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Isolating the net effect of multiple government interventions with an extended Susceptible-Exposed-Infectious-Recovered (SEIR) framework: empirical evidence from the second wave of COVID-19 pandemic in China

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ABSTRACT

Objective By using a data-driven statistical approach, we isolated the net effect of multiple government interventions that were simultaneously implemented during the second wave of COVID-19 pandemic in China.

Design, data sources and eligibility criteria We gathered epidemiological data and government interventions data of nine cities with local outbreaks during the second wave of COVID-19 pandemic in China. We employed the Susceptible-Exposed-Infectious-Recovered (SEIR) framework model to analyse the different pathways of transmission between cities with government interventions implementation and those without. We introduced new components to the standard SEIR model and investigated five themes of government interventions against COVID-19 pandemic.

Data extraction and synthesis We extracted information including study objective, design, methods, main findings and implications. These were tabulated and a narrative synthesis was undertaken given the diverse research designs, methods and implications.

Results Supported by extensive empirical validation, our results indicated that the net effect of some specific government interventions (including masks, environmental cleaning and disinfection, tracing, tracking and 14-day centralised quarantining close contacts) had been significantly underestimated in the previous investigation. We also identified important moderators and mediators for the effect of certain government interventions, such as closure of shopping mall and restaurant in the medium-risk level areas, etc. Linking the COVID-19 epidemiological dynamics with the implementation timing of government interventions, we detected that the earlier implementation of some specific government interventions (including targeted partial lockdown, tracing, tracking and 14-day centralised quarantining close contacts) achieved the strongest and most timely effect on controlling COVID-19, especially at the early period of local outbreak.

Conclusions These findings provide important scientific information for decisions regarding which and when government interventions should be implemented to fight against COVID-19 in China and beyond. The proposed analytical framework is useful for policy-making in future endemic and pandemic as well.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ The data-driven statistical approach was adopted to quantitatively isolate the net effect of multiple government interventions.
⇒ The implementation of government interventions was included to extend the Susceptible-Exposed-Infectious-Recovered framework model, which can estimate the net effect of different government interventions reliably.
⇒ Correlation analysis was conducted to demonstrate the strength of relationship between the implementation timing of some specific government interventions and the incidence of COVID-19.
⇒ The study areas were limited to nine cities in China, and potential confounding effects of some unmeasurable seasonal factors were not ruled out completely.

INTRODUCTION

Since its emergence in December 2019, COVID-19 has been rapidly spreading globally and seriously threatening world public health security. This pandemic has created ramifying public health, economic and political crisis throughout the world.[1 2] As of 29 January 2021, the COVID-19 outbreak has affected 223 countries and territories, 100 455 529 have been confirmed positive for COVID-19, and 2 166 440 have died.[3] In particular, some new variants of COVID-19, which were first identified in the UK and South Africa, appeared to be more infectious. During the second wave of COVID-19 pandemic, these new variants with up to 70% higher transmissibility, caused a rapid rise in infections worldwide. One big challenge is that there is currently no clear and convincing evidence showing the effect of existing pharmacological interventions or vaccines to treat or prevent these new COVID-19 variants.[4] Therefore, non-pharmaceutical interventions (NPIs) implemented for fighting against COVID-19 outbreak previously are treated as the priority to delay even contain the spread of these new variants.[5 6] For example, many studies have investigated the influence of a single NPI or a multiple NPIs implemented in China,[7] the UK,[8] Singapore,[9] Germany,[10] Italy,[11] South Korea and the USA,[12] or compared the effect of many NPIs implemented in 34 European countries,[13] 79 territories[14] and 190 countries.[15]

Focused on the first wave of COVID-19 pandemic (from December 2019 to June 2020), most previous studies used the mathematical models (eg, Susceptible-Infectious-Recovered, Susceptible-Exposed-Infectious-Recovered (SEIR), agent-based simulation model) backed by experimental epidemiological parameters to simulate the COVID-19 transmission processes.[16–18] These simulation results, which are used to estimate the effect of different NPIs, are heavily dependent on the epidemiological assumptions, parameter estimations and data variations. First, some epidemiological assumptions are overly simplified, such as using a fixed transmission probability (β) or the same contact rate (c) in different countries. These assumptions overlook the heterogeneities in susceptible population and their contact patterns. Therefore, based on these assumptions, it is challenging to use a simulated R_t (the effective reproductive number) as the typical representative parameter for estimating the NPIs effect. Second, the estimation of NPI effect could be highly sensitive to the estimated values of some vital epidemiological parameters, such as generation time or incubation period. The same parameters with different estimated values cloud lead to the different effect of the same NPIs. Third, during the first wave of COVID-19 pandemic, only symptomatic testing is conducted, resulting in a large proportion of asymptomatic cases undetected. That is the challenge of finding reliable data on daily reported cases. Later, in most countries, the rapid rise of reported cases might be driven by expanding testing coverage or increasing testing rates. Therefore, due to the unknown changes in different countries' testing capabilities, early studies using data from the first wave of COVID-19 pandemic, do not provide a reliable assessment of NPI effect.

This study bridges this tap in the previous literature by adopting a data-driven statistical approach to quantitatively isolate the net effect of multiple government interventions implemented in nine cities of China during the second wave of COVID-19 pandemic. Relying on the epidemiological data (including the characteristics of the reported cases and the 14-day travel history) collected from the official website of Municipal Health Commission, the data-driven statistical approach could apply accurate and reliable statistical treatments to disentangle net effect from different themes of government interventions. This would considerably reduce the structural uncertainties of the previous mathematical models.

In addition, our study focuses only on the government interventions and excluded NPIs initiated and implemented by any non-government institutions due to the difficulties of measuring their effect reliably. Many studies found that government-led NPIs were critical to combat a resurgence of COVID-19 or any other future respiratory outbreak. These interventions, also known as legal NPIs, are announced and implemented by the governments to mandate the public and private sectors to take some specific measures. These government-enforced interventions are more effectively implemented in the community than non-legal NPIs (such as voluntary isolation and voluntarily wearing masks), which could ensure highly public compliance for quantifying the effect accurately.

Previous studies also overlook the different local effect of the same government interventions that were rolled out in different phases. By using a city-level dataset, another significant contribution of this study is to analyse the different net effect of government interventions implemented with different timelines across a large geographic region. Our comparative analysis has shown that certain themes of government interventions implemented earlier are the 'backbone' to contain the COVID-19 outbreak.[19] This finding bears a significant implication for the strategies to prevent or contain future waves of COVID-19.

Although it is tempting to compare government interventions from multiple countries or regions, aggregating evidence from different parts of the world might blur the picture instead. This is because different governments implemented the same government interventions with a significant level of variability. For example, during the first lockdown in the UK, face-covering was encouraged, not mandatory and people were told to use their 'good solid British common sense' to make their own decision. Meanwhile, face masks were mandatory in China throughout the pandemic and strictly enforced by both the government and the broad community. Therefore, the observed effect of the same government interventions will inevitably be confounded by these institutional variations. To isolate the net effect of multiple government interventions, we choose to use data from China, where these interventions were implemented effectively and efficiently across the country. In particular, based on the widespread implementation of epidemiological investigation in China, more epidemiological data become available. Our study also benefited from the accurate and efficient epidemiological data (included the characteristics of reported cases and their 14-day travel history), covering the location-specific transmission, the case identification and the COVID-19-infected sources by city and date. The research design and empirical strategy enable the reliable isolation of the net effect of multiple government interventions. Our findings can be used as the upper bound of the effect range of such interventions, given the strict and effective implementation of government interventions in China. The results can guide policy decisions to deal with

