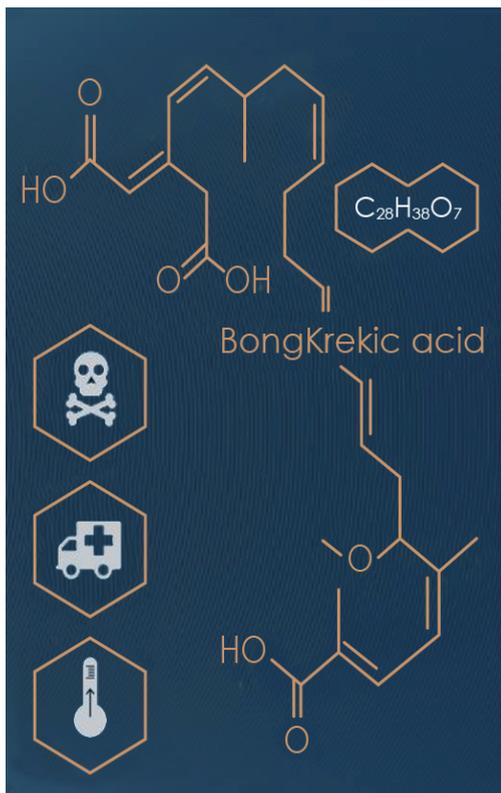


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## 中国疾病预防控制中心周报



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## Outbreak Reports

## A Foodborne Bongkrelic Acid Poisoning Incident — Heilongjiang Province, 2020

Yuan Yuan<sup>1,&</sup>; Rui Gao<sup>2,&</sup>; Qiang Liang<sup>3,&</sup>; Li Song<sup>4</sup>; Jun Huang<sup>3</sup>; Nan Lang<sup>1</sup>; Jing Zhou<sup>1,#</sup>

### Summary

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

Poisoning incidents caused by bongkrelic acid (BA), one of the metabolites of *Burkholderia gladioli* pathovar *cocovenenans* (*B. cocovenenans*), have been reported in Indonesia, Mozambique, and China. The reported case fatality rates averaged 60%, 32%, and 26.5%, respectively. In China, *B. cocovenenans* is often called *Pseudomonas cocovenenans* subsp. *farinofermentans*.

#### What is added by this report?

In October 2020, 9 persons in Jidong County, Heilongjiang Province died after consuming a homemade fermented corn flour product — sour soup — with a case fatality rate of 100%. BA was detected in both food samples and biological samples with a content of 330 mg/kg and 3 mg/L, respectively. The doses of BA consumed by the cases were approximately 22–33 times the lethal dose in human.

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

The consumption of fermented corn flour products, deteriorated fresh tremella, or black fungus and metamorphic starch products may cause BA poisoning. Health education should be strengthened so that homemade-starch-fermented food should be avoided and foods that have been kept for a long time should not be consumed. Meanwhile, training and emergency capacity building for primary healthcare workers should be strengthened to provide timely diagnosis and response.

On October 6, 2020, Jidong County CDC received a report that a family in Sihai Community, Xingnong Town had a suspected foodborne poisoning incident. By the investigation of the county, municipal, and provincial CDC, the incident was due to consumption of the local homemade specialty food, a sour soup, for breakfast on October 5. In the homemade processing and storage, this food was contaminated by *Burkholderia gladioli* pathovar *cocovenenans* (*B. cocovenenans*) which can produce bongkrelic acid

(BA), resulting in deaths for all persons exposed due to poisoning. The case attack and fatality rates were both 100% in the persons who consumed the sour soup. Improper processing and storage of fermented corn flour products can cause BA poisoning.

### INVESTIGATION AND FINDINGS

On October 4, a total of 12 persons involving 5 families gathered for lunch and dinner. At around 8:00 am on October 5, the 12 persons had breakfast together and left separately. Among them, 9 persons consumed the sour soup, while 3 did not and all the 12 persons had consumed the other food items. The 9 persons then successively developed gastrointestinal symptoms such as nausea, vomiting, and abdominal pain. Finally, all 9 cases died after treatment.

