

# **Title: Impact of lockdown on COVID-19 incidence and mortality in China: an interrupted time series study.**

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## **DISCLAIMER**

This paper was submitted to the Bulletin of the World Health Organization and was posted to the COVID-19 open site, according to the protocol for public health emergencies for international concern as described in Vasee Moorthy et al. (<http://dx.doi.org/10.2471/BLT.20.251561>).

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## **RECOMMENDED CITATION**

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## Abstract

**Objective:** to evaluate the effectiveness of strict social distancing measures applied in China in reducing the incidence and mortality from COVID-19 in two Chinese provinces.

**Methods:** We assessed incidence and mortality rates in Hubei and Guangdong before and after the lockdown period in cities in Hubei. An interrupted time series study was conducted to evaluate the effectiveness of lockdown on reducing the number of cases and deaths from COVID-19. We assumed a slope change following a lag impact model and analysed scenarios with different time-lag periods.

**Findings:** Daily relative risk reduction in cases was 6.43% (CI -10.25% / - 2.31%) in a scenario with a 17 day time-lag in Hubei. In Guangdong province, this reduction was 8.43% (CI -14.07% / -2.09%) in a scenario with a 7 day time-lag. Daily relative risk reduction in mortality in Hubei was 7.88% (CI -11.06% / -4.39%) in a scenario with a 10 day time-lag.

**Conclusion:** Strict social distancing measures were effective in reducing incidence and mortality rates. Our results suggest that the onset of reduction effects on incidence and mortality are observed after a period ranging from 7 to 17 days and 10 days, respectively. Effectiveness and the time required for changes seem to be associated with the number of undiagnosed patients and post-lockdown home transmission. Improving epidemiological surveillance may help stakeholders make decisions in a timely manner, enabling the use of more effective and specific social isolation strategies with less economic and social impact.

## Introduction

Cases of pneumonia of unknown origin were reported to the World Health Organization (WHO) on December 31, 2019 in Hubei province in China. A new type of coronavirus (SARS-CoV-2) was isolated from infected patients, characterizing the appearance of a new pathology, later called COVID-19.<sup>1</sup>

The lack of specific treatment or vaccines makes non-pharmaceutical interventions (NPIs) at the individual and collective level the only actions capable of containing the spread of the epidemic and reducing its impact on population health. There is a relative consensus on the use of individual protection measures as these measures have a low capacity to cause damage to health and the economy.<sup>2</sup> Social distancing

measures for patients with respiratory infections or symptoms show evidence of effectiveness in controlling the spread of respiratory disease epidemics and, therefore, should be used as a way to reduce the spread of the epidemic.<sup>2</sup> More comprehensive social distancing measures, such as temporary suspension of school activities, events involving large crowds, or closing borders, are also recommended in specific situations, despite the lack of evidence of effectiveness.<sup>2</sup>

China initiated measures to contain the epidemic with the closure of the Wuhan Wet Market, which was identified as the first place of COVID-19 spread on January 1, 2020.<sup>3</sup> The spread of the epidemic and the confirmation of human-to-human transmissibility led to the lockdown of the Wuhan city on January 23.<sup>3,4</sup> This measure resulted in travel restrictions to and from Wuhan.<sup>3,4</sup> Public places such as schools and universities were closed and mass gatherings were prohibited.<sup>5</sup> Strict social distancing measures were adopted and outside activities were extremely limited to reinforce home quarantine.<sup>5</sup> These measures were followed by actions to reduce mobility and mass gatherings across China, using different strategies based on the epidemic situation in each region.<sup>5</sup> Despite these measures, there was an increase in cases and deaths by COVID-19 in China, especially in Hubei province. In early February, community transmission outside of China was confirmed, starting a new phase of expansion of COVID-19 that has culminated in the current pandemic situation.<sup>6</sup>

Research on factors that influence COVID 19 transmissibility is limited. Estimated basic reproduction numbers before January, 23 in Hubei ( $R_0$ ) vary, ranging from 1.6 to 2.6, indicating a high capacity for sustained transmission.<sup>4</sup> SARS-CoV-2 has an average incubation period of 5.1 days, with 97.5% of cases progressing to COVID-19 at around 11.5 days.<sup>7</sup> Thus, it is assumed that some of the cases diagnosed in the first days after the lockdown were infected before January the 23<sup>rd</sup>. Close contact with family members may be another important route of transmission as has been shown in some studies.<sup>8,9</sup> Thus, familiar transmission could play a role in incidence increases during home quarantine.<sup>9</sup> These factors suggest that the effectiveness of lockdown in reducing incidence may be perceived only days after its implementation.

COVID 19 case fatality rate is associated with older age.<sup>10</sup> However, there is limited research on factors which influence COVID-19 mortality in community settings. There are no population studies that show the average time elapsed between exposure to the virus and the evolution to death. However, data from the COVID-19 outbreak on the

Princess Diamond cruise ship indicate that deaths started 15 days after the first cases were reported.<sup>11</sup> Due to these characteristics, lockdown effects on mortality should be observed progressively after a lag of days. Strict social distancing measures have a high economic and social impact and it is, therefore, necessary to understand their effectiveness and effects. The aim of this study is to evaluate the effectiveness of lockdown measures on reducing incidence and mortality from COVID-19 in two Chinese provinces.