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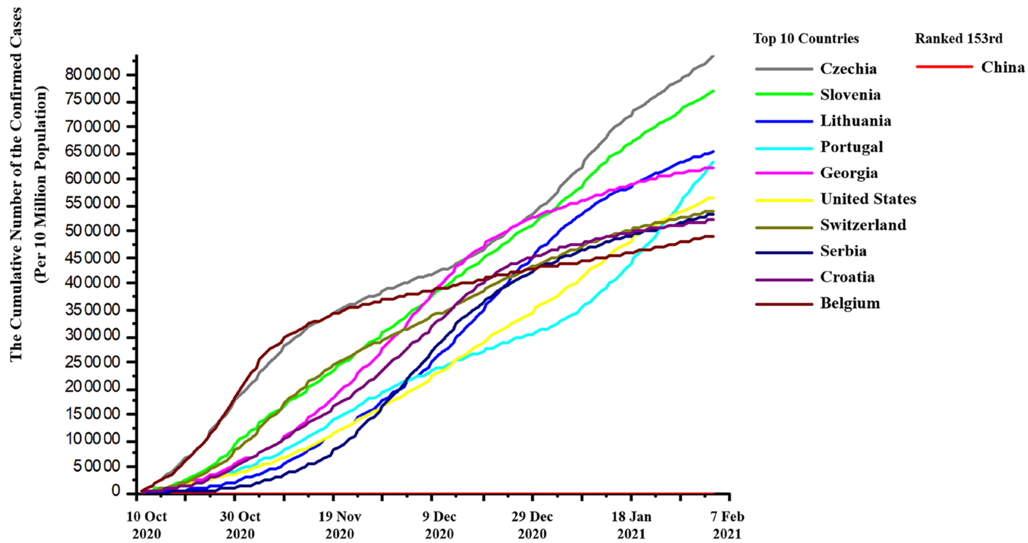

Figure 1 The cumulative number of confirmed cases (per 10 million population) in top 10 countries and China from 11 October 2020 to 4 February 2021.

the rapidly changing epidemiological situations in other countries when fighting against the COVID-19 pandemic, and the spread of similar raspatory transmissive diseases in general.

DATA AND METHODS

COVID-19 case data

A country-level dataset on daily confirmed COVID-19 cases per 10 million people included a total of 156 countries from 11 October 2020 to 4 February 2021, which was extracted from a data repository sourced from Johns Hopkins University Center for Systems Science and Engineering and the Wind Financial database Dong *et al*.[20] By ranking these countries according to the cumulative number of confirmed cases (per 10 million population), figure 1 shows the evolution of cumulative confirmed cases (per 10 million population) in the top 10 countries. Compared with these top 10 countries, the cumulative number of confirmed cases (per 10 million population) in China was >1000 times lower than in these top 10 countries. From 11 October 2020 to 4 February 2021, this pandemic has progressed just through the local outbreak and community transmission stages in 21 cities of China without high infections and widespread transmission. Local governments judiciously and timely implemented some specific themes of government interventions to prevent the local outbreak from shifting into national transmission. Such evidence has supported that the government interventions played an important role in containing the COVID-19 outbreak in China.

In China, focus on 21 cities occurred local outbreak, the data on the characteristic of reported cases and their complete and detailed 14-day travel history were available in 9 cities (eg, Beijing, Chengdu, Shanghai, Tianjin, Shenyang, Dalian, Qingdao, Changchun, Heihe), while some critical data were unavailable in other 12 cities (eg, Suihua, Qiqihar, Harbin, Daqing, Xingtai, Shijiazhuang, Langfang, Baoding, Tonghua, Songyuan, Manzhouli, Kashi). This limited our study areas to these nine cities. Between 11 October 2020 and 4 February 2021, figure 2 shows the distribution of medium-risk level areas in these nine cities.

According to the Chinese COVID-19 Risk Classification Scheme, low-risk level areas were defined as the communities with no confirmed cases or no new

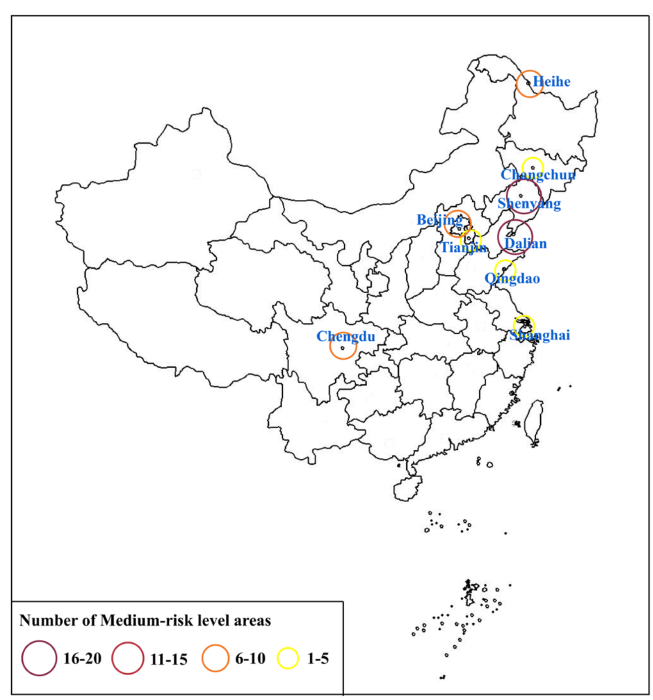

Figure 2 The distribution of medium-risk level areas in nine cities from 11 October 2020 to 4 February 2021.

confirmed cases reported in 14 days. Medium-risk level areas were defined as the communities where the cumulative number of confirmed cases was no more than 50, or there was no cluster of COVID-19 cases in 14 days. High-risk level areas were defined as the communities where the cumulative number of confirmed cases was >50 or some clusters of COVID-19 cases in 14 days. From 11 October 2020 to 4 February 2021, there was no high-risk level area in each city. Therefore, the number of medium-risk level areas (figure 2) indicated the final size of COVID-19 outbreak in these nine cities.

Our observation period covered the entire transmission period of COVID-19 in all nine cities. In each city, the transmission period began when the first case was reported, and ended when the last case was reported. Each city had a different transmission period with a different start date and end date, such as Qingdao (11 October 2020 to 14 October 2020), Tianjin (8 November 2020 to 24 November 2020), Chengdu (7 December 2020 to 17 December 2020), Dalian (15 December 2020 to 8 January 2021), Shenyang (23 December 2020 to 10 January 2021), Beijing (23 December 2020 to 29 January 2021), Changchun (23 December 2020 to 3 February 2021), Heihe (29 December 2020 to 7 January 2021) and Shanghai (21 January 2021 to 4 February 2021).

In nine cities, Municipal Health Commission kept a daily record of reported cases. From 11 October 2020 to 4 February, epidemiological data were collected from the official website of Municipal Health Commission, respectively, including Qingdao (http://wsjkw.qingdao.gov.cn/), Tianjin (http://wsjk.tj.gov.cn/), Chengdu (http://cdwjw.chengdu.gov.cn/), Dalian (http://hcod.dl.gov.cn/), Shenyang (http://wjw.shenyang.gov.cn/), Beijing (http://wjw.beijing.gov.cn/), Changchun (http://wjw.changchun.gov.cn/), Heihe (http://zwgk.heihe.gov.cn/) and Shanghai (https://wsjkw.sh.gov.cn/). And epidemiological data included the characteristics of reported cases (including age, gender, home address, confirmed or asymptomatic cases, wearing masks or not, quarantined or not, etc) and their 14-day travel history. The accuracy and efficiency of 14-day travel history was demonstrated by the mandatory use of Health QR Code (mobile app supported). Health QR Code is a surveillance system shared by all Chinese cities and regions to record all people's travel trajectory (ie, where have they been, who have they met with, whether have they travelled to medium-risk or high-risk level areas; whether have they met with the reported cases). We merged the epidemiological data to form a city-level dataset of each city, which was used to analyse the location-specific transmission, the case identification and the COVID-19-infected sources by city and date. As a contact transmission, COVID-19 transmission is primarily due to person-to-person contact. Therefore, high population density has substantially increased social contacts in public.[21] Considering the different population densities, we focused on the cumulative number of reported cases (including confirmed cases and asymptomatic cases) (per 10 million population) to indicate the growth rate of infections in nine cities of China (figures 3 and 4).