On October 6, the investigation revealed that the 9 cases included 4 males and 5 females with an average age of 61 years (range: 45–72 years). Detailed clinical data were collected on the initial patient and her husband. Physical examination of the initial case showed tenderness in the upper abdomen. Laboratory abnormalities include progressive dysfunction of liver function, renal function, and coagulation function in her and her husband, and imaging indicated diffuse changes in the liver (Table 1). The attack rate was 100% in the persons who consumed sour soup and the attack rate was 0% in those who did not consume it, which suggested that the sour soup was the likely source of exposure. The median latency period was estimated as 3 hours (range: 2–8 hours) according to the time of consumption of sour soup and the onset time of the case. The median course of disease in 9 cases was 53 hours (range: 20–341 hours). The patients and cases were numbered 1–9 according to the latency period from short to long (Figure 1). Patient 9 had the longest latency period, and he returned home after receiving prescription medication from the outpatient department. He then died at home with the shortest course of illness, which was only 20 hours.

According to the investigation, the process of

TABLE 1. The clinical characteristics list of two typical cases in the foodborne bongkreik acid poisoning incident in Jidong County, Heilongjiang Province, 2020.

Patient	Gender	Age (years)	Latency period (h)	Course of disease (h)	Clinical manifestation			Physical examination	Liver function			Coagulation function			Renal function			Imaging
					Nausea, vomiting	Diarrhea	Dizziness, fatigue		Oliguria	Tenderness in the upper abdomen	ALT (U/L)	AST (U/L)	PT (s)	APTT (s)	PLT ( $10^9/L$ )	UREA (mmol/L)	CREA ( $\mu\text{mol/L}$ )	
Initial patient's husband	Male	49	4	61	+	+	+	+	+	22,640 $\uparrow$	43,900 $\uparrow$	>120 $\uparrow$	88.3 $\uparrow$	30 $\downarrow$	8.87 $\uparrow$	466 $\uparrow$	Liver diffuse lesions	
Initial patient	Female	47	2	341	+	-	+	+	-	7,199 $\uparrow$	10,630 $\uparrow$	71.4 $\uparrow$	46.6 $\uparrow$	27 $\downarrow$	1.84 $\downarrow$	213 $\uparrow$	Liver diffuse lesions	

Note: Marks: + : indicates symptoms that do occur; - : indicates symptoms that do not occur;  $\uparrow$ : means increasing;  $\downarrow$ : means decreasing.

Abbreviations and reference ranges: ALT: Alanine aminotransferase 0–40 U/L; AST: Aspartate aminotransferase 0–40 U/L; PT: Platelets ( $100\text{--}300$ ) $\times 10^9/L$ ; APTT: Activated partial thromboplastin time 23–35 s; PT: Prothrombin time 10.5–13 s; UREA: Urea nitrogen 2.3–7.2 mmol/L; CREA: Creatinine 44–110 mmol/L

making the homemade sour soup was as follows: one year ago, the corn was soaked in water for about a month to ferment. After mill grinding, the corn husks were filtered out in the water, and the delicate parts were kept to be dried in flour bags and formed into dough and then noodles with a specialized tool. It was consumed as soon as the noodle-based sour soup was ready and the rest of the dough was put in the refrigerator and frozen. This fall, because the refrigerator was used to store other foods, the dough was made into cornmeal powder and then stored in the refrigerator again to save space. After the corn dough was taken out, it was first exposed to air outside and covered with a simple porous plastic net. After drying for a day, it was transferred to dry in the house due to cloudy and rainy weather.

On October 5, the local public security department extracted all the types of residual food and detected them. No poisonous substances such as cyanide, organophosphorus, carbofuran, psychostimulant, or tetramine were found. On October 7, the municipal CDC tested all the types of food and a patient's gastrointestinal decompression fluid for salmonella, and the results were negative. The local hospital tested the food and found the aflatoxin was in excess. As this toxin is a common contaminant of corn, and it generally does not cause acute poisoning manifestations as the latency period is usually 2–3 weeks (1), which caused it to be excluded. On October 10, the provincial CDC detected BA in the remaining raw material for the sour soup, the corn flour, and the gastrointestinal decompression fluid. In accordance with national standard (2), the concentration of BA was 330 mg/kg and 3 mg/L, respectively. Combined with the epidemiological investigation result, the patient's clinical manifestations and laboratory test results, the investigation team confirmed this poisoning incident was caused by BA when bacteria contaminated the corn flour and was used to make the sour soup.

