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## Preplanned Studies

## Predicted Impact of the COVID-19 Responses on Deaths of Tuberculosis — China, 2020

Caihong Xu<sup>1,&</sup>; Tao Li<sup>1,&</sup>; Dongmei Hu<sup>1</sup>; Hui Zhang<sup>1</sup>; Yanlin Zhao<sup>1,&</sup>; Jianjun Liu<sup>1,&</sup>

### Summary

#### What is already known about this topic?

The World Health Organization has estimated the impact of reductions in the performance of global tuberculosis (TB) detection and care on TB deaths. However, the actual impact of COVID-19 pandemic on TB deaths in China remains unclear.

#### What is added by this report?

The stringent public interventions to fight COVID-19 including lockdown led to more than 20% decrease of TB detection in China. It was predicted that the reduction of TB detection might result in 11,700 excess deaths based on assumption of no detection rebound. Based on the prediction the total deaths will be 51,100 in 2020 which might surpass the deaths in 2011.

#### What are the implications for public health practice?

Rapid restoration of TB diagnosis and care services is critical for minimizing the potential effects on TB-related deaths and bringing TB burden back to control. It is urgent to ramp up case detection including active case finding and to provide an uninterrupted supply of quality-assured treatment and care for TB cases in post-COVID-19 outbreak.

In order to reduce transmission of coronavirus disease 2019 (COVID-19), China implemented a series of public health interventions including cancelling public transportation; prohibiting public gatherings; closing schools, libraries, and other public spaces; recommending a 14-day home quarantine for individuals from highly-affected areas; and deploying a large amount of resources and dispatched health workers to fight the epidemic (1–3). All these interventions have successfully brought COVID-19 under control. But at the same time, these interventions have adversely affected other public health issues that deserve the public's concern and should be addressed including tuberculosis (TB) control (4–5).

TB is a bacterial disease predominantly affecting the lungs. During 2018, an estimated 10 million new TB cases occurred globally, while 0.86 million cases were registered in China, which ranks second in the world (6). Although, TB-related mortality declined from 8.7/100,000 person-years (PY) in 2000 to 2.6/100,000 PY in 2018, TB still caused an estimated 39,400 deaths (including TB/HIV deaths) in 2018 in China (7).

Some studies have discussed the possible impact of COVID-19 on the performance of TB control regarding diagnosis, treatment, and management (8). The World Health Organization (WHO) has estimated the impact of reductions in the performance of global TB detection and care on TB deaths (9). However, the actual impact of COVID-19 pandemic on TB deaths in China remains unclear.

The TB detection data was extracted from Tuberculosis Information Management System (TBIMS) on July 15, 2020. Considering the epidemic of COVID-19, the study estimated excess TB deaths in 3 geographic areas (Wuhan City, Hubei Province and China overall) and 4 phases (Phase I: January 23, 2020 to February 11, 2020; Phase II: February 12, 2020 to March 24, 2020; Phase III: March 25, 2020 to April 8, 2020; Phase IV: April 9, 2020 to June 30, 2020). These phases were divided based on 4 events: 1) January 23, 2020, lockdown of Wuhan City; 2) February 11, 2020, China CDC issued a notice to guide management of TB patients during the COVID-19 epidemic; 3) March 24, 2020 (World TB day), China promoted a campaign of “Jointly fighting COVID-19 and TB, and breathing healthy together” and the National Health Commission issued a “Notice on Further Strengthening TB Control and Prevention” and 4) April 8, 2020, China lifted the 76-day lockdown on Wuhan which meant the whole country started gradually returning to normal life.

Excess TB mortality  $\Delta M$  resulting from the perturbation to TB detection was calculated using the following formula (9):

$$\Delta M = \sum_b [(1-d)(f_u^b - f_t^b) T^b] \quad (1)$$

The perturbation  $d$  of TB detection was expressed in terms of a reduction in the number of treated cases as compared to the expected number in the absence of the COVID-19 pandemic. Subscript  $u$  denotes untreated TB and subscript  $t$  denotes treated TB. Distributions of  $f$  are taken from the death surveillance points of China. It is assumed that the value of  $d$  is the same among HIV-positive and HIV-negative individuals. The  $b$  represent HIV status.

The number of detected active TB cases in China, Hubei, and Wuhan were found to decrease by 20%, 29%, and 44%, respectively, during January 23 to June 30, 2020 when compared with the same period in 2019. The highest reduction appeared in phase I nationwide and in phase II in Hubei and Wuhan. Wuhan had an especially large reduction at 74% (Figure 1).

The estimated additional TB deaths would be 186 cases, 760 cases and 11,700 cases which brought the total TB deaths to 478 cases, 2,520 cases and 51,100 cases in Wuhan, Hubei, and China, respectively. The

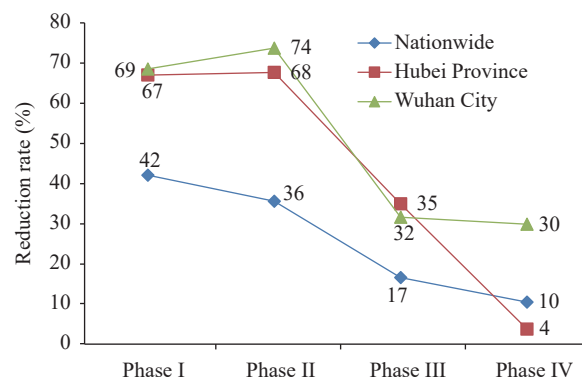


FIGURE 1. The reduction in tuberculosis case detection in China overall, in Hubei, and in Wuhan in different phases in 2020.

Phase I: January 23, 2020 to February 11, 2020; Phase II: February 12, 2020 to March 24, 2020; Phase III: March 25, 2020 to April 8, 2020; Phase IV: April 9, 2020 to June 30, 2020.

estimated nationwide number of deaths surpassed the level of TB deaths in 2011 (50,900) and caused a serious setback in the progress towards the End TB strategy milestones and targets. More than half of the

TABLE 1. The predicted number of tuberculosis deaths including tuberculosis (TB) deaths in HIV-negative and in HIV-positive cases during different phases in China overall, in Hubei, and in Wuhan in 2020.

	Perturbation	Predicted excess deaths among HIV-positive cases (N)	Predicted excess deaths among HIV-negative cases (N)	Predicted total excess deaths (N)	Excess deaths/annually deaths in 2018 (%)
<b>Wuhan City</b>					
Phase I	0.962	0	34	34	11.8
Phase II	0.915	1	77	78	26.6
Phase III	0.987	0	12	12	4.1
Phase IV	0.932	1	61	62	21.3
Subtotal		2	184	186	63.8
<b>Hubei Province</b>					
Phase I	0.963	2	201	203	11.5
Phase II	0.963	4	427	430	24.4
Phase III	0.986	1	79	79	4.5
Phase IV	0.922	0	47	47	2.7
Subtotal		6	753	760	43.1
<b>Nationwide</b>					
Phase I	0.977	24	2,827	2,851	7.2
Phase II	0.959	43	5,022	5,065	12.9
Phase III	0.993	7	835	842	2.1
Phase IV	0.976	25	2,917	2,942	7.5
Total		98	11,601	11,700	29.7

Note: The study estimated excess TB deaths in 3 geographic areas (Wuhan City, Hubei Province and China overall) and 4 phases (Phase I: January 23, 2020 to February 11, 2020; Phase II: February 12, 2020 to March 24, 2020; Phase III: March 25, 2020 to April 8, 2020; Phase IV: April 9, 2020 to June 30, 2020).



excess deaths were due to the reduction in case in Phase II. The estimated excess deaths during the COVID-19 pandemic accounted for 63.8%, 43.1%, and 29.7% of annual deaths in Wuhan, Hubei, and China, respectively (Table1).