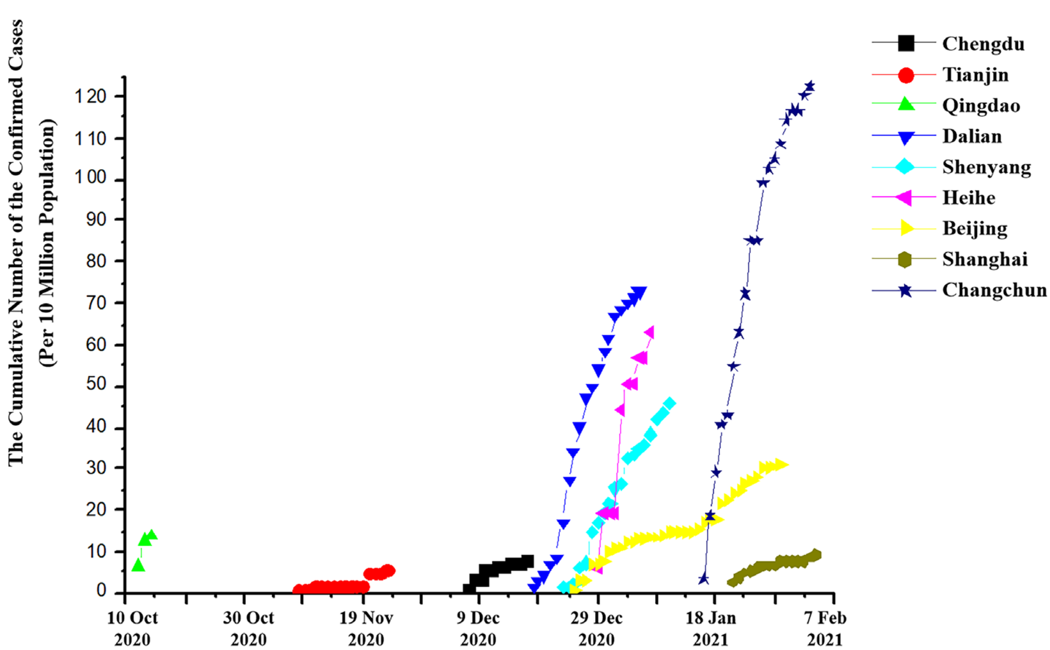

Figure 3 The cumulative number of confirmed cases (per 10 million population) in nine cities from 11 October 2020 to 4 February 2021.

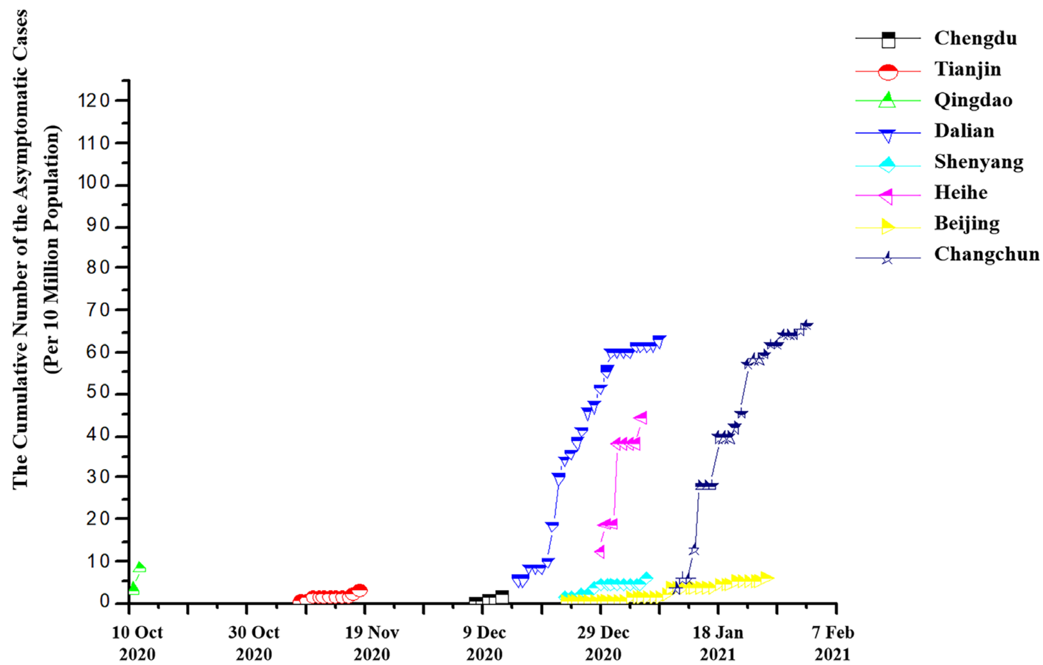

Figure 4 The cumulative number of asymptomatic cases (per 10 million population) in nine cities from 11 October 2020 to 4 February 2021.

Government interventions data

The publicly available Complexity Science Hub COVID-19 Control Strategies List (CCCSL) dataset and CoronaNet COVID-19 Government Response Event (CoronaNet) Dataset on NPIs were used to define and categorise the government interventions implemented in nine cities, respectively. The CCCSL dataset provided a hierarchical taxonomy of 6068 NPIs covered 56 countries, and CoronaNet dataset contained 31 532 interventions covered 247 territories. In this study, we used a dynamic version of CCCSL and CoronaNet. From 11 October 2020 to 4 February 2021, in each city, COVID-19 Prevention and Control Headquarter, as the responsible sector, released the updated NPIs through the news conferences and announcements on the official website of Municipal Health Commission, respectively. And each NPI was treated as 'on' when it was announced to be implemented in each city. We collected and recorded all legal NPIs (as government interventions) and their implementation date, not non-legal NPIs. Then, using the same criterion for the CCCSL and CoronaNet datasets, we formed a four-level hierarchical coding scheme to define and categorise all recorded government interventions. This scheme included 5 themes (level 1, L_1), 10 categories (level 2, L_2), 12 subcategories (level 3, L_3) and 12 codes (level 4, L_4). Each L_1 (theme) is composed of several categories (L_2) that contained subcategories (L_3), which were further subdivided into codes (L_4). Details pertaining to this four-level hierarchical coding scheme are summarised in table 1. Figure 5 shows the implementation timing of government interventions in nine cities from 11 October 2020 to 4 February 2021.

Susceptible-Exposed-Infectious-Recovered framework model linked with government interventions implementation

The SEIR model, as an experimental simulation model, is widely used to assess and predict the epidemic curve of COVID-19 in many previous studies. In the standard SEIR model, the population was stratified as susceptible (S), exposed (E), Infectious (I) and recovered (R) compartments. Nevertheless, most previous studies have used the SEIR modelling method to simulate the epidemic without considering the effect of NPIs implementation,[22] or just investigating the effect of a single NPI or a group of NPIs, which was estimated by the experimental population-based data.[23] These modelling studies lacked a discussion of NPIs effect, could not help public-health officials make decisions on the public's adoption of protective action. Furthermore, we argued that the lack of experimental population-based data on some NPIs (such as environmental cleaning and disinfection, and periodic testing, etc) could not be equated with these specific NPIs in effect. In particular, the low acceptability and tolerability of some specific NPIs (such as masks, etc) induced low public compliance in some countries. This has tended to overlook these NPIs effect, which might be a reason against their recommendation. Therefore, in this study, we employed the SEIR framework model to analyse the transmission pathways between cities within government interventions implementation. We used the legal NPIs data implemented by the local governments of nine cities to provide direct evidence about the net effect of government interventions (selected and categorised as a four-level hierarchical coding scheme, including 5 themes (L_1), 10 categories (L_2), 12 subcategories (L_3) and

Table 1 Definition and categorisation of the government interventions

L_1 theme	L_2 category	L_3 subcategory	L_4 code
Case identification, contact tracing and related measures	Tracing and ttracking	Close contacts	GI_1
	14-day centralised quarantining	Close contacts	GI_2
	Testing	Targeted testing	GI_{3a}
		Periodic testing	GI_{3b}
		Mass testing	GI_{3c}
Environmental measures	Environmental cleaning and disinfection		GI_4
Social distancing	Mass gathering cancellation	Medium-risk level areas	GI_5
	Closure of educational institutions	Medium-risk level areas	GI_6
	Closure of non-essential businesses	Medium-risk level areas	GI_7
	Closure of shopping mall and restaurants	Medium-risk level areas	GI_8
Travel restriction	Lockdown	Medium-risk level areas	GI_9
Health resources	Personal protective equipment	Masks	GI_{10}

12 codes (L_4)) on COVID-19 transmission, respectively. However, isolating the net effect was statistically challenging because most cities implemented two or more government interventions simultaneously according to the implementation timing of these government interventions in nine cities from 11 October 2020 to 4 February 2021 (figure 5).[24 25] Focusing on 'viewing the goals as the centre point, the typical themes of government interventions were implemented to achieve some specific goals (including reducing the number of susceptible population; protecting the susceptible population; reducing the number of exposed cases and identifying the exposed cases and infected cases), which reflected with the new-formed compartments (including the protected susceptible population (S_p), the quarantined exposed cases (E_q) and the hospitalised infected cases (I_h)) in SEIR framework model (figure 6).