## PUBLIC HEALTH RESPONSE

Local CDC and the National Early Warning Information Dissemination Center has issued a warning message about BA poisoning. China CDC tracks the handling of incidents, provides technical guidance on epidemiological investigation and sampling detection, and at the same time obtains information from surveillance systems and carries out risk assessments regularly.

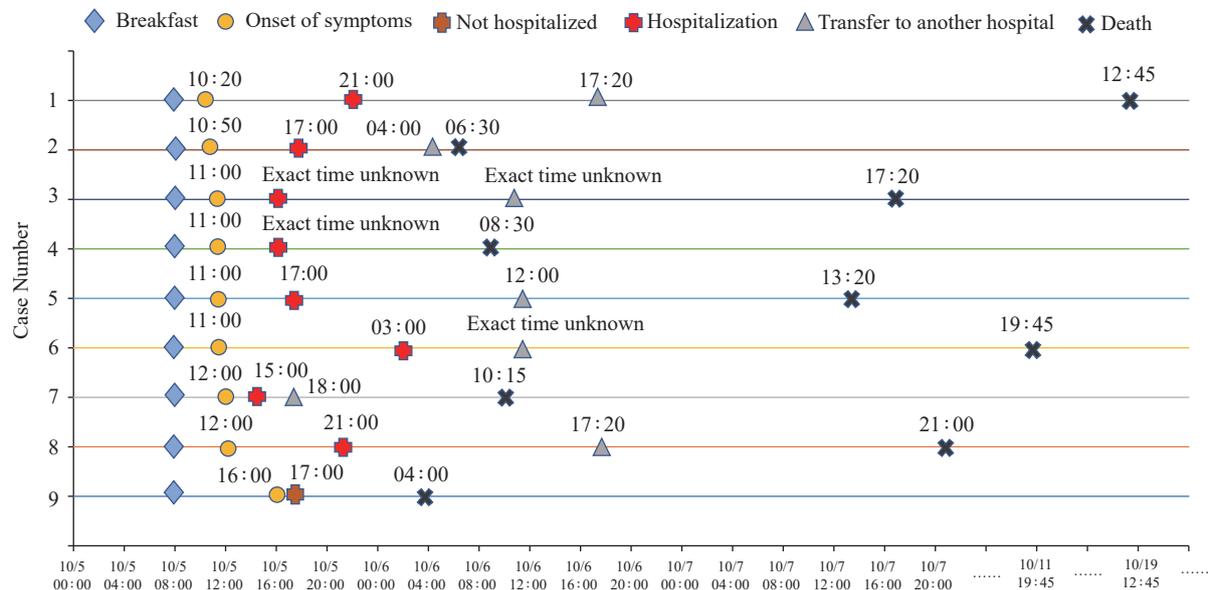


FIGURE 1. Sequence diagram of the course of disease of patients in the foodborne bongkrekkic acid poisoning incident in Jidong County, Heilongjiang Province, 2020.

## DISCUSSION

Based on the consumption of staple food of 100 g per person, the BA concentration of corn flour and the remaining raw food material collected on the scene, was 22–33 times higher than the lethal dose of 1–1.5 mg (3) and resulted in all 9 deaths. Laboratory studies have shown that coconut, corn, and other foods that are rich in oleic acid, are suitable for the growth of *B. cocovenenans* at a neutral pH of 22–30 °C. When *B. cocovenenans* is cultured on coconut medium under ideal conditions, toxin production can reach 2–4 mg/g by the second day of culture (4). Although it is not clear how the corn flour used to make the sour soup was contaminated in this incident, we can learn from the production process that the poisoned sour soup was made in the same batch as last year. There was no abnormal consumption last year, and the contamination probably occurred after the food was taken out of the refrigerator. The corn dough was likely contaminated with bacteria when it was dried outside. The natural air drying speed was slow as the environment likely had poor ventilation, high relative humidity, and a suitable temperature for bacterial growth. These factors provide favorable conditions for the bacteria to multiply and produce the toxin. Despite the destruction of *B. cocovenenans* during cooking, the BA produced by them has a heat-stable character. Therefore, the storage, processing, and sanitary conditions of raw food materials were closely related to

the occurrence of poisoning.

