relax restrictions should be informed by a variety of factors including the capacity and resilience of the healthcare system; and may be best made at provincial / district rather than national levels in some countries.

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Contributors

YL, HC and HN conceptualised the study. YL led data acquisition, analysis and visualisation. HN, HC and YL led the data interpretation with substantial contribution from DK, AH, MN and XW. YL wrote the draft report and all other authors revised the report critically for important intellectual content. All authors have read and approved the final version of the report.

Declaration of interests

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Table 1. Change in the R ratio over time on Day 7, Day 14 and Day 28 since the introduction/relaxation of each NPI

NPI	Day 7	Day 14	Day 28
School closure			
Introduction	0·89 (0·82-0·97)	0·86 (0·72-1·02)	0·85 (0·66-1·1)
Relaxation	1·05 (0·96-1·14)	1·18 (1·02-1·36)	1·24 (1·00-1·52)
Workplace closure			
Introduction	0·89 (0·83-0·96)	0·89 (0·78-1·02)	0·87 (0·73-1·03)
Relaxation	1·04 (0·97-1·13)	1·10 (0·97-1·24)	1·01 (0·83-1·25)
Public events ban			
Introduction	0·90 (0·82-0·99)	0·83 (0·68-1·00)	0·76 (0·58-1·00)
Relaxation	1·02 (0·93-1·11)	1·07 (0·92-1·24)	1·21 (0·97-1·50)
Ban on gathering size of >10 persons			
Introduction	0·93 (0·87-0·99)	0·98 (0·87-1·10)	0·97 (0·83-1·14)
Relaxation	0·99 (0·93-1·06)	1·07 (0·96-1·20)	1·25 (1·03-1·51)
Public transport closure			
Introduction	0·97 (0·91-1·04)	0·98 (0·87-1·11)	0·99 (0·84-1·18)
Relaxation	1·00 (0·93-1·07)	1·08 (0·96-1·22)	1·04 (0·85-1·27)
Requirements to stay at home			
Introduction	0·90 (0·85-0·97)	0·89 (0·79-1·00)	0·97 (0·83-1·14)
Relaxation	0·97 (0·91-1·03)	1·02 (0·92-1·13)	1·11 (0·94-1·32)
Internal movement limits			
Introduction	0·97 (0·90-1·03)	0·97 (0·87-1·10)	0·93 (0·79-1·10)
Relaxation	0·98 (0·92-1·04)	1·06 (0·95-1·18)	1·13 (0·94-1·37)
International travel limits			
Introduction	0·89 (0·81-0·98)	0·97 (0·81-1·16)	1·08 (0·85-1·38)
Relaxation	0·95 (0·84-1·07)	1·02 (0·81-1·28)	0·98 (0·68-1·40)

For each NPI, the reference period is the day before introduction/relaxation of that NPI. R ratio >1 indicates increased transmission and R ratio <1 indicates decreased transmission. NPI = non-pharmaceutical intervention.

Table 2. Modelled change in the R ratio over time on Day 7, Day 14 and Day 28 since the introduction of different composites of NPIs

NPIs introduced	Day 7	Day 14	Day 28
Candidate 1: **Ban on public events & gathering (>10)**	0·94 (0·85-1·03)	0·87 (0·73-1·05)	0·71 (0·55-0·93)
Candidate 2: **Workplace closure +** **ban on public events & gathering (>10)**	0·84 (0·76-0·93)	0·78 (0·64-0·94)	0·62 (0·47-0·82)
Candidate 3: **Workplace closure +** **ban on public events & gathering (>10) +** **internal movement limits**	0·81 (0·71-0·92)	0·76 (0·60-0·95)	0·58 (0·41-0·81)
Candidate 4: **School & workplace closure +** **ban on public events & gathering (>10) +** **internal movement limits +** **stay at home requirement**	0·65 (0·54-0·78)	0·58 (0·42-0·78)	0·48 (0·32-0·71)

The reference period is the day before introduction. R ratio >1 indicates increased transmission and R ratio <1 indicates decreased transmission. NPI = non-pharmaceutical intervention.

Figure 1. Schematic figure presenting calculation of R ratio. NPI = non-pharmaceutical intervention.

Figure 2. Frequency (A) and order (B) of introducing and lifting NPIs. In Panel A, each number denotes the frequency of the co-occurrence of NPIs in the x and y axis. Numbers on the diagonal (from bottom left to top right) denotes the frequency of the occurrence of NPIs (with and without co-occurrence). In Panel B, each number in the graph denotes the percentage of NPI in the y axis that occurred earlier than the NPI in the x axis among countries with both NPIs ordered or lifted. NPIs are ranked from earliest to latest based on the average percentage of the row. NPI = non-pharmaceutical intervention.

Figure 3. Change over time in the R ratio following the introduction and relaxation of individual NPIs. For each NPI, the reference period is the day before introduction/relaxation of that NPI. R ratio >1 indicates increased transmission and R ratio <1 indicates decreased transmission. The error bars present the 95% confidence intervals of the R ratios derived from the model. NPI = non-pharmaceutical intervention.

Figure 4. Change over time in the R ratio following the introduction and relaxation of ban on gathering size (>10 persons vs >100 persons). The error bars present the 95% confidence intervals of the R ratios derived from the model.