## DISCUSSION

Our study showed that stringent responses to COVID-19 that have slowed transmission of the virus also caused and might continue causing disruptions to TB programs in the short and long terms. Lockdowns have already severely reduced TB notification rates by 20%–44% in various areas between January 23 and June 30, 2020. The reduction in TB detection during the 5-month period was estimated to lead to a 30% increase in TB deaths in 2020, bringing the total TB deaths to 51,100 TB, which will setback progress in reducing TB deaths to levels seen in 2011 in China. Globally, the 3-month lockdown is estimated to reduce TB detection rates by 50% and bring the number of TB deaths to 1.85 million, which is similar to global levels seen in 2012 (9).

The public interventions to fight the COVID-19 pandemic adversely impacted TB detection and mortality in the following ways. First, the restriction of traffic has created barriers for patients to access healthcare, difficulties for health providers in tracing presumptive TB cases, transporting sputum samples, managing TB patients' daily medication, and visiting patients' households for close contact tracing. Second, healthcare staff from TB programs, TB laboratories, and TB wards have been re-assigned to fight against COVID-19, which reduced capacity of TB diagnosis, treatment, and management. Third, concerns of COVID-19 transmission has reduced willingness of patients to visit health facilities. Finally, supply interruptions and low supplies of TB drugs and lack of care for TB cases could lead to delays in initializing TB treatment or involuntary treatment interruption.

The results of the study need to be interpreted with caution since the estimation of the excess deaths was on the assumption that the beneficial effect of lockdown and social distancing policies on TB reproductive number may be offset by increased duration of infectivity under lower case detection and treatment performance. The estimation did not address the interaction between TB and the COVID-19 virus.

Our results have certain implications for the

National Tuberculosis Program (NTP) in China. Generally, rapid restoration of TB diagnosis and care services is critical for minimizing the potential effects on TB-related deaths and bringing TB burden back to control. Specifically, it was pivotal to maintain awareness of recognizing and responding to symptoms suggestive of TB; it is urgent to ramp up case detection including active case finding and to provide an uninterrupted supply of quality-assured treatment and care for TB cases. Systemic evaluation, referral, and management of complications at diagnosis of the disease should also be prioritized. Meanwhile, the COVID-19 pandemic also provided opportunities for simultaneous testing of TB and COVID-19, better implementation of infection control measures, and effective contact tracing investigations.

This study was subject to some limitations. Only the excess deaths caused by declines in detection of TB patients were estimated, while the impact on TB deaths may be more complicated. For example, measures devoted to screening based on symptoms and temperature monitoring during the disease-response period may increase the sensitivity of patients' detection. In addition, results among different areas with different controls strategies were not compared to further measure potential impact of the lockdowns.

In conclusion, the response to fight the COVID-19 pandemic has caused directly impacted TB case detection and might result in potential effects on TB deaths, which may wipe out the TB control program efforts made in the last few years. To cope with the adverse effects, comprehensive measures should be implemented in the aftermath of the pandemic, including strengthening human resources for TB control, scaling up of laboratory testing, ensuring an uninterrupted supply of medicines, providing holistic treatment management care, and other measures. These will help to ensure timely TB diagnosis and full course treatment for all TB cases.

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## Notes from the Field

## Two Reemergent Cases of COVID-19 — Hebei Province, China, January 2, 2021

Shunxiang Qi<sup>1,✉</sup>; Xiang Zhao<sup>2,✉</sup>; Peter Hao<sup>3</sup>; Nankun Liu<sup>3</sup>; George F. Gao<sup>3</sup>; Yang Song<sup>2</sup>; Wenbo Xu<sup>2,✉</sup>; Qi Li<sup>1,✉</sup>

On January 2, 2021, 2 cases of coronavirus disease 2019 (COVID-19) were identified in 2 cities of Hebei Province, and genomic sequencing suggested that the cases likely resulted from the same origin. The first case (Patient A) was identified as positive at 12:18 in Shijiazhuang City, the capital of Hebei Province, and the second case (Patient B) was identified as positive at 21:00 in Xingtai City.

Patient A is a 61-year-old female residing in a rural village in Gaocheng District of Shijiazhuang City and had a history of hypertension and multiple mild cerebral infarctions. Patient A experienced discomfort in her pharynx starting around 21:30 on January 1, 2021 and general malaise and fever around 04:00 on January 2. At 05:00, she took a taxi accompanied by her husband and eldest son (all wearing masks) to a hospital for treatment and was sent to the fever clinic for testing. Her temperature measured 38.6 °C and she tested positive at 12:18. At 17:50, she was transferred by a negative pressure ambulance to a designated hospital in Shijiazhuang for isolation and treatment.

In the two weeks prior to her diagnosis, Patient A had a history of staying at home, visiting family, and attending religious gatherings in the village with sporadic mask wearing. However, on December 28, she attended a wedding in the village at a restaurant with roughly 250 people in attendance. Of these 250 people, several were known to be traveling from Xi'an City of Shaanxi Province and Beijing Municipality.

Patient B is a 34-year-old male residing in Nangong City, a county-level city of Xingtai City. At 14:00 on January 1, he recorded a self-tested temperature of 38.1 °C and drove to the fever clinic of Nangong City for a COVID-19 test at his own expense. His results were found to be positive at 21:00 on January 2, and he was immediately isolated via ambulance and placed under medical observation. He was retested by Xingtai CDC and confirmed to be COVID-19 positive.

In the two weeks prior to his diagnosis, Patient B had a history of performing work-related tasks, staying at home, and meeting guests without going to high-risk areas. He was possibly exposed on December 25

when traveling to Shijiazhuang City to see his daughter at a children's hospital or on December 28 when attending an agricultural conference without wearing a mask. Based on the full investigation of Patient B's epidemiological history, 137 close contacts have been preliminarily identified.

On January 4, the sequences of the COVID-19 samples from Patients A (Shijiazhuang) and B (Xingtai) were obtained using Illumina Miseq and Illumina Nextseq550 platform, respectively (Sequence ID: 512 and 519). Compared with the Wuhan reference sequence (EPI\_ISL\_402119) (1–2), the Shijiazhuang strain had 21 nucleotide variation sites and the Xingtai strain had 22 nucleotide variation sites. The Xingtai strain shared the 21 nucleotide variation sites presented by the Shijiazhuang strain and also presented an additional unique variation. The 2 strains both contained the 7 single nucleotide polymorphisms (SNPs) that defined L-lineage European branch I (C241T, C3037T, C14408T, A23403G, G28881A, G28882A, and G28883C) (Figure 1). Furthermore, the 2 sequences shared an additional 14 unique nucleotide variation sites (T2392C, C6354T, T7075C, C10747T, A11794G, C15342T, C15360T, G15666A, C16733T, C21727T, T22020C, C25416T, C27213T, and C29835T) and were both identified as belonging to B.1.1.123 Pangolin lineage (3), which suggested that the Shijiazhuang and Xingtai strains had the same transmission route. However, the Xingtai strain had an additional variation site T23227C. The sequencing results indicated that the genomic characteristics of the Hebei strains differed from recent strains detected in several COVID-19 epidemics in China (4–6) and were unrelated to recent variants discovered in the United Kingdom.

After accessing the public database GISAID and GenBank, 3 Russian strains detected in July were found to share the 10 variation sites with the 2 Hebei strains (GISAID IDs: EPI\_ISL\_596266, EPI\_ISL\_569792, and EPI\_ISL\_569793). Despite relatively few shared variation sites, the 3 unique sites detected from the Russian strains were only seen in the Hebei strains

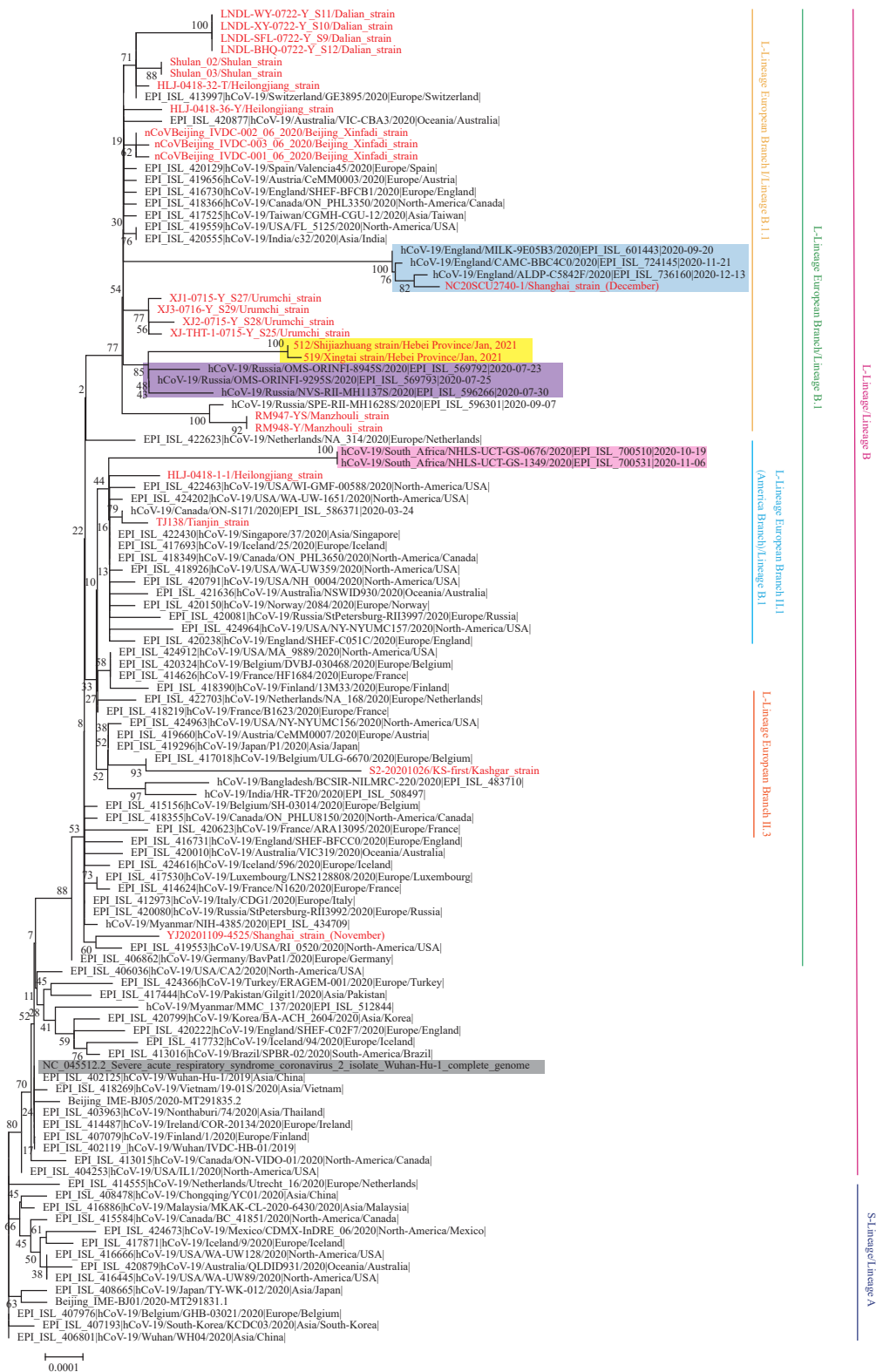


FIGURE 1. Phylogenetic tree based on the full-length genome sequences of the COVID-19 virus. Strains associated with specific outbreaks in China were marked and colored in red letters. The Shijiazhuang and Xingtai strains from Hebei Province are highlighted in yellow, and the Russian strains that shared 10 nucleotide variation sites with the Hebei strains are highlighted in purple. The UK VUI-202012/01 variants and South African 501.V2 variants are highlighted in blue and pink, respectively. The Wuhan reference strain is shaded in gray. The S(A)- or L(B)-lineage and sublineages of the COVID-19 virus were marked and colored on the right.

(Figure 1). The databases have not recorded many recently uploaded strains from Russia, but evidence indicates that these the Shijiazhuang and Xingtai strains may have originated from these Russian strains. Continued monitoring of COVID-19 in Hebei Province is vital to prevent further transmission.

Since the initial identification of the cases on January 2, 2021, 39 confirmed cases and 83 asymptomatic infections in Hebei Province have been identified as of January 5, 2021. Before this outbreak was identified, Hebei Province had no COVID-19 cases for approximately 160 days with the last cases being found on June 25, 2020.

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## Notes from the Field

# A Case of New Variant COVID-19 First Emerging in South Africa Detected in Airplane Pilot — Guangdong Province, China, January 6, 2021

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Nankun Liu<sup>3</sup>; Chunliang Lei<sup>1,✉</sup>; Changwen Ke<sup>2,✉</sup>

On January 6, 2021, Guangdong CDC successfully isolated the 501Y.V2 variant of coronavirus disease 2019 (COVID-19) virus from a throat swab of a patient. The 501Y.V2 variant was first detected in South Africa, and the patient is a 55-year-old male airline pilot of South African nationality. He entered Guangzhou City, the capital of Guangdong Province, from Singapore on the evening of December 8, 2020 and was subject to a COVID-19 test. The result returned positive and he was transferred to the designated hospital for further isolation and treatment. On December 31, 2020, Guangdong CDC received the samples and began virus isolation and gene sequencing analysis. The analysis and subsequent verification have concluded that the virus genome belongs to lineage B.1.351, inferring classification as the 501Y.V2 variant. The patient is still receiving treatment.

On January 5, 2021, the sample and virus isolates were sequenced using Nanopore MK1C. Compared with the Wuhan reference strain (EPI\_ISL\_402119) (1–2), this strain displayed 23 nucleotide variation sites including the single nucleotide polymorphisms (SNPs) that defined the L-lineage European branch II.1 and belonged to the Pangolin lineage B.1.351 (3) (Figure 1). Furthermore, 10 amino acid mutation sites (D80A, L242del, A243del, L244del, R246I, K417N, E484K, N501Y, D614G, and A701V) were detected in the spike protein that corresponded to the features of the South African 501Y.V2 variant. The 501Y.V2 variant has 3 specific mutations, K417N, E484K, and N501Y, on the spike protein (4) and shares the N501Y and D614G mutations with the 501Y.V1 variant (also known as the B.1.1.7 lineage and variant of concern (VOC) 202012/01) recently detected in the United

Kingdom. This is the second recent detection of a major international variant following the detection of the United Kingdom 501Y.V1 variant in a patient in Shanghai (NC20SCU2740-1) in December 2020 (5). The transmissibility and pathogenicity of these mutant variants urgently needs further study.

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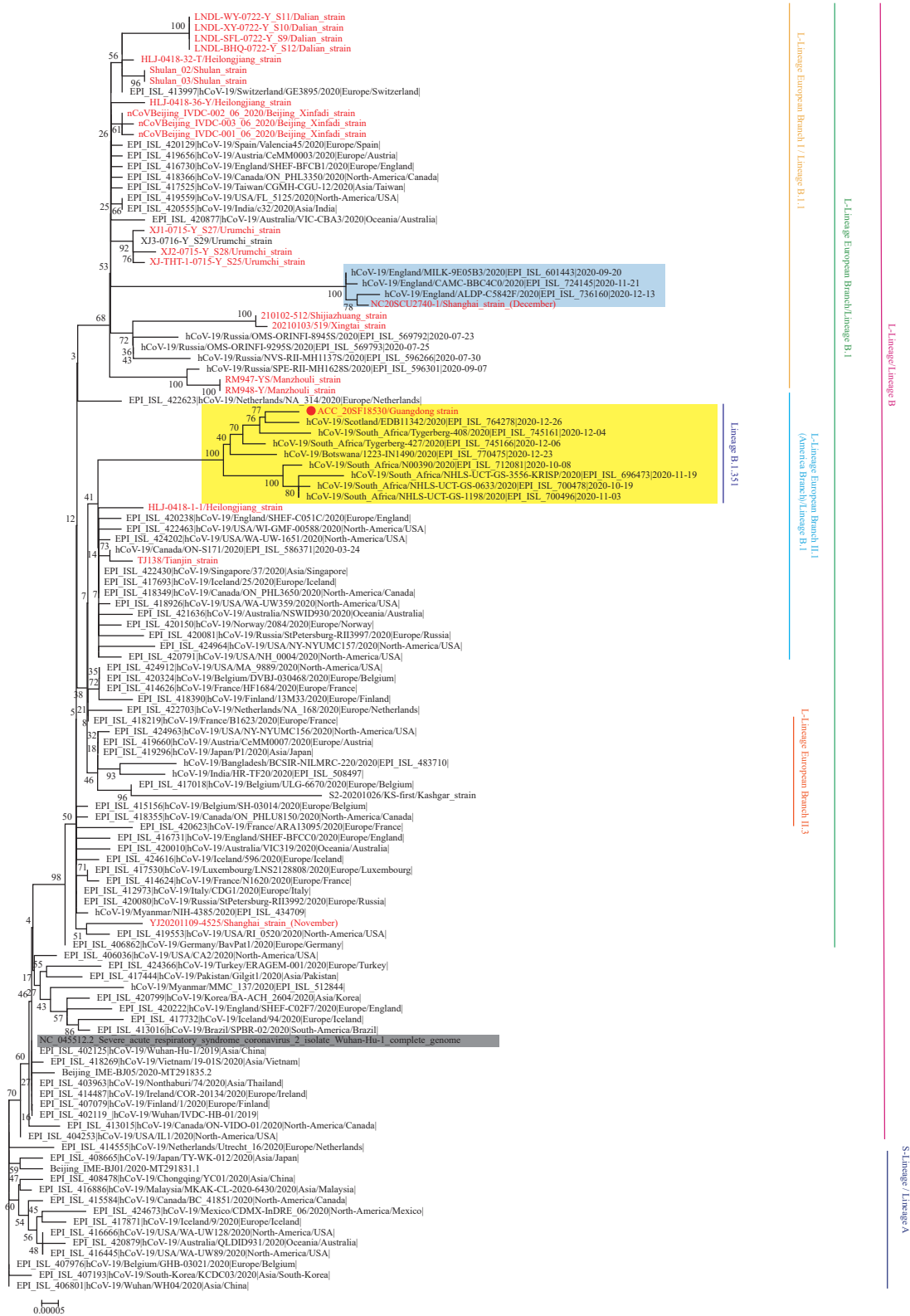


FIGURE 1. Phylogenetic tree based on the full-length genome sequences of the COVID-19 virus. Strains associated with specific outbreaks in China are marked using red letters. The South African 501Y.V2 variants are highlighted in yellow and the Guangdong imported 501Y.V2 variant is marked with a red dot. The UK VUI-202012/01 variants are highlighted in light blue. The Wuhan reference strain is shaded in gray. The S(A)- or L(B)-lineage and sublineages of the COVID-19 virus were marked and colored on the right.

## Controlling COVID-19 Transmission due to Contaminated Imported Frozen Food and Food Packaging

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### BACKGROUND

The emergence of the coronavirus disease 2019 (COVID-19) has been sharply increasing with more than eighty million confirmed cases worldwide (1). It has been contained in China through stringent non-pharmaceutical interventions (2). A combination of strict border control and quarantine measures have effectively prevented the spread of the virus from infected travelers, but the risk of resurgence caused by other routes of transmission (fomite transmission) has been identified in a number of localized outbreaks (3–7). Although the COVID-19 virus is highly unlikely to cause an epidemic through foodborne transmission, epidemiological investigation on the source of infection have found that all these outbreaks in different cities in China could be tracked to fomite transmission originating from workers at port cold storage, seafood processing facilities, and market sites related to imported cold-chain food (Table 1) (3–4). Furthermore, COVID-19 viral RNA has been detected on the surface of frozen food (salmon, white shrimp, lophiiformes, cod fillets, frozen hairtail, frozen beef, frozen pig elbow, frozen chicken wings, and frozen pork) and their packaging materials imported from countries with significant COVID-19 epidemics across 18 provincial level administrative divisions (PLADs) in China (Figure 1).

Additionally, several COVID-19 outbreaks have occurred in meat and poultry processing facilities abroad. COVID-19 was diagnosed in 18.2% workers in some states of the USA (8). Those who work in these cold, high humidity, and congregate locations are at high risk for both the acquisition and transmission

of respiratory infections. Thus, the food and food packaging materials are likely to become contaminated through droplets expelled from COVID-19 carriers by breathing, coughing, singing, sneezing, or even talking. Moreover, scientific studies have shown that COVID-19 virus remained highly stable under refrigeration (4 °C) and freezing conditions (–20 °C and –80 °C), on fish, chicken, and pork for 21 days (9). In the investigation of the COVID-19 outbreak in Qingdao, live COVID-19 virus was successfully isolated and cultured from samples taken from imported frozen seafood packaging (10). These findings indicated that COVID-19 virus could survive on cold-chain food and food packaging during long distance shipping and may cause human infection, in particular to high-risk people (such as dockworkers or stevedores). It was confirmed in these studies that COVID-19 outbreak could be caused by fomite transmission in the cold food chain, although the likelihood of this food-to-human transmission is considered lower when compared with other routes of transmission.

Keeping all workers in the whole food supply chains healthy and safe is vital for their personal wellbeing, for their families, and for ensuring that consumers' needs are met. This is also important for maintaining consumer trust and confidence in securing safe and sustainable food supply. In this regard, Chinese authorities have developed a series of guidance documents to protect food workers from contracting COVID-19, to prevent cross-contamination of COVID-19 virus across the whole food chain to avoid possible exposure of the virus to consumers, and to strengthen food hygiene and sanitation practices.

TABLE 1. Coronavirus disease 2019 outbreaks related with the cold-chain food and food packaging in 2020.

Date	City	Place	Zero patient	Cold-chain food contamination
June 11	Beijing	Wholesale market	Employee	Imported salmon
July 22	Dalian	Dock	Dockworker	Food packaging of imported fish
September 24	Qingdao	Dock	Dockworker	Food packaging of imported frozen cod
November 8	Tianjin	Cold storage	Stevedore	Food packaging of frozen pork

## GUIDANCE RELATED TO IMPORTED COLD-CHAIN PRODUCTS

The Joint Prevention and Control Mechanism of the State Council of the People's Republic of China rapidly promulgated eight technical guidance documents at a national level for the prevention and control of COVID-19 transmission related to cold-chain food production according to the COVID-19 epidemic situation in China (Figure 2). More than 30 guiding documents were promulgated by municipal or provincial governments based on the State Council documents. These documents could be classified into four categories: guidance to prevent human infection,

guidance for detection methods, guidance for disinfection, and guidance for source tracing.

### Guidance to Prevent Human Infection

Transmission of the COVID-19 virus has been linked to close contact between individuals within closed settings. In addition, outbreaks have happened in port cold storage, meat/seafood processing facilities, and wholesale markets. Four documents were proposed including the following: “Guidance for normalizing prevention and control of COVID-19 outbreaks in key locations, key units, and key populations in low-risk areas in summer (revised edition)” Guidance [2020]-192 (Jun 17, 2020) (11), “Guidelines on prevention

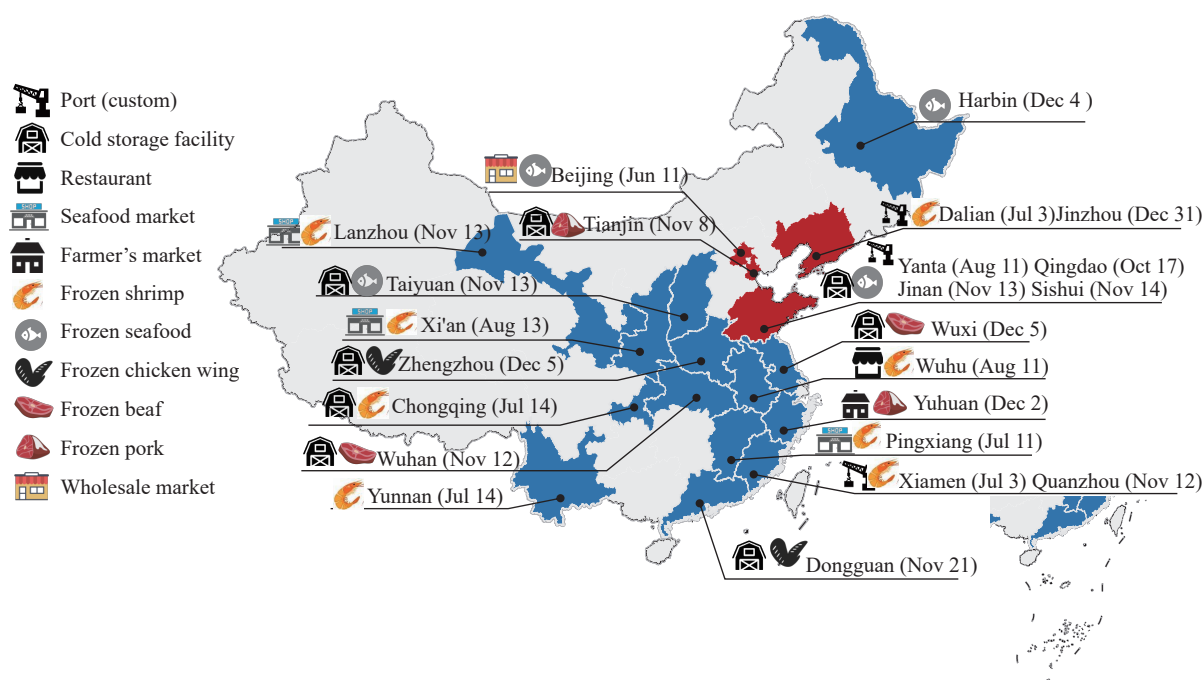


FIGURE 1. Detection of COVID-19 virus on imported frozen raw foods across China from early June 2020 to the end of December 2020.

The blue regions represent areas where the viral RNA has been detected, while the red regions represent areas with both viral RNA having been detected and outbreaks having occurred.

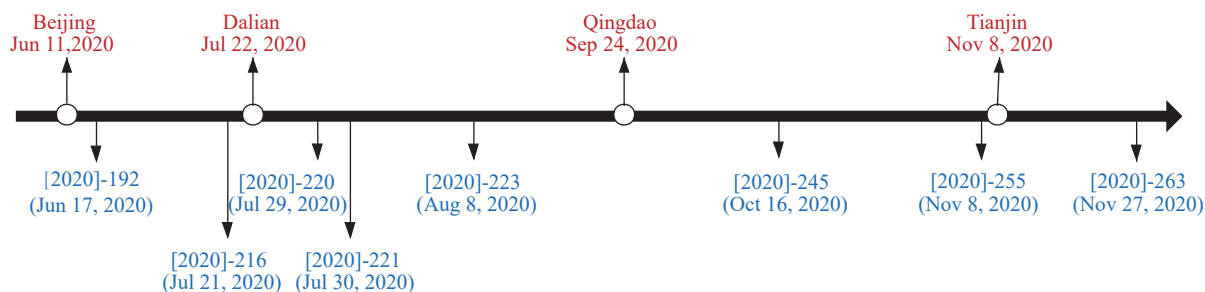


FIGURE 2. The timeline of the onset of coronavirus disease 2019 outbreak and the prevention and control technical guidance documents in 2020.

and control of COVID-19 for meat processing facilities” Guidance [2020]-216 (Jul 21, 2020) (12), “Technical guidance for COVID-19 prevention and control in farmers’ markets” Guidance [2020]-223 (Aug 8, 2020) (13), and “Technical guidance for prevention and control of COVID-19 in cold food production chain and technical guidance for disinfection in cold food production chain to prevent and control of COVID-19” Guidance [2020]-245 (Oct 16, 2020) (14). These guidance documents are intended for stakeholders to ensure compliance with measures to protect food workers and consumers from contracting COVID-19, to prevent exposure to the virus or transmission of it, and to strengthen food hygiene and sanitation practices.

### Guidance for Detection Methods

COVID-19 viral RNA has been detected on frozen food and food packaging and the contaminated cold-chain food and food packaging might lead to a systematic risk for COVID-19 virus transmission. In order to implement the “four early” (early detection, early report, early isolation, and early treatment) prevention and control strategy and strengthen epidemic prevention and control, it is required to strengthen the epidemic risk surveillance to prevent potential additional risks. The most important factor is to strengthen the testing of food, its environment, and the workforce. As a result, “Guidance on strengthening the detection of COVID-19 virus in the cold-food chain” Guidance [2020]-220 (Jul 29, 2020) (15) and “Technical guidance of environmental monitoring of COVID-19 virus in farmers’ markets” Guidance [2020]-221 (Jul 30, 2020) (16) were proposed. COVID-19 virus laboratory testing technical methods as well as a sampling plan and laboratory biosafety is included.

### Guidance for Disinfection

Environmental surfaces are more likely to be contaminated with the COVID-19 virus in manufacturing chain where outbreaks have taken place. Therefore, “Technical guidance for prevention and control of COVID-19 in cold food production chain and technical guidance for disinfection in cold food production chain to prevent and control of COVID-19” Guidance [2020]-245 (Oct 16, 2020) (14) and “Work plan for preventive and comprehensive disinfection of imported cold-chain food” Guidance

[2020]-255 (Nov 8, 2020) (17) were proposed. The purpose of these documents is to provide guidance on the cleaning and disinfection of environmental surfaces (disinfection of internal and external packaging of loading and transportation tools and products) in the context of COVID-19.

### Guidance for Source Tracing

Rapid cold-chain food tracking provided strong support for the prevention and control of COVID-19 outbreaks in Dalian, Qingdao, and Tianjin. As a result, the “Notice on further improving tracking management of cold-chain food” Guidance [2020]-263 (Nov 27, 2020) (18) was proposed. In accordance with this guidance document, the national tracking platform was built for imported cold-chain food and has been connected to more than 9 provincial tracking systems (including Beijing, Zhejiang, and Guangdong, etc.) in real time of the production chains.

## SHORT-TERM RESULTS AFTER IMPLEMENT

In accordance with the requirements of the Joint Prevention and Control Mechanism of the State Council of the People’s Republic of China (Guidance [2020]-220), sampling and testing of cold-chain food and food packaging in the market and the environment were conducted at the national level. The positive rate of COVID-19 testing in the imported cold-chain food was relatively higher than before. By November 30, 2020, COVID-19 viral RNA was detected in food or food packaging samples collected nationwide, with an overall positive rate of 0.048‰ (19). As COVID-19 continues to spread around the world, relevant departments should strengthen the inspection of inbound cold-chain goods from foreign countries, especially those countries or regions with serious outbreaks.

Furthermore, workers needed to be protected as the main route of COVID-19 virus transfer to food and food packaging is assumed to be via cross contamination from infected individuals. Workers who have frequent contact with cold-chain food have a high possibility to be contaminated by COVID-19 virus without effective protection. It is suggested to enhance the awareness of protection and take preventive measures for food workers, especially the high-risk employees.



## CONCLUSION

Since June, several COVID-19 outbreaks in China have been linked to the cold-chain food and food packaging. With increasingly reported evidence, food and food packaging contaminated by COVID-19 virus may pose a risk of spreading the virus under certain conditions. According to a range of different situations, the government has issued a series of guidance documents to prevent both human-transmission and fomite-transmission, which has become a widely adopted practice of epidemic prevention and control. Moreover, technical guidances for cold-chain food tracking are also necessary. So far, the epidemic of COVID-19 has been contained in China through stringent non-pharmaceutical interventions and the integrity of the food chain has been maintained and adequate supplies of safe food is available for all consumers.

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## Policy Notes

# Guidelines for the Prevention and Control of Tuberculosis in Schools: Recommendations from China CDC

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China is still a high tuberculosis (TB) burden country, and the number of new cases of TB was 833,000 in 2019 (1). School campuses are highly-crowded places with potential for close contact, which suggests that a few cases of TB may lead to a large outbreak. Thus, TB prevention and control in schools is an important disease control challenge for educational and health departments at all levels. In 2017, the former National Health and Family Planning Commission (now known as the National Health Commission, NHC) and the Ministry of Education jointly revised and issued the “School Tuberculosis Prevention and Control Work Regulations (2017 Edition)” (hereafter referred to as “School Regulations”) (2). Based on the regulations, China CDC organized experts to formulate the “Guidelines for the Prevention and Control of Tuberculosis in Chinese Schools” (referred to as “School Guidelines”) to standardize and refine the recommendations for implementation.

## BACKGROUND

The total number of students in China has remained as around 250 million since 2008. Students in nurseries/kindergartens, elementary schools, junior and senior high schools, and colleges/universities account for about 20%, 40%, 30%, and 10% of all students (3), respectively. The majority of students were between 3–24 years old, and the proportion of boarding school students is increasing.

In recent years, TB notified case numbers in students were around 48,000 per year with a reported incidence of about 1/3 of the general population. About 85% of all student cases were reported from senior high schools and colleges, aged between 15–24 years old (4). Most reported TB public health emergencies happened in senior high schools with several common features: cases mainly occurred in boarding schools; the proportion of bacteriologically confirmed cases was low; and emergencies in low-risk areas mostly occurred in schools with concentrated students immigrated from high-risk areas.

## METHODS

China CDC organized the first expert discussion meeting in Chongqing Municipality in July 2017. During this meeting, experts determined the main structure and details of the “School Guidelines”. A total of 18 experts from different disciplines participated, formed the drafting group, and then developed the first draft of the guidelines based on existing research evidence and practical experiences. In November and December 2018, the draft was sent to all 31 provincial-level administrative division (PLADs) agencies for TB prevention to collect their opinions for revision. In January 2019, an educational system expert seminar was held in Nanjing City, and several small-scale expert seminars were organized later. In November 2019, 20 experts from the NHC, the National TB Expert Advisory Committee, China CDC, provincial-level educational administrative departments, and university hospitals that specialized in TB diagnosis, TB treatment, epidemiology, laboratory techniques, TB prevention and control, education and school health, reviewed and finalized the guidelines.

## RATIONALE

The school regulations specify prevention and control measures in 3 different scenarios: routine control with no active cases, detection of sporadic cases, and public health emergencies (Figure 1). Based on research evidence and field experiences, the school guidelines refined control measures, gave guidance on the application of several new technical instruments, and provided more practical recording tools for practice.

## RECOMMENDATIONS

### Health Examination

The school entrance examination for newly enrolled

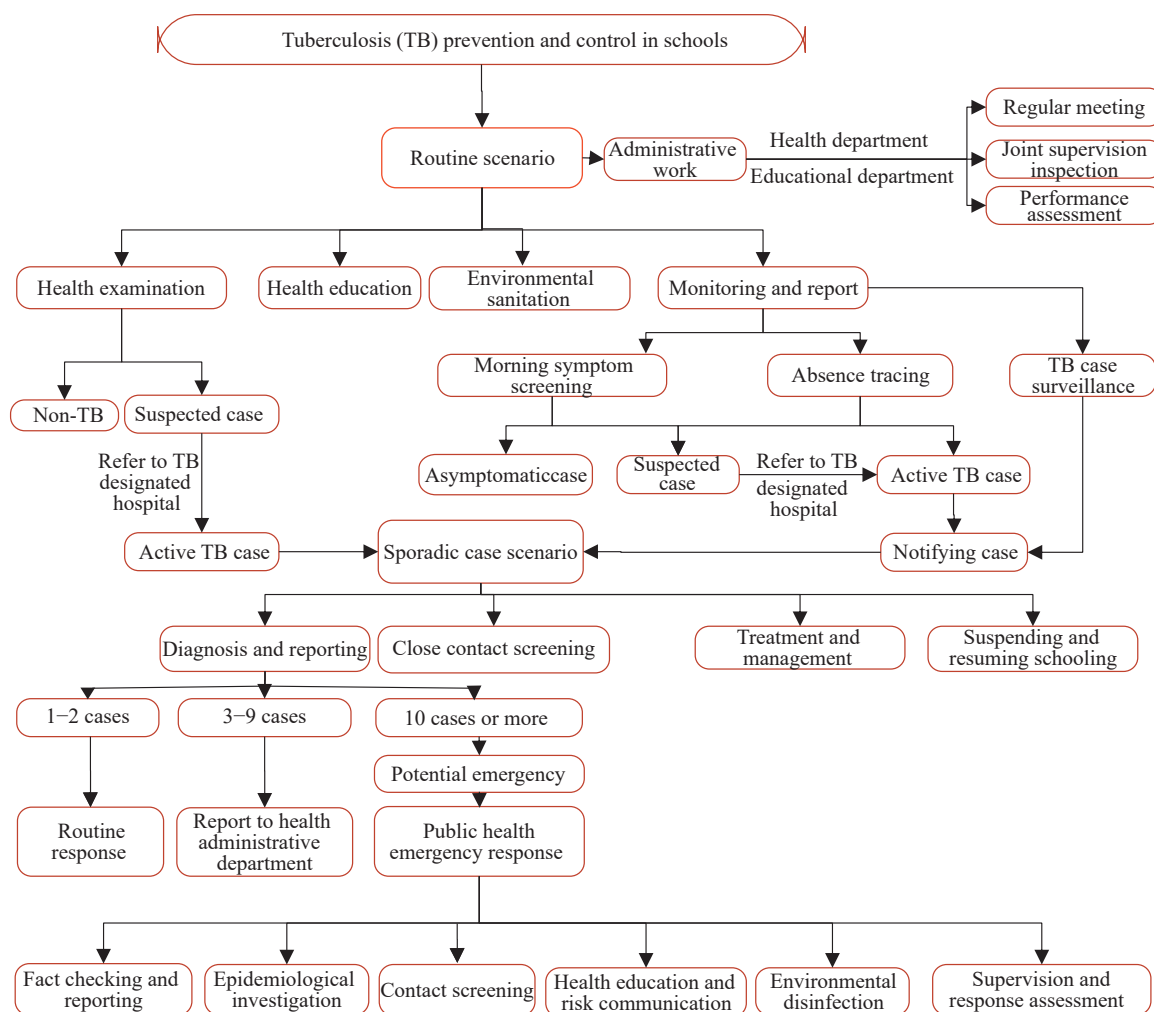


FIGURE 1. Tuberculosis prevention and control measures in school in three different scenarios.

The 3 different scenarios including: routine control with no active cases, detection of sporadic cases, and public health emergencies.

students should be completed before entering the school, or as latest as within 1 month after the start of school life (examinations required were listed in Table 1). All faculty and staff must undergo a health examination before joining the school, and routine health examinations should be performed once a year.

### On-campus Health Education and School Environmental Sanitation

Various sorts of health education should be conducted for educational administrative departments, school principals, school doctors, teachers, students, and their parents. According to national school hygiene standards, schools should guarantee space per capita for classrooms and dormitories and strengthen the ventilation and sanitation of mass gathering venues.

### On-campus Symptom and Absence Monitoring and Reporting

Nurseries/kindergartens, elementary and high schools should carry out morning symptom checks every day (5). Symptoms, such as cough and expectoration, should be recorded and reported to the school medical office. The student with suspicious symptoms of TB should be transferred to the local designated TB hospitals for diagnosis. For absent students, their teachers should verify whether the absence is due to illness, especially for students with presumptive TB or with suspicious symptoms of TB. For suspected or diagnosed TB patients, isolation or suspending schooling may be necessary.

### Active Surveillance By Medical Facilities

For pulmonary tuberculosis (PTB) patients aged

TABLE 1. Health examination at entry of different schools.

School type	Examination methods
Nurseries /kindergartens, elementary schools, and non-boarding junior high schools	First, history of close contact with tuberculosis (TB) patients and TB-like symptoms are checked. For children and students with a history of close contact with TB cases or suspicious symptoms, tuberculin skin test (TST) should be performed. For students who have contraindications for TST testing, the $\gamma$ -interferon release test (IGRA) can be used for instead. For those with suspicious symptoms or strongly positive TST ( $\geq 15$ mm or with double circle, blistering, necrosis or lymphangitis) or IGRA positive results, chest X-ray examination should be performed.
Senior high schools and boarding junior high schools	First, TB-like symptoms are checked and TST or IGRA tested. Chest X-rays should be performed on those with suspicious symptoms or strongly positive TST tests or IGRA positive results.
Colleges and universities	First, TB-like symptoms should be checked, and chest X-ray examination taken. High risk areas and high-risk schools can carry out TST or IGRA test at the same time.

between 3–24 years old, hospitals must check whether the patient is a student and report the name of the school, class, and other information in the National Infectious Disease Reporting System. The National Infectious Diseases Automatic Alert and Response System will send a single-case alert for every PTB case notified as being “in nursery/kindergarten”, “student”, “teacher”, and/or aged 3–24 years old (6). After receiving an alert, the local CDC should promptly verify the information, contact the school, and start contact screening. The local CDC should also regularly analyze the TB epidemic situation in schools within their jurisdiction and conduct public media monitoring to detect clustered epidemics at an early stage.

### Patient Diagnosis, Treatment And Management

TB diagnosis should be made based on patient contact history, symptoms, signs, imaging, and laboratory examination results (7). Treatment course will be determined based on reliable drug susceptibility test results, considering age, weight, and conditions of disease. Supervision of drug intake and support will be performed through the whole course of treatment. Students may need to suspend schooling until getting proof of recovery and non-infectivity.

### Contact Screening

Contacts can be divided into 3 categories (Table 2). The primary screening is generally limited to the close contacts. If a new case is detected or a high tuberculin skin test (TST) strongly positive rate is observed, screening should be expanded to general contacts or even larger scales. See Table 2 for screening approaches and post-screening actions.

### Preventative Treatment

The preventative treatment subjects are those

excluding active PTB and including one or more scenarios: a strongly positive TST test result, TST net value increasing by  $\geq 10$  mm within two years,  $\gamma$ -interferon release test (IGRA) positive, or HIV/AIDS positive and TST  $\geq 5$  mm. Preventative treatment will be given with informed consent, choices of regimen are 3 months of rifampicin+isoniazid/rifapentine+isoniazid, 6–9 months of isoniazid, or 4 months of rifampicin (8). A drug intake supervision will be provided. Routine blood tests and liver and kidney function tests will be performed at the second weekend and the end of every month after.

### Infection Control

Schools should construct the building properly and establish a ventilation system in accordance to the national standards (9). Suspected and diagnosed TB patients who meet the conditions of schooling suspension will be placed under medical isolation or home isolation. UV radiation, chemical disinfection, etc., should be used in classrooms, dormitories, and other places that infectious patients have stayed.

### Response To Clustered Epidemic

Once  $\geq 3$  TB cases are detected in the same school, the local county CDC should complete a field epidemiological survey within 3 working days and contact screening within 10 working days. The school should conduct health education, symptom monitoring, and environmental disinfection promptly. When a school has  $\geq 10$  epidemiologically-linked TB cases or  $\geq 1$  death from TB in the same semester, the county level (or its superior level) health administrative department can determine whether to declare a public health emergency. Once confirmed, the emergency should be reported within 2 hours, an emergency plan should be initiated (10), and an emergency response carried out according to risk assessment results.

TABLE 2. Pulmonary tuberculosis case contact screening and post-screening actions.

Subject	Definitions/Approaches/Actions
Screening subject classification	
Close contacts <sup>*</sup>	Teachers and students in the same class with the index patient (diagnosed pulmonary tuberculosis cases including tuberculosis pleurisy patients), and students who live together in the same dormitory with the index patient. Family members who have been in contact with the index patient in the same residence for $\geq 7$ days within 3 months prior to diagnosis and 14 days after initiation of treatment. Other close contacts that are difficult to define in classes and dormitories, who have direct contact with the index patient (bacteriologically confirmed cases, or bacteriologically negative but having severe tuberculosis or showing obvious symptoms) in an enclosed space for $\geq 8$ hours continuously or for $\geq 40$ hours cumulatively within 3 months prior to diagnosis and 14 days after initiation of treatment. For other bacteriologically negative patients, the cumulative contact period of 40 hours is only calculated for the month prior to diagnosis of the index case.
General contacts	Those who study and live together with the index patient on the same floor of teaching or dormitory building.
Occasional contacts	Those who are in the same teaching or dormitory building but not on the same floor with the index patient, or other teachers and students who occasionally have contact.
Screening approaches	
Contact age <15 years old	Symptom screening and tuberculin skin test (TST)/ $\gamma$ -interferon release test (IGRA); if TST strongly positive or IGRA positive, should add chest X-ray examination.
Contact age $\geq 15$ years old	Symptom screening, TST/IGRA, and chest X-ray examination.
Suspected tuberculosis (TB) cases (those with suspicious symptoms of TB, TST strongly positive /IGRA positive, or abnormality in chest X-rays)	Bacteriological tests, including smear, culture, and molecular diagnostic tests.
Bacteriologically confirmed TB cases	Strain identification and drug susceptibility test. If feasible, it is recommended to keep the strains in order to carry out homology testing between strains collected from other cases afterwards.
Post-screening actions	
Active TB patients	Start standard anti-TB treatment and drug taking supervision and management as soon as possible
Suspected TB patients	Be quarantined temporarily, after diagnosis or exclusion, taking follow-up actions accordingly.
Those with strongly positive TST ( $\geq 15$ mm) or positive IGRA results	Should receive preventive treatment with informed consent. For those who refuse, monitoring and follow-up observation should be strengthened to make sure they will go to the TB designated hospital in time if TB-like symptoms appear. Also, they should take a chest X-ray examination at 3, 6, and 12 months later. When the contact screening finds 3 or more epidemiological-related TB cases in a school, preventive treatment is strongly recommended for all eligible students.
Those with moderately positive (10–14 mm) and mildly positive TST (5–9 mm) results	Should receive health education and strengthened follow-up observation, once TB-like symptoms appear, they should go to a TB-designated hospital promptly. When there are 3 or more epidemiologically-linked cases, it is recommended to perform chest X-ray examination again after 3 months.
Those with negative TST ( $< 5$ mm) or IGRA results <sup>†</sup>	Should receive health education and strengthened follow-up observation. If TB-like symptoms occur, they should go to a TB-designated hospital for TB examination promptly.

\* If time from the onset of symptoms to diagnosis is more than 3 months, the above definitions of infectious period of index patient should be updated to be from the onset of symptoms to 14 days after initiation of treatment

<sup>†</sup> For contacts with negative TST/IGRA results, when the outbreak in school is defined as a public health emergency, TST or IGRA should be performed again after 3 months, and chest X-rays should be taken for those with positive conversion. When there are 3 or more epidemiologically linked cases that have not yet constituted a public health emergency, it is recommended to conduct TST or IGRA again after 3 months.

## COMMENT

The school guidelines are developed for health and educational administrative departments, schools, CDCs, medical institutions (TB designated hospitals and other medical institutions), and primary health care facilities at all levels to engage in school TB prevention and control. It has more clearly defined the responsibilities of various departments and pointed out how to handle various problems in practice, which will

firmly guide the national school TB prevention and control work to be more standardized, prompt, and effective.

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## Commentary

## Sino-EU Intergovernmental Collaboration in the Campaign Against the COVID-19 Pandemic on Food via EU-China-Safe Framework

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The coronavirus disease 2019 (COVID-19) pandemic has swept across the planet with more than 81 million confirmed cases and deaths surpassing 1.8 million in over 222 countries (1). Since the first outbreak found in Wuhan in late December 2019, the capital city in Hubei Province of China, healthcare workers and scientists having been working relentlessly to fight against this invisible enemy. It is very clear that starting from nowhere, our Chinese colleagues have made tremendous contributions to the knowledge of the virus and have shared among their counterparts globally (2–4). There is little doubt that this knowledge has been of substantial support to the rest of world to initiate mitigation strategies and undertake vaccine development. The state government acted quickly by following scientific advice and put into place a coherent control plan. All the available evidence points to China having successfully contained and controlled domestic cases of the virus within a few months of the original outbreak.

There was no early evidence from monitoring data based on whole genome sequencing and RNA testing (5) to show the transmission of COVID-19 virus could occur via food. However, there was a growing body of knowledge to suggest that the virus could have a longer survival time at lower temperatures (6). When the new regional outbreak occurred in Xinfadi and was linked to the wholesale market that serves Beijing, positive COVID-19 RNA results were found on food samples that the association between virus spread and food became apparent (7). Subsequently, transmission of the virus was also linked to Dalian (8), Qingdao (9) and Tianjin (10) harbor workers who, in all likelihood, became infected due to contact with frozen food and its packaging. The isolation of live virus in the Qingdao case study have further confirmed the transmissibility from food packaging to humans (11). In response to this mounting scientific evidence, the Chinese government issued a series of 8 updated notifications/guidelines (12–19) since June 2020 (More insights could be found on the newly released

Policy Note) (20) to enhance the monitoring and regulations and cover the whole refrigerated food supply chain in China from entry into the country to entry into the markets.

The highly important and ambitious EU-China Intergovernmental Horizon 2020 EU-China-Safe program was jointly founded by the Chinese Ministry of Science and Technology (grant no 2017YFE0110800) and the European Commission (H2020 grant no727846). The purpose of this four-year (2017–2021) flagship research project is to establish an efficient, trusted, and robust network of scientists between the two regulatory systems. The project has aimed to deliver mutually recognized information sharing systems and knowledge transfer systems and harmonized testing methods in both food safety and authenticity spheres. The project has been running for three years and has been externally reviewed by both Chinese and European scientists, and the evaluations have been extremely positive. Since the beginning of this pandemic, members of the network in China and the EU have been actively involved in the efforts to control the virus. With an excellent degree of collaborations already in place, the ability to share knowledge and information has been achieved in a very fast and smooth manner. For example, protocols for sampling and analysis have been shared via the ‘virtual laboratory’ established at the outset of the project. All this information is being made available on the EU-China-Safe website (<http://euchinasafe.eu>) to help further disseminate the combined China and EU protocols. This project is exemplary of what can be achieved when the very best scientists from China and the EU have the means to work together and help develop high impact solutions to complex problems.

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