In Indonesia and Mozambique, the reported case fatality rate of BA poisoning were 60% and 32%, respectively (4–6). As of January 1, 2004, China CDC launched the Public Health Emergency Management Information System, which is a surveillance system for public health emergencies that may occur or have already occurred, which is reported online by medical and health institutions at all levels. The surveillance data showed that 15 BA poisoning incidents, 136 poisoned individuals, 36 resulting deaths, and a case fatality rate of 26.47% was reported during 2010–2019 in the mainland of China. These occurred in the provincial-level administrative divisions of Yunnan, Guizhou, Guangxi, Guangdong, Liaoning, and Shandong. Compared with 545 such incidents from 1953–1994, 3,352 persons were poisoned, among which 1,401 died (case fatality rate was 41.80%), and the scale showed a significant decline (7). According to the reported 15 incidents of foodborne poisoning caused by BA, there was 1 incident of sour soup poisoning at Liaoning Province in northeastern China, in which 4 persons were poisoned and all died. There were 2 incidents of poisoning caused by nonfermented rice noodle product at Guangdong Province in southern China, 8 people were poisoned and 5 died (case fatality rate was 62.5%). There were 5 incidents of poisoning caused by Diaojiangba (hanging syrup cake) in Yunnan Province, 47 people were poisoned and 15 people died (case fatality rate was 32%), suggesting that different types

of starch products may lead to different case fatality rates.

There are few BA detection reports for past incidents, and they are mainly inferred based on exposure and clinical manifestations. The reason why the fatality rate of this incident was much higher than that of previous incidents was likely related to the exposure dose being much higher than the lethal dose.

The Health Emergency Information Platform for Poisoning Emergencies (an information system for emergency work for poisonings in provincial-level medical and health institutions) showed that up to July 2020 among the 81 institutions that were provincial CDCs, provincial treatment bases for poisoning, and designated medical institutions in China, only 7% had reserved and had access to the detection technology of BA in their daily work. It took 5 days and 6 days to get the qualitative and quantitative test results in this incident, respectively, which represents a shortcoming in the detection capacity of early and rapid diagnosis of BA.

At the same time, studies on the toxicokinetics of BA are lacking. There is no specific antidote (8) or standardized treatment guidelines for BA poisoning. The treatment of patients is mainly to terminate toxic contact, remove toxins that have not been absorbed in the body, and provide symptomatic support treatment. If the cases of this incident were treated in time at a hospital capable of treating severe poisoning, the case fatality rate may be reduced.

The investigation had several limitations. Because the patient who made the poisoned food fell ill and died, it was impossible to know all the details of how it was prepared. Most patients had a short course of illness with limited or unavailable clinical records. Not all patients had biological specimens collected for BA quantitative detection.

In high-risk areas, prevention of exposure to *B. cocovenenans* and BA and safer fermentation processes should be adopted. Meanwhile, training in BA poisoning and confirmative testing in primary health

care facilities should be strengthened to improve emergency response capacity for timely diagnosis and response. In addition, scientific institutions should conduct studies on the distribution of *B. cocovenenans*, the laws of toxin production, and toxicokinetics of BA and develop commercial products for rapid detection of toxins in food.

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## Preplanned Studies

## Reducing Canine Echinococcus Infection with Smart Deworming Collars — Tibet, China, June–November, 2020

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### Summary

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

Existing manual deworming programs launched have made great progress in reducing the *Echinococcus* infection rate of domestic dogs, but significant challenges remain in scattered nomadic communities inhabiting the Tibetan Plateau. The low deworming frequency and low levels of coverage were responsible for the high infection rate of *Echinococcus* spp. among dogs.

#### What is added by this report?

Smart deworming collars controlled by a remote management system (RMS) was found to increase the deworming frequency and coverage and subsequently reduce the canine infection rates with *Echinococcus* spp..

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

As an innovative tool, smart deworming collars may drive the paradigm shift from manual deworming to smart deworming and stop the transmission of echinococcosis.

Endemic echinococcosis is still a serious challenge in northwestern China. We employed smart deworming collars controlled by remote management system (RMS) to deliver baits containing praziquantel (PZQ), a medication used to treat parasitic worm infections, for dogs. Compared with existing manual deworming techniques, the deworming coverage increased from 57.7% (173/300) to 85.7% (945/1,103) following the smart collars implementation, and the monthly deworming rate increased from 40.3% (121/300) to 91.4% (1,008/1,103). The positive rates of *Echinococcus* antigen in canine feces were reduced to zero, which suggests that this may be a novel effective alternative to reduce the transmission of echinococcosis.

Echinococcosis is a severe cross-species transmitted

parasitic disease (1), and cystic echinococcosis (CE) caused by *Echinococcus granulosus* and alveolar echinococcosis (AE) caused by *Echinococcus multilocularis* are the two main forms in human. In China, CE is widely endemic in at least 368 counties of 9 provincial-level administrative divisions (PLADs) and AE is co-endemic with CE in 115 of these counties (2). China remains the region with the most serious endemic disease burden, which comprised 40% of the world's CE disability-adjusted life years (DALYs) and 91% of new cases of AE per year globally (3–4).

Existing studies demonstrated that dogs were the most definitive host for *Echinococcus* spp. and its role in transmission of both CE and AE was significant (5). Periodic deworming of dogs is a highly effective measure against echinococcosis recommended by the World Health Organization (WHO) and Office International Des Epizooties (OIE) (6). In China from 2006, a monthly deworming program was employed to control the transmission of canine echinococcosis to livestock and humans (7–8), and significant progress has taken place to reduce the population prevalence of echinococcosis and the infection rate of *Echinococcus* spp. in dogs (2). However, in harsh climate and high altitude areas such as the Qinghai-Tibet Plateau, the unique humanistic values and nomadic production methods caused the implementation of manual monthly deworming for every dog encountered to become difficult and challenging, and the real data on the deworming coverage and frequency was difficult to obtain. Even in a county where the National Control Program struggled to achieve monthly deworming from 2010, the deworming coverage for dogs was not higher than 63.2% (9). In another county earmarked for the comprehensive control of echinococcosis in 2016–2017, only 21.7% (30/138) of dog owners performed deworming once a month (10). The low deworming frequency and coverage was responsible for

the high prevalence of echinococcus among dogs, including 2.96% in Sichuan, 3.03% in Ningxia, 4.91% in Gansu, 7.3% in Xizang (Tibet), 13.0% in Qinghai, and 41.3% in Hobukesar County, Xinjiang, China (2,9).

In this study, we employed a smart deworming collar controlled by RMS, a platform specially developed for managing and controlling smart deworming devices, to deliver bait containing PZQ (100 mg per bait; Beijing Zhongnong Warwick Pharmaceutical Co., Ltd., Beijing, China. batch: 20190613) for dogs automatically, regularly, and quantitatively to increase the deworming frequency and coverage, reduce the dogs' infection rate of *Echinococcus*, further reduce the abundance of parasitic eggs in the environment, and ultimately prevent the transmission of echinococcosis from dogs to humans and livestock.

From June to November, 2020, a six-month field evaluation was performed in Kangma County, Shigatse City, Tibet Autonomous Region of China, which is a semi-agricultural and semi-pastoral border county with a severe epidemic of echinococcosis, an average altitude of >4,300 m, and an annual average temperature of about 4 °C. The population is around 34,000, of which >99% are ethnic Tibetans, the population prevalence of echinococcosis is 1.74%, and the overall positive rates of *Echinococcus* antigen in canine feces is 7.5%. Based on the production style, the population prevalence of echinococcosis, the number of dogs, and the positive rates of *Echinococcus* antigen in canine feces, a stratified cluster sampling method was conducted, and 5 towns were identified as smart collar group with 1,103 registered dogs and the other 4 townships as manual deworming group with 605 registered dogs. Local staff attached the smart deworming collars to all the dogs in the smart collar group according to the product specifications. The steps for attaching the smart collar to the dogs were as follows: 1) matching the information of the dogs, the owners, and the smart collars and uploading the information to the RMS; 2) set deworming frequency such as once a month, once a quarter, even once every

six months according to the local prevalence of echinococcosis; 3) set the PZQ baits dose for each dog according to the dog's weight and size; and 4) set deworming time (8:00 or 18:00 on the deworming date), and then the smart deworming collar will run according to the set procedure. The dogs in the manual deworming group remained to be dewormed by the existing manual deworming methods.

In the smart deworming group, the deworming coverage and frequency of the smart collars were counted by the RMS. In the manual deworming group, due to remote locations of nomadic settlements, 300 dog owners (their dogs were randomly selected to collect dog feces once a quarter) were surveyed through questionnaires to obtain the information of monthly deworming. The total fecal sample size was estimated by the Walters normal approximation method and determined to be 600 (300:300). Each quarter, 300 dogs were randomly selected from the 1,103-dog category and the other 300 dogs from 605-dog category by an accurate random sampling method followed by collection of the fecal samples from each of the chosen dogs. The fecal samples were tested once a quarter with the coproantigen ELISA Kit for Canines (produced by Shenzhen Combined Biotech Co., Ltd., Shenzhen, China) in the National Health Commission (NHC) Key Laboratory of Echinococcosis Prevention and Control. IBM SPSS (version 20.00; International Business Machines Corporation, New York, USA) was used to analyze the data.

Over 85.7% (945/1,103) deworming coverage was achieved with the smart collars, and 91.4% (1,008/1,103) of dogs in smart deworming group were dewormed 6 times during the 6 months. The smart deworming collar increased the deworming coverage and frequency (Tables 1 and 2). The positive rate of *Echinococcus* antigen in canine feces decreased from 5.7% (17/300) to 0 after six months of smart-collar deworming (Table 3).

## DISCUSSION

As stated above, the existing manual deworming

TABLE 1. Deworming coverage between the two groups in Kangma County, Shigatse City, Tibet from June to November 2020.

Group	Number of dogs (n)	Beginning deworming		Three months later		Six months later	
		Actual number covered (n)	Rate (%)	Actual number covered (n)	Rate (%)	Actual number covered (n)	Rate (%)
Smart collar deworming group	1,103	1,103	100.0	1,032	93.6	945	85.7
Manual deworming group	300	129	43.0	158	52.7	173	57.7

TABLE 2. Deworming frequencies between the two groups in Kangma County, Shigatse City, Tibet from June to November 2020.

Deworming frequency	Smart collar deworming group		Manual deworming group	
	Number of dogs (n)	Constituent ratio (%)	Number of dogs (n)	Constituent ratio (%)
0	0	0.0	19	6.3
1	9	0.8	43	14.3
2	16	1.5	29	9.7
3	23	2.1	25	8.3
4	21	1.9	30	10.0
5	26	2.5	33	11.0
6	1,008 <sup>a</sup>	91.4	121	40.3
Total	1,103	100.0	300	100.0

<sup>a</sup>The number 1,008 sums 945 and 63, where 945 is the number of the dogs with smart deworming collars still attached after six months, and 63 is the number of the dogs which although the smart deworming collars were removed by their owners, the smart deworming collars still ran well to deliver the bait containing praziquantel once a month, and the owners fed the baits to the dogs.

TABLE 3. Positive rates of *Echinococcus* antigen in canine feces between the two groups in Kangma County, Shigatse City, Tibet, from June to November 2020.

Deworming time	Smart deworming group			Manual deworming group			$\chi^2$	p
	Test numbers (n)	Positive numbers (n)	Positive rate (%)	Test numbers (n)	Positive numbers (n)	Positive rate (%)		
Before deworming	300	17	5.7	300	15	5.0	0.132	>0.05
Three months later	300	1	0.3	300	13	4.3	10.531	<0.05
Six months later	300	0	0.0	300	14	4.7	14.334	<0.05

methods (each dog, once a month) involved significant challenges, especially in China's less developed and more dispersed nomadic communities. In this study, the smart deworming collar was employed to deliver bait containing PZQ for dogs with many advantages: 1) deworming automatically as the smart collar only needs to be attached to the dog once a year and will deliver bait containing PZQ 12 times automatically, which greatly saves originally planned manpower and cost; 2) deworming regularly; 3) deworming quantitatively and with conditions for each individual dog; 4) digital smart telemanagement and control as after the dog is attached a smart collar, the RMS will automatically identify and analyze the related information and remotely monitor the status of the collar in real time without having to enter the scene; and 5) predominant characteristics of being waterproof, anti-collision, and cold-proof to ensure it runs well in the harsh climate. The results of this study illustrated that over 85.7% (945/1,103) of deworming coverage was achieved by the smart collar, and a 91.4% (1,008/1,103) monthly deworming rate was achieved in which the dogs in smart deworming group were dewormed 6 times within 6 months. These conditions basically met the standard of '4–8 times per year' and

'at least >90% of registered dogs' recommended by the WHO/OIE (6). Although the deworming coverage and frequency of the smart collar group were decreased, it was still much higher than those of manual deworming group.

The acceptable prevalence of canine echinococcosis recommended by WHO is <0.01% after an 'attack' phase of 5–10 years of regular dosing for registered dogs (7). In this study, after 6-months of smart deworming, the positive rates of *Echinococcus* antigen in canine feces decreased significantly from 5.7% (17/300) to 0, but in manual deworming group, the change of the positive rates of *Echinococcus* antigen in canine feces was not yet significant. The results implied that deworming by smart collar was a more efficient alternative to reduce the positive rate of *Echinococcus* antigen in canine feces.

The six-months evaluation has shown that there are obvious advantages and significant public health significance in improving the deworming coverage and frequency, reducing the positive rate of *Echinococcus* antigen in canine feces, and providing stronger protection than manual deworming. This study was limited by its relatively short evaluation period, and the actual effect of implementation still needs to be evaluated for a longer time.

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Based on the findings of this study, the government should increase funds to support the application of the smart deworming collar, professional institutions should make further improvements based on the problems discovered in the actual application, and health promotion and education for dog owners should also be strengthened to improve their willingness and skills in attaching smart collars. In addition, the potential impact on dogs and associated economics all need further investigation.

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## Notes from the Field

## The Two Reemergent Confirmed COVID-19 Cases — Manzhouli City, Inner Mongolia Autonomous Region, China, November 20, 2020

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On November 20, 2020, a 55-year-old male went to the Zhongmeng Hospital of Manzhouli City, Inner Mongolia Autonomous Region for diagnosis and treatment of pain in the waist and lower extremities. His wife, a 55-year-old female, accompanied him to the hospital also feeling unwell. They were first tested for coronavirus disease 2019 (COVID-19) in Manzhouli People's Hospital based on China's policy of ensuring that "all those in need are tested, isolated, hospitalized, and treated." Later that day, Manzhouli People's Hospital reported their nucleic acid test results were positive. In the early hours of November 21, the municipal and district-level CDCs confirmed their nucleic acid test results were positive, and after consultation with experts, comprehensive clinical examination, and inspection of imaging results, the COVID-19 diagnosis was confirmed for both patients.

On November 24, the sequences of the two Manzhouli COVID-19 patient samples were acquired using the Illumina MiSeq platform. These two Manzhouli genome sequences were identical, and when compared with the Wuhan reference sequence (EPI\_ISL\_402119) (1), 17 nucleotide variation sites were detected in the both of the Manzhouli strains, from which 8 sites (C241T, C3037T, C14408T, C18877T, A23403G, G28881A, G28882A, G28883C) were single nucleotide polymorphisms (SNPs) that belonged to the L-lineage European branch I/Pangolin lineage B.1.1 (2). Furthermore, the two Manzhouli sequences had nine unique nucleotide variation sites: C5526T, C10078T, C12952T, C14793T, C15654T, A19308G, G25650T, G29553T, and C29739T. A Russian strain was retrieved from the GISAID database (GISAID ID: EPI\_ISL\_5963017) that shared a total of 15 SNPs which included 7 unique SNPs with the 2 Manzhouli strains. This finding suggested it might be highly possible that the Manzhouli strains were imported from Russia. Continued monitoring of imported COVID-19 cases is vital for reducing related outbreaks (Figure 1).

The sequencing results indicated that the genomic characteristics of the Manzhouli cases were different from recent cases detected in Kashgar Prefecture, Tianjin Municipality, and Shanghai Municipality (3–5). The source of the virus was not likely a spillover event from a host or intermediate host.

Since November 21, the Manzhouli Government carried out large-scale epidemiological investigations and comprehensive nucleic acid testing. All persons that had contact with the cases or entered from the land port at Manzhouli underwent nucleic acid testing. Further investigation is still being conducted.

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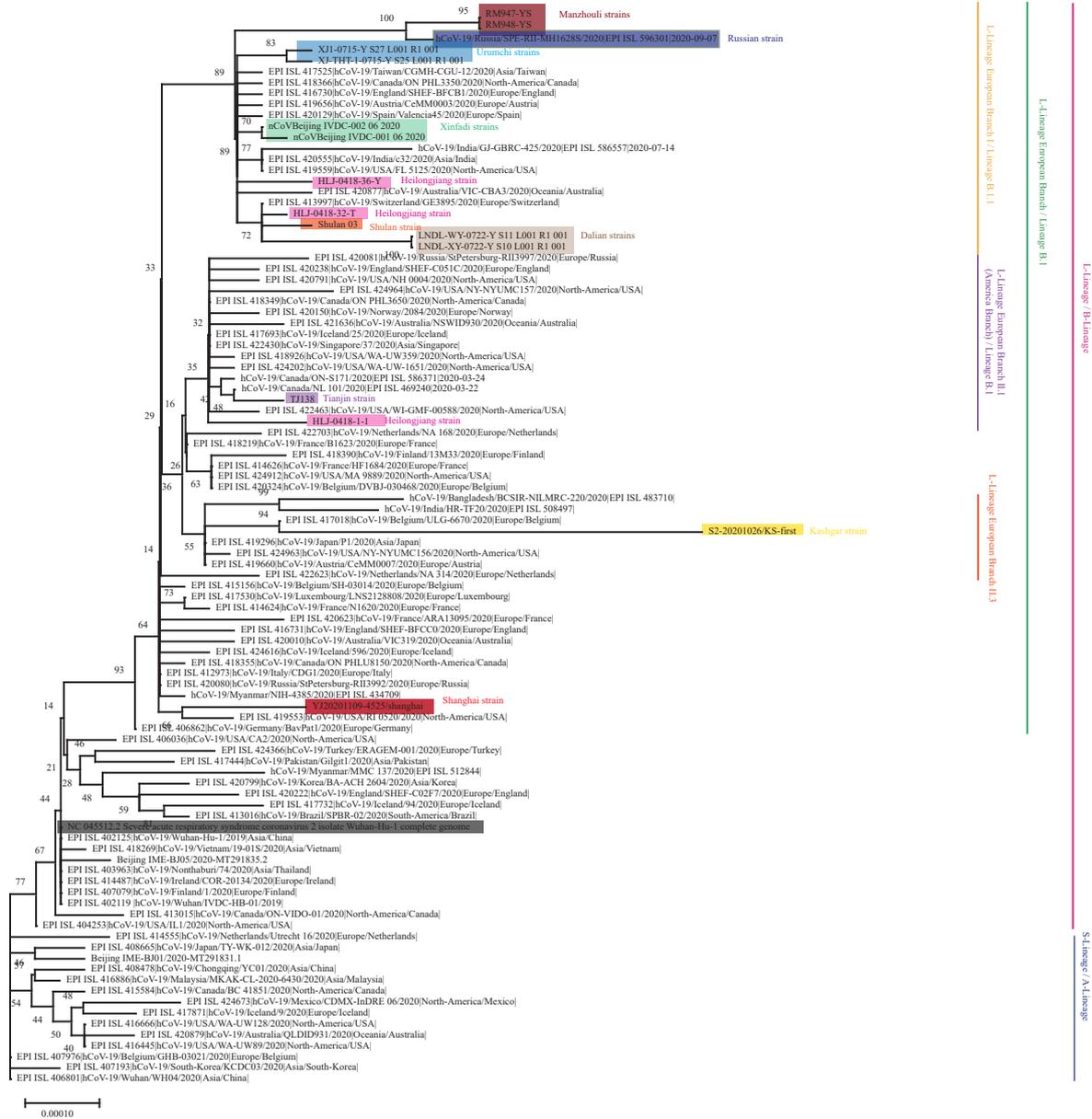


FIGURE 1. Phylogenetic tree based on the full-length genome sequences of the COVID-19 virus. The strains associated with specific outbreaks are as follows: Manzhouli City (crimson) Shanghai Municipality (red); