Reduction in effective reproduction number of COVID-19 is higher in countries employing active case detection with prompt isolation

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Highlight: Countries that implemented liberal testing with active case finding and prompt isolation, combined with contact tracing and quarantine, were more successful in reducing the reproduction number compared to countries that primarily relied on social distancing and lockdown measures.

As the coronavirus disease 2019 (COVID-19) pandemic is progressing rapidly, many countries implemented control measures to contain the COVID-19 outbreak. In this study, we estimated a time-varying reproduction number, $R_t$, to assess the effectiveness of control measures employed in 10 selected counties. The time-varying reproduction number, $R_t$, is the average number of secondary cases of disease caused by an infected individual over his or her infectious period. A value of $R_t$ greater than the threshold of 1 indicates that the infection could be able to spread in the population at time $t$, whereas $R_t < 1$ indicates that the epidemic size is shrinking at time $t$. The goal of the control measures is, therefore, to reduce $R_t$ below 1. Close monitoring of $R_t$ over time can provide a real-time assessment on the effectiveness of control measures and guide adjustments in intervention strategies.

We employed a method proposed by A. Cori et al.\(^1\) to estimate $R_t$ in 10 selected countries, namely Belgium, China, France, Germany, Iran, South Korea, Spain, Thailand, United States, and United Kingdom, using the EpiEstim Microsoft Excel spreadsheet (available at http://tools.epidemiology.net/EpiEstim.xls). This $R_t$ estimation method only requires the number of daily new cases and the distribution of the serial interval, which is the time between the onset of symptoms of a primary case and the onset of symptoms of secondary cases, as an input (see Supplementary Information for more details). In this study, the number of daily confirmed cases of COVID-19 in the selected countries were obtained from the Center for Systems Science and Engineering (CSSE) at Johns Hopkins University,\(^2\) and the distribution of the serial interval was assumed to be a discretized Gamma distribution with the mean serial interval of 3.96 days and the standard deviation of 4.75 days.\(^3\) We also calculated the reduction in $R_t$ ($\Delta R_t$): a higher $\Delta R_t$ is indicative of more successful control measures.
Figure 1 (A – J) illustrates the time series of the estimated $R_t$ on weekly windows with 95% confidence interval (CI) in 10 selected countries starting from the date at which the number of cumulative confirmed cases in each country exceeds 100 and Figure 1K shows the reduction in $R_t$ ($\Delta R_t$) in each country after the control measures have been implemented for 3 weeks. We found that among the selected countries, as of 7th April 2020, only China and South Korea were successful in controlling the disease: implementing the control measures for 3 weeks, the median of $R_t$ decreases more than 2 (Figure 1K), and have since remained below or close to 1 (Figure 1A and 1B).

In China, the epicentre was Wuhan where COVID-19 first emerged in December 2019. By 23rd January 2020, Wuhan implemented a strict lockdown with a total standstill and stay-at-home policies, combined with contact tracing and quarantining of all contacts.\(^4\) In addition to a strict lockdown, from February onwards, China also added extensive active case finding including isolation of all cases, even mild cases, in Fangcang shelter hospitals.\(^5\) As a result, the median of $R_t$ in China declined from 3.19 (95% CI: 3.11-3.28) to a value lower than the self-sustaining threshold of 1 in approximately 3-4 weeks (Figure 1A).

In South Korea, the first COVID-19 case was reported in late January 2020. In contrast to China, South Korea did not implement a strict lockdown but focused on active case-finding with average testing of 12,000 patients per day, with the peak capacity as high as 20,000 tests per day, since 25th February 2020.\(^6\) The median of $R_t$ in South Korean rapidly decreased from 2.56 (95% CI: 2.38-2.74) to a value lower than 1 in approximately 3-4 weeks (Figure 1B). In contrast, by 7th April 2020, the medians of $R_t$ in the United States, United Kingdom, Spain, Iran, Italy, and France were still greater than 1, associated with a much lower $\Delta R_t$.

Our analysis suggests that to contain the COVID-19 transmission either a very strict lockdown combined with rigorous active case-finding, prompt case isolation, and with strict enforcement of physical distancing (the measures employed in China) or without a lockdown but with rigorous active case-finding, prompt case isolation, and quarantine of all contacts (the measures employed by South Korea)\(^6\) may be needed to be successful in containing the outbreak. House-to-house surveys, drive-in testing, policies for isolation of all cases, enhanced
contact tracing with digital technologies, and close monitoring of all quarantined contacts to identify new cases were hallmarks of the public health measures in China and South Korea.\textsuperscript{7,8} As of 7\textsuperscript{th} April 2020, neither Italy nor any of the other epicentres in Europe or the United States had employed all the above measures. In most of these countries, only severe cases were isolated in hospitals, while mild and moderate cases were told to stay at home, thereby continuing within-household transmission\textsuperscript{9}, resulting in a lower $\Delta R_t$.

Our estimation of $R_t$ also has some limitations. First, the estimation of $R_t$ was based on the reported case number only. Second, we assumed that testing and reporting were constant over time. Finally, country-to-country comparisons of the effectiveness of control measures are problematic due to many confounding factors, such as different population sizes and densities, superspreading events, social mixing patterns, and nuances in social distancing measures. Large-scale epidemiological evaluations of the impact of different public health measures dependent on countries’ characteristics will be needed in the future. Nevertheless, for the time being, the striking differences of the reduction in the effective reproduction number over a period of 3 weeks in 10 countries show that liberal testing, active case-finding, and prompt case isolation reduce the outbreak size more rapidly. While social distancing led to flattening the curve\textsuperscript{10}, only those countries implementing active case detection with prompt isolation experienced a rapid reduction in the reproduction number associated with bending the epidemic curve. Although lockdowns will be necessary when healthcare systems are overwhelmed, the lesson is that basic public health measures that include active case detection with prompt isolation (not just home isolation)\textsuperscript{9} need to be strengthened in all countries in order to effectively curb outbreaks in a timely manner.

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**Author contributions**
CM, PT, and PA conceived and designed the study. CW, CS, NCJ, NY, and CM conducted the study and drafted the manuscript. All authors were responsible for analyses and data interpretation.

**Conflict of interests**
The authors declare that they have no conflict of interests.
Figure 1. Time-varying reproduction numbers after the date at which the number of cumulative confirmed cases exceeds 100 in 10 selected countries. The solid orange line shows the median of $R_t$ in (A) China, (B) South Korea, (C) the USA, (D) the UK, (E) Spain, (F) Italy, (G) France, (H) Germany, (I) Iran, and (J) Thailand. The orange shades illustrate the 95% confidence intervals. The dashed black lines indicate the $R_t$ threshold value of 1. The red star indicates the first date of implementing a lockdown or a massive physical distancing measure in each country. The solid blue lines show the number of daily new confirmed COVID-19 cases (numerical data can be found in Supplementary Results). (K) The reduction in the medians of $R_t$ ($\Delta R_t$) after implementing control measures for 3 weeks.
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