## **Methods**

### **Data Sources and data setting**

We used daily data on confirmed cases and deaths made available by international organizations and systematized by researchers at John Hopkins University from January the 22<sup>nd</sup> 2020.<sup>12</sup> Data on confirmed cases and deaths occurring between 11/01/2020 and 21/01/2020 were extracted from reports of the National Health Commission of the People's Republic of China.<sup>13</sup> Population data used to calculate incidence and mortality rates were extracted from the National Bureau of Statistics of China.<sup>14</sup>

Response variables were incidence and mortality rates (per 10,000 inhabitants) and explanatory variables were time (setting day 1 as the first COVID-19 diagnosed case), lockdown intervention (setting 0 as the period without lockdown and 1 as the period with lockdown), and the interaction between time and intervention period.

### **Design and study population**

This research is an interrupted time series study which assessed COVID-19 incidence and mortality rates in Hubei and Guangdong provinces in China, before and after the lockdown period in Wuhan and other cities in Hubei.<sup>15</sup>

Interrupted time series studies are applied to evaluate the effectiveness of population-based interventions.<sup>15</sup> This methodology analyses the longitudinal effects of an intervention on a given outcome, considering an expected trend in the absence of the intervention (contrafactual) and the trend found after the intervention (intervention).<sup>15</sup> The comparison between the expected tendency without intervention and the existing trend after the intervention allows identification of any changes, in this way evaluating

effectiveness.<sup>15</sup> The characteristics of the intervention and the evaluated outcomes define the parameters of the method adjustments.<sup>15</sup>

Based on information providing in existing literature, we assumed a slope change following a lag impact model to analyse the incidence and mortality trend following the lockdown intervention.<sup>15</sup> Thus, we analysed scenarios with different lag periods and times of observation (until 12/02/2020 or 12/03/2020) in Hubei and Guangdong. Mortality analysis was done only for Hubei, because all deaths in Guangdong occurred after the lockdown

## **Statistical methods**

We specified random effects negative binomial regressions. Random effects for time and interaction were modelled by a random walk of order 1 (i.e., independent increments) for the Gaussian random effects vector.<sup>16,17</sup> As the Bayesian estimation provides greater flexibility (a consequence of its hierarchical strategy), we chose to conduct analyses using a Bayesian framework through the integrated nested Laplace approximations (INLA) approach.<sup>18,19</sup> In summary, initial uncertainty about the effect measures (i.e., relative risks) and the extent of their variation, was first expressed through prior distributions. Next, we combined prior distributions with the so-called likelihood (i.e., the model and the current data), to obtain posterior distribution for the quantities of interest (again, relative risks). We then summarised the posterior distributions through point estimates and credible intervals (analogous to typical confidence intervals, CIs). A small modification in the standard priors (eg, increasing their precision) can imply very different inferences. That is why we need robust priors such as penalising complexity priors, which are invariant to re-parameterisations and always provide the same inferences.<sup>20</sup> One of the advantages of Bayesian analyses (with respect to the classical (or frequentist) analyses) is that they are more suitable for accounting for model uncertainty, both in the parameters and in the specification of the models. Furthermore, only with a Bayesian approach is it possible to model variability with relatively sparse data, whilst it is also easier to specify more complex scenarios. All analyses were carried out with the free software R, available through the INLA library (version 3.6.3).<sup>21</sup>

## **Results**

The incidence in Hubei was 0.07 cases of COVID-19 for 10,000 inhabitants on the 23<sup>rd</sup> of January and 11.44 cases for 10,000 inhabitants on the 12<sup>th</sup> of March 2020. In Guangdong, incidence rates ranged from 0.003 to 0.13 cases for 10,000 inhabitants in the same period (Table 1A – appendix).

Results of the estimated daily reduction of relative risks for each scenario analysed and their respective credible intervals (CI) are shown in figure 1. In the scenario included data collected up until February the 12<sup>th</sup>, the lockdown showed a significant reduction in incidence in the scenario with 17 days of lag in Hubei (Figure 1). In this scenario, the daily reduction in cases was 6.43% (CI -10.25% / - 2.31%). In Guangdong province, this reduction was 8.43% (CI -14.07% / -2.09%) in the scenario with 7 days of lag.

In the scenario that included data collected up until March the 12<sup>th</sup>, the lockdown showed a significant daily reduction in incidence 17 days after the intervention in Hubei (figure 1). In this scenario, the daily reduction in cases was 8.03% (CI -10.31% / - 5.58%). In Guangdong province, the reduction was significant in scenarios with lags from the fourth post-intervention day, with a daily reduction of 13.41% (CI -21.14% / -5.23%) in the scenario including data collected up until March the 12<sup>th</sup> (figure 1). Incidence evolution curve estimations in Hubei and Guangdong are displayed in figure 2.

During the study period, Hubei reported 3,065 deaths from COVID-19 and Guangdong reported eight. The lethality rate was 4.54% in Hubei and 0.59% in Guangdong. Reductions in mortality in Hubei were significant in models using time lag of 13 days in both scenarios of time observation (Table 1B - appendix). This daily reduction was 6.15% (CI -10.50%/-1.15%) and 12.04%, respectively (CI -15.08% / 8.78%). According to the long-term observation model, the reduction in deaths in Hubei was 35.22%. Predicted mortality in Hubei was 13.38 deaths (CI 5.13-48.22) per 10,000 inhabitants, which would be equivalent to 82,101 deaths (CI 30,336-285,303) on March the 12<sup>th</sup> 2020 (Table 1B – supplementary material). A similar mortality applied to all of China would mean 1,936,159 deaths (CI 716,037-6,728,178) at the end of the epidemic. Mortality evolution curve estimations in Hubei are displayed in figure 3.

Analysis models of incidence reduction using data collected up to March the 12<sup>th</sup> 2020 showed reductions in both provinces (figure 4). In Hubei, the reduction in relation to the estimates was 47.43% on the sixth day after lockdown, reaching a reduction of 92.37% after 24 days. Reductions were higher in Guangdong, with 61.26% 6 days after the beginning of measures and 97.75% after the 24<sup>th</sup> day. The reduction in mortality in

Hubei was 68.40% on the sixth day after the intervention and 99.00% after the twenty-fourth day.

## Discussion

The results demonstrate that the lockdown was effective in reducing incidence and mortality rates in Hubei and in adjacent regions like Guangdong. Thus, it can be used as a strategy to reduce the spread of the COVID-19 epidemic.

These were the two Chinese provinces with the highest number of cases of COVID-19 and they were in different situations in relation to the epidemic process at the beginning of the lockdown in Hubei.<sup>12</sup> These provinces have 59.17 and 104.30 million inhabitants, respectively, which together represent 11.72% of the Chinese population in 2018.<sup>14</sup>

As mentioned in the Introduction section and depicted in the results section, the effectiveness of lockdown progressively increased in scenarios that considered time-lags between the intervention initiation and the beginning of the effect, as expected by the dynamics of the infection itself. In that sense, we present in appendix a logic model of transmissibility of COVID-19 in quarantine. According to that, due to the SARS-CoV-2 incubation time, an effective reduction in incidence would be expected between the 5th day and the 11th day after the intervention.

In Guangdong province, there was a significant reduction from the 7th day after introduction of social distancing measures, which is compatible with expected behaviour. In Hubei, significant daily reductions were seen later than those found in Guangdong. It is estimated that 86% of COVID 19 cases were not documented before the start of the lockdown in Hubei.<sup>22</sup> Undocumented cases probably perpetuated the transmission chain in households; sustaining the incidence increases seen in the first weeks of quarantine and reducing the effects observed in our estimates.<sup>8,9,22</sup> These results suggest the importance of considering undiagnosed cases and transmissions between family members in the progression of the epidemic.<sup>8,9</sup> Indeed, our results suggest that in regions where there are a greater number of unidentified cases, the effect of lockdown begins to be observed later.

The COVID-19 epidemic has an exponential growth characteristic and, therefore, the effectiveness of reducing incidence is affected by the time of the epidemic when social distancing measures are established. This hypothesis was confirmed based on the

differences found between the provinces of Hubei and Guangdong. These results suggest that the identification of undiagnosed cases, through intensive testing strategies and social distancing measures, improves the results obtained. A study carried out in China reports that a 3-day delay in measures being introduced in Wuhan could be responsible for the 35.21% increase in the number of cases that occurred outside of this region in late February.<sup>23</sup>

The different moments of implementation of social distancing measures may explain differences in the capacity to contain the number of cases in the province of Hubei and in countries like Italy, where similar measures have been implemented.<sup>24</sup> Italy implemented a lockdown on March the 11<sup>th</sup> when it had an incidence rate of 11.71 cases per 10,000 inhabitants and a mortality rate of 0.11 deaths per 10,000 inhabitants.<sup>12,24,25</sup> Currently, Italy has an incidence of 17.12 for every 10,000, three times higher than that observed in Hubei when it managed to control the epidemic.<sup>12</sup> Analysis of mortality data in the Chinese province of Hubei suggests that lockdown prevented the deaths of thousands of Chinese. A recent study by the Imperial College suggests similar estimates in European countries corroborating our results.<sup>25</sup>

This analysis is based on historical time series data on the number of confirmed COVID-19 cases and deaths. Thus, outcomes are influenced by changes relating to the definition of diagnostic criteria, accuracy of diagnostic tests and access to tests. Estimates of incidence and mortality showed higher values in models shorter observation periods. This pattern can be explained by the fact that in the interrupted time series model, estimates are also influenced by observed data trends in the post-intervention period.<sup>15</sup> Thus, the lower incidences seen following lockdown generated scenarios with lower estimates in models with longer observation periods. With regards to relative daily reductions, differences between the values obtained in the short-term and long-term observations were smaller. This demonstrates the consistency of the model.