1. The theme of travel restriction (lockdown) was implemented to reduce a susceptible population's possibility to contact with the infections. Lockdown (G_{11}) of the medium-risk level areas had statistically significant explanatory power in containing transmission across locations. Therefore, we assumed that the theme of travel restriction was implemented to achieve the goal of reducing the number of susceptible population. And the net effect of this theme could induce a reduced susceptible population (S').
2. The themes of health resources (including masks) and environmental measures (including environmental cleaning and disinfection) were implemented to protect the susceptible population, which played a more prominent role in disease control than that during the first wave of COVID-19 pandemic. Because the increas-

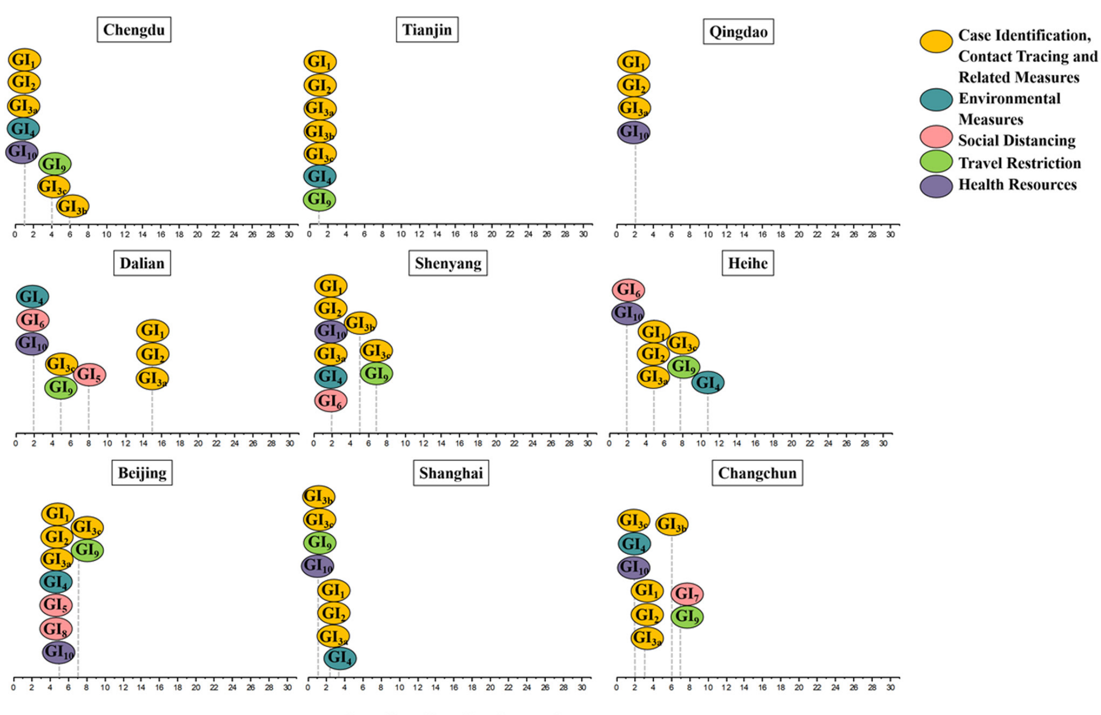

Figure 5 The implementation timing of government interventions in nine cities from 11 October 2020 to 4 February 2021.

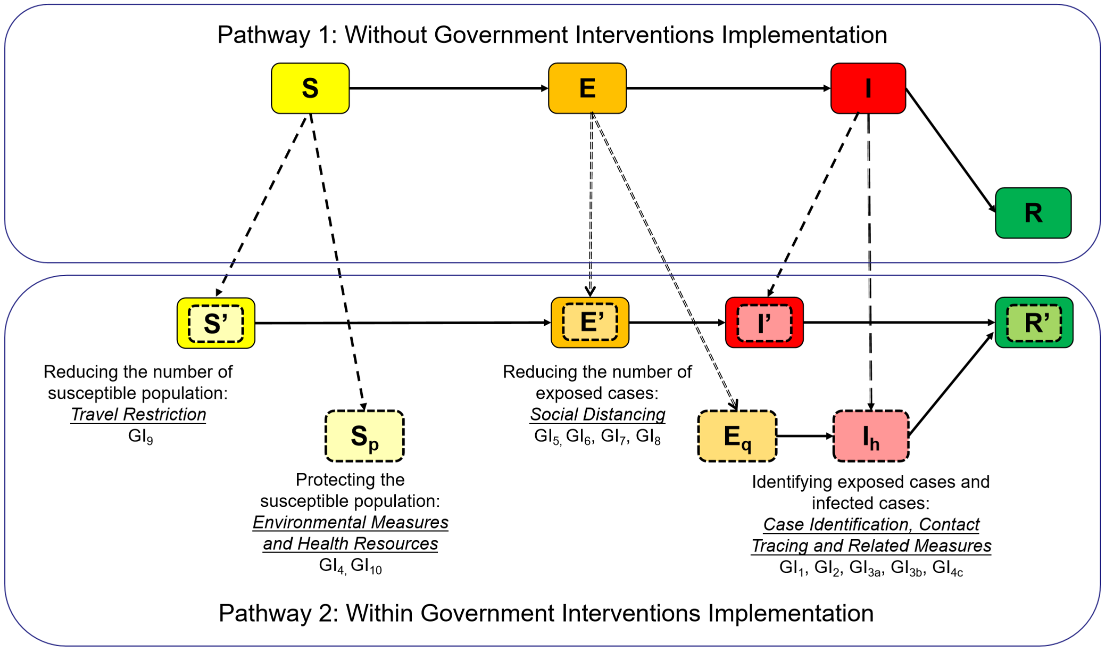

Figure 6 Schematic of the Susceptible-Exposed-Infectious-Recovered framework model for linking government interventions implementation, in which transmission pathways are distinguished between (pathway 1) without government interventions implementation and (pathway 2) within government interventions implementation.

ing spread risk from asymptomatic cases accounted for the higher transmission rate globally during the second wave of COVID-19 pandemic.[26] However, these themes were seldom reported by the governments, and many previous studies ranked these interventions least effective. For example, owing to the lack of valid and robust data in most countries, the effect of environmental cleaning and disinfection (GI_4) might be prone to be ignored. And the contribution of wearing masks (GI_{10}) might also be underestimated due to the probable biases in the masks' coverage ratio in the susceptible population. Unequivocally, when the susceptible population used masks only after the onset of symptoms or a low proportion of the susceptible population wore masks, there were no significant statistics to estimate the effect of masks. In China, the themes of environmental measures and health resources were legally and officially implemented by the national and local governments, which provided direct evidence about their effect on COVID-19 transmission. Therefore, we assumed that the themes of environmental measures and health resources were implemented to achieve the goal of protecting the susceptible population. And the net effect of these themes could separate the protected susceptible population (S_p) from the susceptible population (S). The protected susceptible population had a lower proportion of being exposed to the virus, which further reduced the infection risk.