According to our results strict social distancing measures represent an effective way to slow the progression of COVID-19 epidemics. However, these measures have a great economic, psychological and social impact.<sup>26,27</sup> They should, therefore, be used as extreme options in regions where evolution of the COVID-19 epidemic puts the health system's response capacity and the health of the population at risk. Epidemic surveillance based on effective testing strategies is a central element in determining choices relating to the degree of intensity of social isolation measures. Thus, improving epidemiological



surveillance and expanding the capacity to diagnose people with COVID-19 can help stakeholders make decisions in a timely manner, enabling the use of more specific social isolation strategies with less economic and social impact.

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**Declaration of interests:** We declare no competing interests

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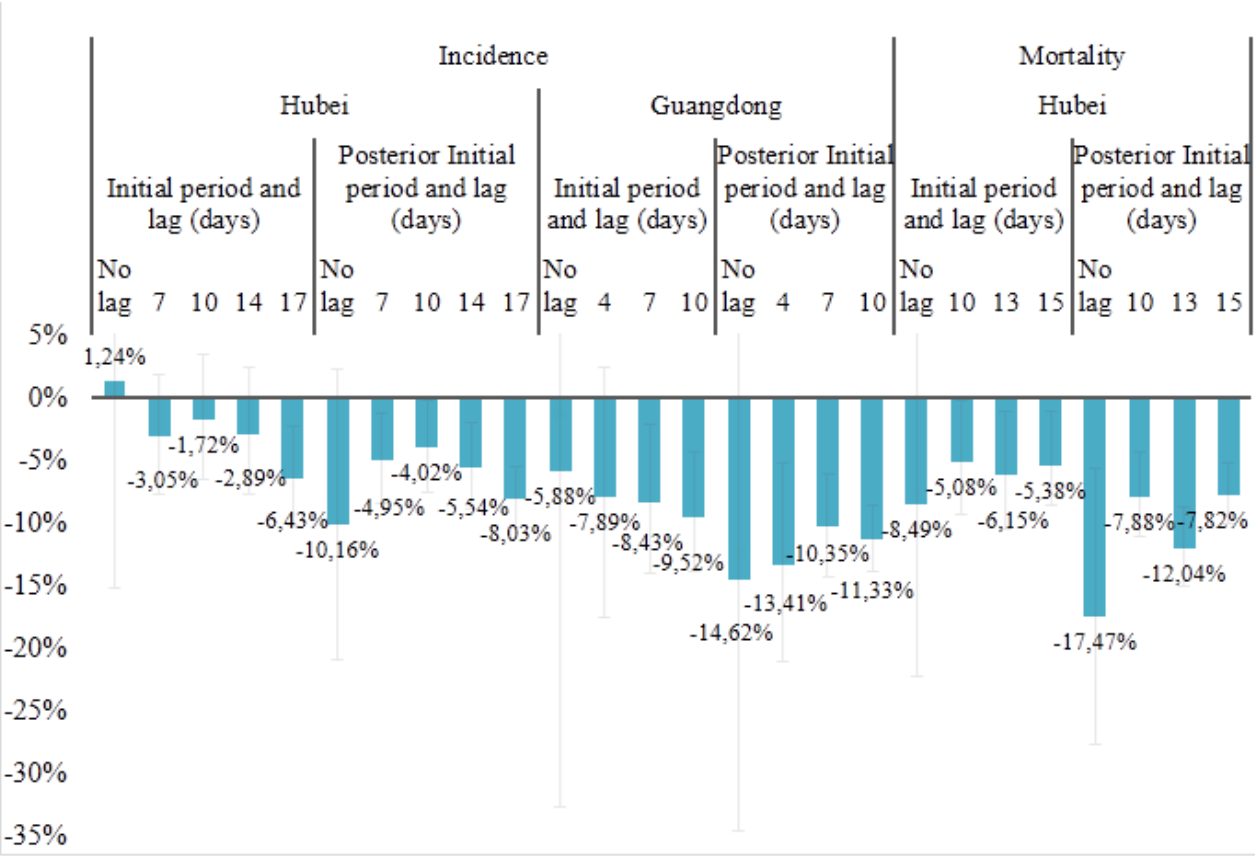
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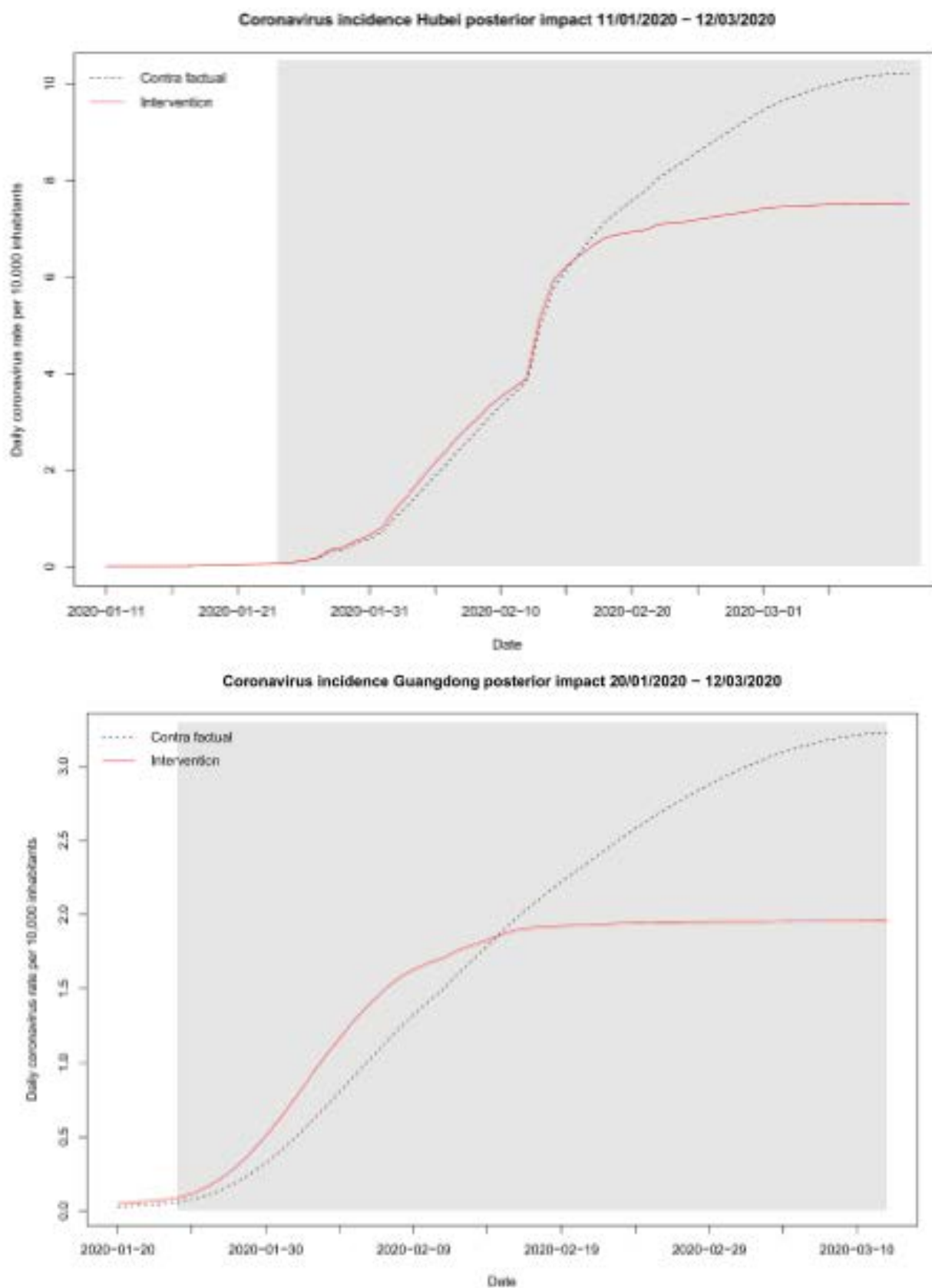
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**FIGURE 1: Estimated daily relative risk reduction due to lockdown (% change and 95% credible intervals)**