3. The theme of social distancing (including but not limited to mass gathering cancellation, closure of educational institutions, non-essential businesses and restaurants) has been implemented in medium-risk level areas or all areas to drastically shift the social mixing pattern. It was especially helpful in curbing the spread of an emerging pathogen to the wider community and reducing the spread risk from asymptomatic or mild infections. Therefore, we assumed that the theme of social distancing was implemented to achieve the goal of reducing the number of exposed cases (E). And the net effect of this theme could induce reduced exposed cases (E'), which could further induce reduced infected cases (I').
4. The theme of case identification, contact tracing and related measures (including tracing and tracking, 14-day centralised quarantining and testing) was encouraged and supported by local governments of nine cities to identify and quarantine the COVID-19 infections as early as possible. For example, tracing and tracking close contacts (GI_1), which was used to understand community interactions, could improve the detection and diagnosis of asymptomatic cases and further control and prevent potential new infections. During the second wave of COVID-19 pandemic, more COVID-19 infections were either asymptomatic or mild symptoms, which induced a large proportion of infections unidentified with only symptomatic testing. Targeted testing (GI_{3a}) of all susceptible population in the medium-risk level areas, periodic testing (GI_{3b}) of health professionals (such as doctors, nurses and other healthcare workers) and essential-workers porters (such as testers and porters of cold-chain food, couriers, public transport drivers, etc) might be less costly and more effective than mass testing (GI_{3c}). Because the significant increase in large-scale testing capability was currently the most challenge faced by many countries. In different countries, a wide range of varying

quarantine strategies (including the quarantine on susceptible population, exposed or infected cases; self-isolation or centralised isolation; voluntary isolation or mandatory isolation; etc) were adapted and tailored to fit the needs of dormitory residents, their living circumstances and the seriousness of COVID-19. However, the existing studies either used data of only confirmed cases or confirmed/death cases to estimate the effect of these quarantine strategies, which cannot provide direct evidence about their effect on COVID-19 transmission. In China, the 14-day centralised quarantining close contacts (GI_2) was strictly enforced to isolate the identified exposed/infected cases from susceptible population. When there were interactions between susceptible population and exposed/infected cases, the close contacts as the potential exposed/infected cases were quarantined to prevent seeding the virus to wider regions. And this quarantine for 14-day was necessary and effective because the incubation period from infection to the appearance of the first symptoms was typically 5–7 days but up to 14 days.[27] Therefore, we assumed that the theme of case identification, contact tracing and related measures was implemented to achieve the goal of identifying exposed/infected cases. And the net effect of this theme could separate the quarantined exposed cases (E_q) from exposed cases (E), and the hospitalised infected cases (I_h) from infected cases (I). The quarantined exposed (E_q) and hospitalised infected (I_h) cases could not contact the susceptible population and hence reduce the recovered cases (R').

Quantifying the net effect of government interventions

Based on the SEIR framework model linked with government interventions implementation, we applied a data-driven statistical approach (including the time series descriptive statistical analysis, the correlation analysis and the linear regression analysis) to quantify the net effect of government interventions implemented in nine cities of China from 11 October 2020 to 4 February 2021, respectively. In different cities, government interventions were implemented with different timelines. Some government interventions had a substantially longer implementation period than others, even an overlapped implementation period with others. Since the combined effect of government interventions was not considered in this study, we hypothesised the net effect of each government intervention was conditionally independent of each other.

1. To test the net effect of travel restriction (lockdown in the medium-risk level areas GI_9) on reducing the number of susceptible population, we used the distribution of reported cases in medium-risk level areas (including the total number of the medium-risk level areas and the percentage of the reported cases in the top three medium-risk level areas) of nine cities. And we conducted the correlation analysis (by assessing the Spearman's rank-order correlation coefficients) to demonstrate the strength of the relationship between the implementation timing of lockdown in the medium-risk level areas and the total number of the medium-risk level areas, or the percentage of the reported cases in the top three medium-risk level areas, respectively. This correlation analysis examined if the earlier implementation of targeted partial lockdown, instead of complete lockdown, could significantly limit the spread scope of COVID-19.
2. To test the net effect of health resources and environmental measures on protecting the susceptible population, we used the distribution of location-specific transmission (including the percentage of the reported cases due to household, community, hospital, workplace, educational institution, non-essential business, shopping mall and restaurant or public transport transmission), and the distribution of COVID-19-infected sources (including imported cold-chain food from other countries, imported cases from other countries, imported cases from other cities or local cases) in nine cities, respectively. The different percentages of reported cases due to different location-specific transmission, combined with the different percentages of different COVID-19-infected sources, indicated if the continued stringent wearing masks in public places, and the targeted environmental cleaning and disinfection in medium-risk level areas, could effectively diminish the possible mode of COVID-19 transmission.
3. To test the net effect of social distancing on reducing the number of exposed cases, we built a linear regression model to ascertain whether different location-specific transmission (including household, community, hospital, workplace, educational institution, non-essential business, public transport and shopping mall and restaurant) was associated with a different impact on the incidence of COVID-19. By assessing the coefficient of each independent variable (including the percentage of the reported cases due to household, community, workplace, educational institution, non-essential business, public transport, shopping mall and restaurant transmission) on dependent variable (the cumulative number of reported cases (per 10 million population) in nine cities), the linear regression model was applied to identify some location-specific transmissions as important moderators and mediators. Moreover, controlling for other independent variables, we treated a 5% increase of each independent variable separably, resulting in different changes in the dependent variable. This model accounted for the different effect of social distancing in both different types of places and different cities.
4. To test the net effect of case identification, contact tracing and related measures on identifying exposed/infected cases, we used the distribution of case identification (including self-diagnosis, close contact tracing or mass testing) and the distribution of quarantine ratio (including quarantined or not quarantined) in nine cities. And we conducted the correlation analysis (by assessing Spearman's rank-order correlation

Table 2 The distribution of reported cases in medium-risk level areas of nine cities from 11 October 2020 to 4 February 2021

Cities	The total number of the medium-risk level areas	The percentage of the reported cases in the top three medium-risk level areas (%)
Chengdu	6	81.25
Tianjin	3	100
Qingdao	1	100
Dalian	16	34.00
Shenyang	19	19.99
Heihe	7	61.53
Beijing	11	13.85
Shanghai	4	95.23
Changchun	4	11.88

coefficients) to demonstrate the strength of relationship between the cumulative number of reported cases (per 10 million population) and the implementation timing of tracing and tracking close contacts, or 14-day centralised quarantining close contacts, respectively. This correlation analysis examined if the earlier implementation of mandatory and targeted tracing, tracking and 14-day centralised quarantining interventions, instead of quarantine on all susceptible population in the medium-risk level areas, could significantly slow down the COVID-19 transmission.

Patient and public involvement

No patients and the public were directly involved in this study. Considering the rapidity of the research, patient and public involvement was not considered viable in this study. However, based on the data-driven approach, our findings provided scientific evidence on the net effect of multiple government interventions against the second wave of COVID-19 in China, which would guide policy decisions for rapidly changing the epidemiological situations in >223 other countries that are fighting against the COVID-19 pandemic. These findings will also be widely disseminated to the public through official, personal and social communication tools.

RESULTS

The net effect of travel restriction

The distribution of reported cases in medium-risk level areas of nine cities from 11 October 2020 to 4 February 2021 is shown in table 2. And the correlation analysis results between the implementation timing of lockdown in medium-risk level areas and the total number of medium-risk level areas, or the percentage of reported cases in top three medium-risk level areas are shown in table 3. In each city, the medium-risk level areas had been ranked due to their announcement date. The significantly positive relationship indicated that the earlier implementation of lockdown in medium-risk level areas had more effectively reduced the total number of medium-risk areas. Furthermore, the significantly negative relationship indicated that the earlier implementation of lockdown in medium-risk areas induced a higher percentage of reported cases concentrated in top three medium-risk areas. For example, in two of nine cities (including Tianjin and Qingdao), this earlier implementation of lockdown in medium-risk areas, which was implemented from the first or second day in their transmission period, strongly limited the progression of COVID-19 pandemic just to less than three medium-risk level areas and ensured 100% reported cases concentrated in top three medium-risk level areas (as the earliest announced medium-risk level areas).

Furthermore, unlike the 'Wuhan Lockdown' during the first wave of COVID-19 in China, the complete lockdown was not implemented in all nine cities. However, the infections were effectively contained in small and local areas without driving into the national transmission. These results suggested that the earlier enforced lockdown in medium-risk level areas had significant net effect in reducing the number of susceptible population, which cloud support our assumption. More importantly, in the early stage of COVID-19 outbreak, this targeted partial lockdown as a substitute for complete lockdown in terms of effect should be implemented earlier. And avoiding complete lockdown could reduce the adverse impacts on society, economy, humanitarian response system and environment.

Table 3 Correlations of the implementation timing of lockdown in medium-risk level areas and the total number of medium-risk level areas, or the percentage of reported cases in top three medium-risk level areas

			The total number of the medium-risk level areas	The percentage of the reported cases in the top three medium-risk level areas
Spearman's rho	The implementation timing of lockdown in the medium-risk level areas	Correlation coefficient	0.884*	−0.676†
		Sig. (two-tailed)	0.002	0.046
		N	9	9

*Correlation is significant at the 0.01 level (two-tailed).
†Correlation is significant at the 0.05 level (two-tailed).

The net effect of health resources

The distribution of location-specific transmission in nine cities from 11 October 2020 to 4 February 2021 is shown in table 4. In most cities, the averagely low percentage (37.39%) of reported cases due to public place transmissions, while the averagely high percentage (8.97%) of reported cases due to household transmissions, provided direct evidence that the mandatory wearing masks in public places could effectively diminish the possible mode of COVID-19 transmission. Changchun, with the highest percentage of reported cases (87.36%) due to non-essential business transmissions, is just due to two mass gatherings (in a beauty club and a health club of Changchun) without wearing masks, where a super-spreader phenomenon had induced a COVID-19 cluster among the elderly (>100 individuals). Moreover, in these nine cities, 27.12% of reported cases were asymptomatic cases, which indicated that an official state-wide requirement to wear masks regardless of symptoms was crucial for minimising the likelihood of susceptible population contracting the virus, which had significant net effect in protecting the susceptible population. This was consistent with our assumption.

Some previous studies stated that a wide range of alternative interventions (such as 'one-metre hats', 'germ bubble') might be equally or more effective than masks,[28] which had been implemented by many countries instead of masks. However, keeping physical distance in many metropolitan areas (such as New York, London) with high population density was more complicated. These metropolitan areas, which had high basic reproductive numbers, were possibly due to the higher population density supported more opportunities for sustained transmission. Owing to a lack of valid and robust data, the net effect of masks was unable to be examined in most of the countries. These results provided sufficient evidence to strongly support the continued stringent wearing masks to be implemented, which was crucial for mitigating the spread of COVID-19 and recommendations by the Centers for Disease Control and Prevention.

The net effect of environmental measures

The distribution of COVID-19-infected sources in nine cities from 11 October 2020 to 4 February 2021 is shown in figure 7. These results indicated that the imported cold-chain food from other countries was a main COVID-19-infected source, which caused the local outbreak in three of nine cities (including Tianjin, Dalian and Qingdao). For example, in Tianjin, the infected cold-chain food had caused the highest percentage of reported cases (44.44%) due to workplace transmission (table 4). The ports and industrial parks, as the major storage and processing sites of infected cold-chain food, had played a vital role in workplace transmission. That was because the porters and workers acquired the virus by loading and contacting the infected cold-chain food, which further caused the local outbreak. In many previous studies, the imported cases from other cities or countries had been widely accepted

Table 4 The distribution of location-specific transmission in nine cities from 11 October 2020 to 4 February 2021

Cities	The percentage of the reported cases due to household transmission (%)	The percentage of the reported cases due to public place transmissions (%)						
		Community	Hospital	Workplace	Educational institution	Non-essential business	Public transport	Shopping mall and restaurant
Chengdu	38.46	61.54	0.00	0.00	0.00	0.00	0.00	0.00
Tianjin	22.22	33.33	0.00	44.44	0.00	0.00	0.00	0.00
Qingdao	9.09	0.00	90.91	0.00	0.00	0.00	0.00	0.00
Dalian	37.5	7.14	7.14	28.57	0.00	0.00	0.00	21.43
Shenyang	41.67	8.33	41.67	5.56	0.00	0.00	0.00	2.78
Heihe	41.67	25.00	0.00	0.00	33.33	0.00	0.00	0.00
Beijing	70.02	0.00	0.00	21.05	0.00	0.00	5.26	3.51
Shanghai	66.67	14.29	4.76	9.52	0.00	0.00	0.00	4.76
Changchun	9.20	0.00	0.00	0.00	0.00	87.36	3.45	0.00

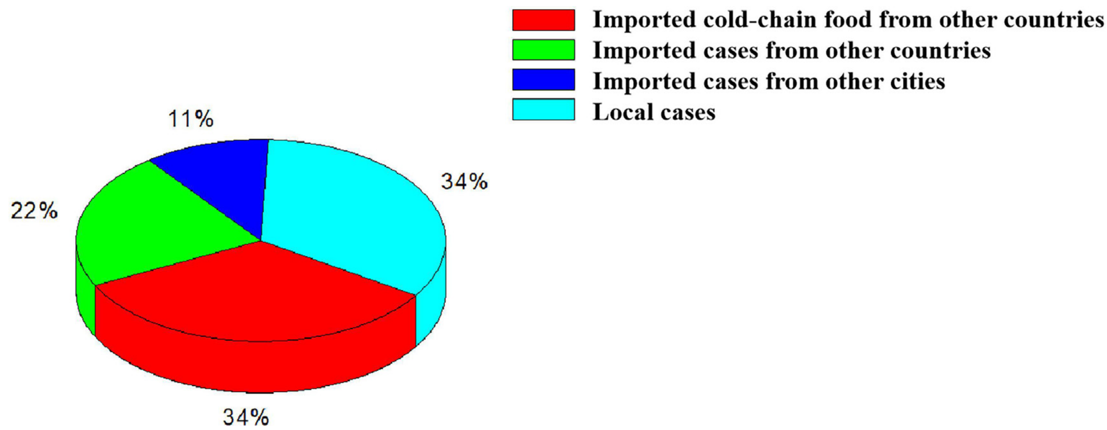

Figure 7 The distribution of COVID-19-infected sources in nine cities from 11 October 2020 to 4 February 2021.

as the main COVID-19 infected sources, when a new local outbreak occurred in many cities or countries. However, due to a lack of widespread implementation of epidemiological investigation, there was unclear and ambiguous available evidence for identifying other COVID-19-infected sources. The distribution of COVID-19-infected sources in nine cities would clearly show that a new local outbreak could be driven by frequent imported cold-chain food, meaning that the net effect of environmental cleaning and disinfection was appeared to be missed in almost all countries. Therefore, environmental cleaning and disinfection should be intensively implemented in all ports and industrial parks, which could effectively protect the susceptible population (especially porters and workers). It was likely to help curb the spread of an emerging infection from other cities or countries.

The net effect of social distancing

The linear regression model was used to estimate different impacts of different location-specific transmission (including household, community, hospital, workplace, educational institution, non-essential business, public transport and shopping mall and restaurant) on the incidence of COVID-19 in nine cities. The different coefficients (table 5) indicated that the increased percentages of reported cases due to household (B=−60.094), community (B=−8.327) or workplace (B=−28.902) transmission could lead to a decreased cumulative number of reported cases. In contrast, the increased percentages of reported cases are due to educational institution (B=290.015), non-essential business (B=159.563), public transport (B=499.106) or shopping mall and restaurant (B=602.949) transmission could cause an increased

Table 5 Linear regression model used to estimate different impacts of different location-specific transmission on incidence of COVID-19 in nine cities

Variables		Unstandardised coefficients		Standardised coefficients		
		B	SE	Beta	T	Sig.
Constant		37.977	32.330		1.175	0.449
The percentage of the reported cases due to location-specific transmission	Household (H)	−60.094	76.675	−0.200	−0.805	0.569
	Community (C)	−8.327	65.227	−0.026	−0.128	0.919
	Workplace (W)	−28.902	82.468	−0.070	−0.350	0.785
	Educational institution (E)	290.015	103.190	0.492	2.810	0.218
	Non-essential business (N)	159.563	61.294	0.710	2.603	0.233
	Public transport (P)	499.106	905.599	0.150	0.551	0.679
	Shopping mall and restaurant (S)	602.949	198.201	0.639	3.042	0.202
N		9				
R^2		0.974				

Independent variable: the percentage of reported cases due to household, community, workplace, educational institution, non-essential business, public transport, shopping mall or restaurant transmission.
Dependent variable: the cumulative number of reported cases (per 10 million population) in nine cities.

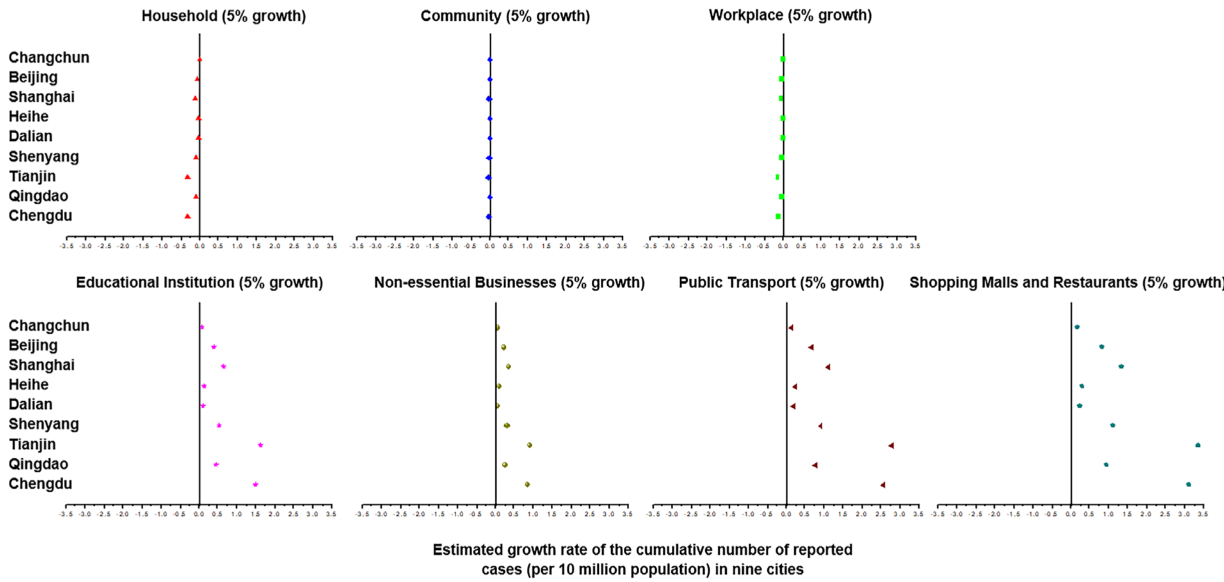

Figure 8 Estimated growth rates of cumulative number of reported cases (per 10 million population) in nine cities, assuming a 5% increased reported cases due to different location-specific transmission, separably.

cumulative number of reported cases. No significant relationship was identified for hospital transmission.

The different growth rates (figure 8) showed that the same increased percentage (5%) of reported cases due to different location-specific transmissions could lead to the remarkable changes in the cumulative number of reported cases in nine cities. For example, controlling for other location-specific transmissions, a 5% increase in reported cases due to shopping mall and restaurant transmission could lead to the largest increased cumulative number of reported cases (per 10 million population) in nine cities, while a 5% increase in reported cases due to household transmission could lead to the largest decreased cumulative number of reported cases (per 10 million population) in nine cities. These results demonstrated that at the price of an increased percentage of reported cases within households, the intervention of stay-at-home cloud effectively reduce the cumulative number of reported cases for the whole city. Furthermore, the percentage of reported cases due to shopping mall and restaurant transmission was an important moderator and mediator, meaning that closure of shopping mall and restaurant in the medium-risk level areas (GI_8) cloud significantly reduce the cumulative number of reported cases (as the exposed cases in SEIR framework model). And the lower percentage of reported cases due to shopping mall and restaurant transmission cloud raise the expectations of slowing or stopping the spread of COVID-19 pandemic.

The net effect of case identification, contact tracing and related measures

The distribution of case identification in nine cities from 11 October 2020 to 4 February 2021 was shown in figure 9. These results showed that tracing and tracking close contacts had significant net effect in identifying exposed/infected cases, which strongly contributed to a rapid resolution of COVID-19 pandemic in these nine cities. For example, tracing and tracking close contacts identified 64.87% of reported cases averagely in all cities, and even up to 92.52% in Changchun. Moreover, targeted testing of all susceptible population in the medium-risk level areas, and periodic testing of health professionals and essential-workers porters had a high risk of exposure to the virus, provided a great benefit for limiting the spread of COVID-19 locally. For example, testing (including targeted, periodic and mass testing) identified 30.81% of reported cases average in nine cities. In particular, periodic testing (once a week) identified the first infected cases in three of nine cities (including Qingdao, Tianjin and Dalian), where the imported cold-chain food from other countries was a main COVID-19-infected source. These first infected cases as the asymptomatic cases were all porters and workers who had a high risk of exposure

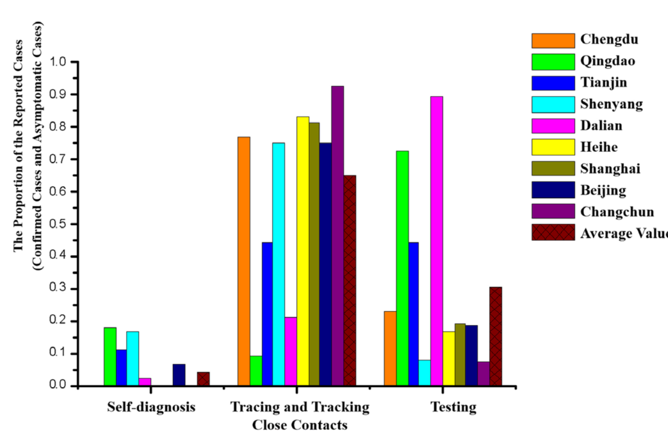

Figure 9 The distribution of case identification in nine cities from 11 October 2020 to 4 February 2021.

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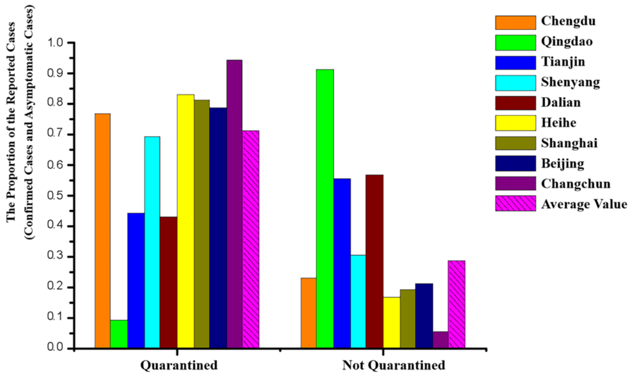

Figure 10 The distribution of quarantine ratio in nine cities from 11 October 2020 to 4 February 2021.

to the infected cold-chain food. The earlier identification was a significant advance in the control of COVID-19 outbreak. Besides, after the medium-risk level areas' lockdown, targeted testing could effectively identify more exposed/infected cases from the susceptible population for interrupting transmission. Therefore, the enforced partial lockdown could be relieved safely in the presence of targeted testing, which could be used to determine the reopening phases of communities. In contrast, in nine cities, the lowest percentage (4.3%) of reported cases were found by self-diagnosis averagely, which indicated that only symptomatic testing was problematic to identify all actual infected people.

The distribution of quarantine ratio in nine cities from 11 October 2020 to 4 February 2021 is shown in figure 10. In nine cities, the high quarantine ratio (averagely 71.35%) implied that the 14-day centralised quarantining close contacts had quarantined most reported cases before confirmed diagnosis. In particular, more than half of these reported cases started to get symptoms after being quarantined for 3–10 days. These results provided precise and direct evidence about the significant net effect of 14-day centralised quarantining close contacts on separating the quarantined exposed cases from exposed cases, and the hospitalised infected cases from infected cases, which further stabilised the cumulative number of reported cases.

The correlation analysis results between the cumulative number of reported cases (per 10 million population) and the implementation timing of tracing and tracking close contacts, or 14-day centralised quarantining close contacts are shown in table 6. These significantly positive relationships indicated that the earlier implementation of tracing and tracking, or 14-day centralised quarantining close contacts both had effectively reduced the cumulative number of reported cases in nine cities. Tracing and tracking close contacts were necessary and effective to identify the exposed/infected cases earlier and more accurately. Combined with tracing and tracking, 14-day centralised quarantining close contacts cloud isolate these identified exposed/infected cases (including the quarantined exposed cases and the hospitalised infected cases) from the susceptible population, which could avoid quarantining all susceptible population in the medium-risk level areas. Therefore, these mandatory and targeted tracing, tracking and quarantining interventions considerably shifted the epidemiological dynamics of COVID-19 pandemic without significant and unpredictable economic and social consequences. Meanwhile, the significant effect of these interventions relied on the full promotion of location tracking app (such as Health QR Code in China) which stronger local governments mandated, and the sufficiently tracing and testing capacities of the public health institutes.

DISCUSSION AND CONCLUSION

The strengths of our study lied in presenting a data-driven approach to analyse the net effect of five themes of government interventions in nine cities of China from 11 October 2020 to 4 February 2021, respectively. First, compliance rates of NPIs were crucial for quantifying NPIs effect accurately. Because some NPIs effect might be overestimated due to their wide implementations, while some NPIs effect might be underestimated due to the low degree of implementations. Therefore, we just focused on the government interventions implemented in nine cities. And community workers combined with the mandatory use of Health QR Code (mobile app supported) ensured all people's compliance with some specific government interventions no matter in communities or public places. If a person went to the medium-risk or high-risk level areas or met with the reported cases, Health QR Code would be changed from 'green code' into 'yellow code', even 'red code'. Without 'green code', any person could not go into any public places (such as railway stations, airports,

Table 6 Correlations of the cumulative number of reported cases (per 10 million population) and the implementation timing of tracing and tracking close contacts, or 14-day centralised quarantining close contacts

			The implementation timing of tracing and tracking close contacts	The implementation timing of 14-day centralised quarantining close contacts
Spearman's rho	The cumulative number of reported cases (per 10 million population)	Correlation coefficient	0.749*	0.749*
		Sig. (two-tailed)	0.020	0.020
		N	9	9

*Correlation is significant at the 0.05 level (two-tailed).

ports, office buildings, shopping mall, restaurant, parks, etc). And by interviewing community workers and local government officials in nine cities, the coverage rates of Health QR Code were very high (>95%). It ensured the high compliance rates demonstrate the accuracy and reliability of our results.

Second, we selected five themes of government interventions (including 10 categories, 12 subcategories and 12 codes) from CCCSL and CoronaNet datasets, which featured non-homogeneous data completeness across different territories. Notably, some government interventions could belong to more than one category but were recorded only once. We tried to mitigate this issue by validating our findings on these two databases.

Third, we linked the SEIR framework model with government interventions implementation to solve the difficulties in isolating net effect, when many government interventions were proceeding simultaneously. Four specific goals defined the targeted contributions of different themes of government interventions implementation. Moreover, in nine cities, Municipal Health Commission provided unique, consistent and reliable epidemiological data (including the characteristics of reported cases and their 14-day travel history). Compared with the previous mathematical models, it avoided the large statistical uncertainties in simulating COVID-19 transmission processes.

Fourth, the local COVID-19 response was far less coordinated: different cities implemented different themes of government interventions at different timing. This played a crucial role in local pandemic control and had large effect on the final size of COVID-19 outbreak locally. Our study conducted the correlation analysis to demonstrate the strength of relationship between the implementation timing of some specific government interventions and the incidence of COVID-19 in nine cities. We proposed prioritising 'what can be done' at the city-level to plan the government interventions' maximal effect against the spread of COVID-19.

The detailed findings of our study included the following: first, our results suggested that different themes of government interventions were implemented to achieve different goals, which had different net effect. Aimed at reducing the number of susceptible population, the theme of travel restriction had a significant role in preventing the spread of COVID-19 across China. Compared with the complete lockdown, the earlier enforced lockdown in medium-risk level areas (GI_9) had much larger effect on containing the local outbreak across locations, while not carrying with the significant and unpredictable economic and social consequences. Aimed at protecting the susceptible population, the themes of health resources and environmental measures were likely to diminish the possible mode of COVID-19 transmission. The continued stringent wearing masks (GI_{10}) in public places had significant effect in reducing the reported cases due to public place transmissions, especially in metropolitan areas with a high density or a high proportion of asymptomatic cases. The environmental cleaning and disinfection implemented in targeted specific workplaces (including ports and industrial parks) are particularly effective when the imported cold-chain food from other countries was a main COVID-19-infected source. However, previously, due to a lack of wide implementation, the net effect of these two themes was appeared to be missed or underestimated in almost all countries.

Aimed at reducing the number of exposed cases, the theme of social distancing implemented in different locations had different net effect. Closure of educational institutions (GI_6), non-essential businesses (GI_7), shopping mall and restaurant (GI_8) in the medium-risk areas had positively influenced the incidence of COVID-19. In particular, containing the shopping mall and restaurant transmission as an important moderator and mediator had dramatically reduced the cumulative number of reported cases. In contrast, a larger percentage of household transmission could significantly reduce the cumulative number of reported cases. Therefore, stay-at-home could be an effective policy option in such circumstances. Aimed at identifying exposed/infected cases, the theme of case identification, contact tracing and related measures had significant effect in controlling the COVID-19 outbreak. Tracing and tracking close contacts identified 64.87% of reported cases average. Addressing the transmission within medium-risk level areas and high infection risk groups, testing (including targeted, periodic and mass testing) identified 30.81% of reported cases average. Fourteen-day centralised quarantining close contacts had quarantined 71.35% reported cases averagely before confirmed diagnosis. Therefore, considering the increasing proportion of asymptomatic cases, the combination of these government interventions had significant effect in isolating the identified exposed/infected cases from susceptible population, which prevented and delayed the arrival of second wave in China. In particular, the earlier implementation of tracing and tracking, or 14-day centralised quarantining close contacts had effectively induced a greater reduction in the incidence of COVID-19, which was found by the significantly positive correlations. This evidence from nine cities provided information that the theme of case identification, contact tracing and related measures should be enacted earlier to maximise their benefits and minimise the health, social and economic effect of COVID-19 in other countries or cities.

Despite the comprehensive findings, our study has several limitations. First, due to the current limited availability of epidemiological data, our study areas were just limited to nine cities in China. Second, in nine cities, we assumed that the apparent fall in the incidence of COVID-19 was likely to be attributed to the government interventions implementation, we cannot rule out the possibility that this fall was partially attributed to other unknown seasonal factors, for example, temperature and absolute humidity. Third, we only examined five themes of government interventions included in CCCSL and CoronaNet datasets. Other unobserved NPIs might also be an important part of effective COVID-19 response. Future research should consider expanding the themes of government interventions to include more government interventions implemented, as this would allow a more precise comparison of their net effect.

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Patient consent for publication Not applicable.

Ethics approval This study did not receive nor require ethics approval, because it used secondary data, and government published databases.

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Data availability statement All data relevant to the study are included in the article.

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