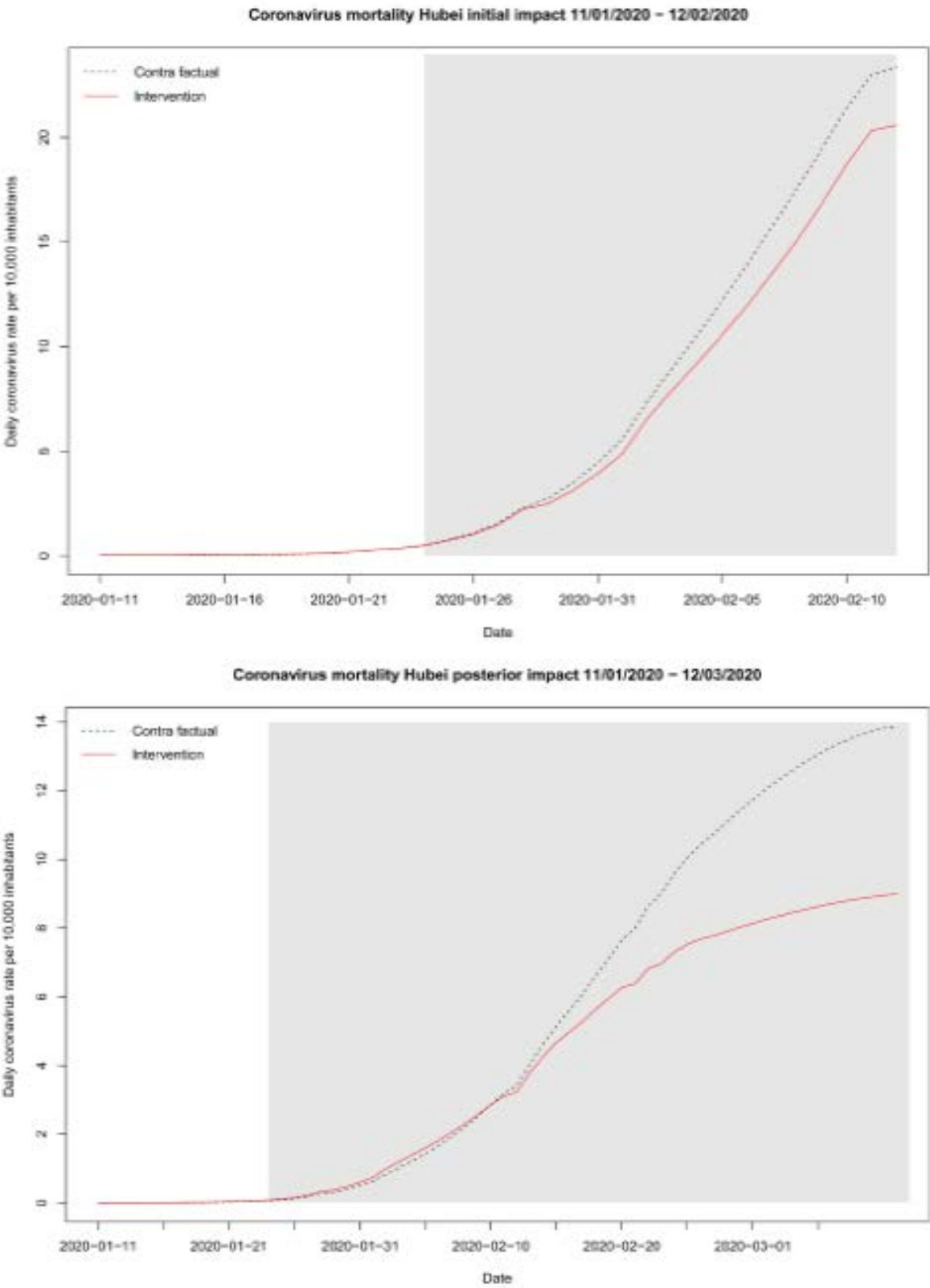


Note: Relative risk of the interaction between the intervention (lockdown) and time (1 day)

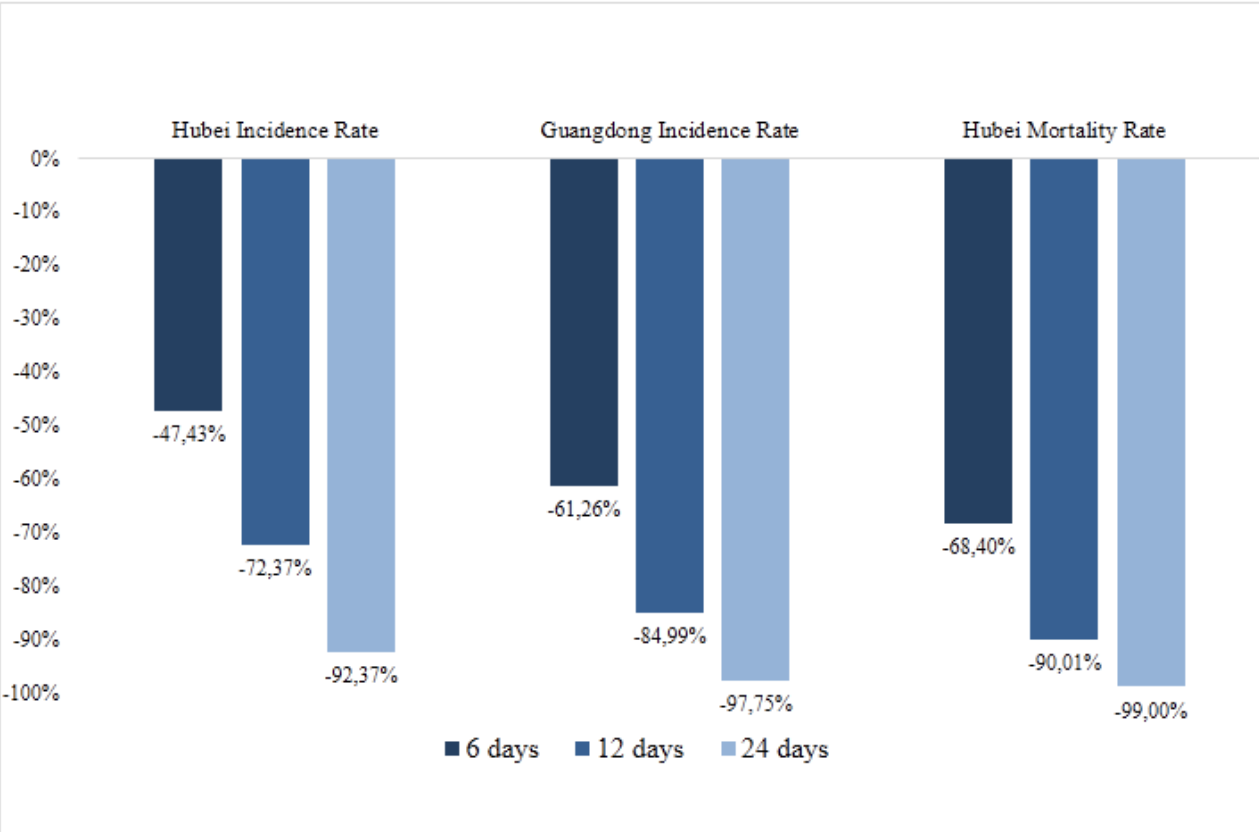
**FIGURE 2: Expected incidence trends in the absence of the intervention (contrafactual) and following intervention (intervention) in Hubei and Guangdong. Scenarios including data collected up until March the 12<sup>th</sup>.**



**FIGURE 3: Expected mortality trends in the absence of the intervention (contrafactual) and following intervention (intervention) in Hubei – scenarios including data collected up until Februaray 12<sup>th</sup> and March the 12<sup>th</sup>.**



**FIGURE 4: Estimated relative risk reduction according to different lockdown durations**





**FIGURE 1 APPENDIX – Logic model of transmissibility of COVID-19 in quarantine**

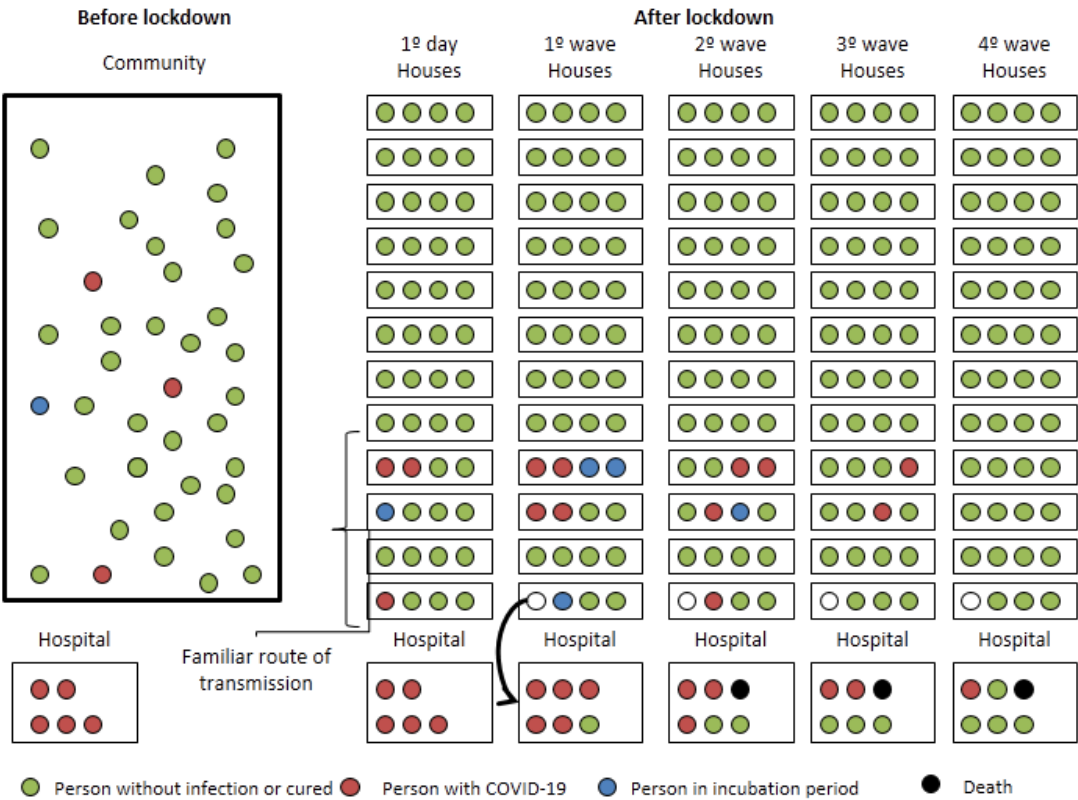


TABLE 1A APPENDIX

Outcome	Province	Observation time*	Lag	Observed rate per 10,000	Estimated rate per 10,000 without lockdown			Estimated rate per 10,000 without lockdown			Estimated rate averted*	Estimated daily RR reduction due to lockdown**			Estimated RR reduction according to different times since the lockdown started (follow-up period)		
					Point estimation	Lower95% CI	Upper95% CI	Point estimation	Lower95% CI	Upper95% CI		Point estimation	Lower CI 95%	Upper95% CI	6 days	12 days	24 days
Incidence	Hubei	Until February 12	No lag	5.64	22.14	6.36	77.63	22.45	13.89	35.53	140%	1.24%	-15.20%	21.63%	7.66%	15.90%	34.32%
			7	-	-	-	-	-	-	-	-	-3.05%	-7.72%	1.81%	-16.97%	-31.05%	-52.46%
			10	-	-	-	-	-	-	-	-	-1.72%	-6.59%	3.50%	-9.91%	-18.84%	-34.12%
			14	-	-	-	-	-	-	-	-	-2.89%	-7.70%	2.38%	-16.14%	-29.68%	-50.55%
			17	-	-	-	-	-	-	-	-	-6.43%	-10.25%	-2.31%	-32.87%	-54.94%	-79.69%
		Until March 12	No lag	11.46	10.22	3.85	35.46	7.52	5.69	9.76	-26.41%	-10.16%	-20.89%	2.28%	-47.43%	-72.37%	-92.37%
			7	-	-	-	-	-	-	-	-	-4.95%	-8.42%	-1.33%	-26.28%	-45.66%	-70.47%
			10	-	-	-	-	-	-	-	-	-4.02%	-7.55%	-0.29%	-21.84%	-38.91%	-62.68%
			14	-	-	-	-	-	-	-	-	-5.54%	-8.88%	-1.94%	-28.94%	-49.51%	-74.51%
			17	-	-	-	-	-	-	-	-	-8.03%	-10.31%	-5.58%	-39.49%	-63.38%	-86.59%
	Guangdong 9	Until February 12	No lag	0.12	5.05	1.73	16.56	4.04	2.89	5.6	-19.99%	-5.88%	-32.61%	31.62%	-30.50%	-51.70%	-76.67%
			4	-	-	-	-	-	-	-	-	-7.89%	-17.53%	2.38%	-38.92%	-62.70%	-86.08%
			7	-	-	-	-	-	-	-	-	-8.43%	-14.07%	-2.09%	-41.04%	-65.24%	-87.91%
			10	-	-	-	-	-	-	-	-	-9.52%	-13.95%	-4.36%	-45.13%	-69.89%	-90.94%
		Until March 12	No lag	0.13	3.23	1.39	9.41	1.96	1.61	2.39	-39.29%	-14.62%	-34.58%	11.43%	-61.26%	-84.99%	-97.75%
			4	-	-	-	-	-	-	-	-	-13.41%	-21.14%	-5.23%	-57.85%	-82.23%	-96.84%
			7	-	-	-	-	-	-	-	-	-10.35%	-14.30%	-6.15%	-48.09%	-73.06%	-92.74%
			10	-	-	-	-	-	-	-	-	-11.33%	-13.87%	-8.67%	-51.41%	-76.39%	-94.43%

\* Relative difference between the estimated rates WITHOUT and WITH the intervention from the date with the first case detected until the initial or posterior period (12/02 or 13/03, respectively)

\*\*Relative Risk (of the interaction between the intervention (lockdown) and time (1 day))

TABLE 1B APPENDIX

Outcome	Province	Observation time*	Lag	Observed rate per 10,000	Estimated rate per 10,000 without lockdown			Estimated rate per 10,000 without lockdown			Estimated rate averted*	Estimated daily RR reduction due to lockdown**			Estimated RR reduction according to different times since lockdown started (follow-up period)		
					Point estimation	Lower 95% CI	Upper 95% CI	Point estimation	Lower 95% CI	Upper 95% CI		Point Estimation	IC 95% Lower	IC 95% Upper	6 days	12 days	24 days
Mortality	Hubei	Until February 12	No lag	0.18	23.35	5.86	101.2	20.58	11.68	34.73	-11.85%	-8.49%	-22.18%	8.79%	-41.27%	-65.51%	-88.11%
			10	-	-	-	-	-	-	-	-	-5.08%	-9.27%	-0.19%	-26.87%	-46.52%	-71.39%
			13	-	-	-	-	-	-	-	-	-6.15%	-10.50%	-1.15%	-31.67%	-53.31%	-78.20%
			15	-	-	-	-	-	-	-	-	-5.38%	-8.63%	-1.14%	-28.26%	-48.53%	-73.51%
		Until March 12	No lag	0.52	13.88	5.13	48.22	8.99	6.67	11.88	-35.22%	-17.47%	-27.65%	-5.69%	-68.40%	-90.01%	-99.00%
			10	-	-	-	-	-	-	-	-	-7.88%	-11.06%	-4.39%	-38.89%	-62.66%	-86.06%
			13	-	-	-	-	-	-	-	-	-12.04%	-15.08%	-8.78%	-53.67%	-78.54%	-95.39%
			15	-	-	-	-	-	-	-	-	-7.82%	-10.09%	-5.23%	-38.65%	-62.36%	-85.83%

\* Relative difference between the estimated rates WITHOUT and WITH the intervention from the date with the first case detected until the initial or posterior period (12/02 or 13/03, respectively)

\*\*Relative Risk (of the interaction between the intervention (lockdown) and time (1 day))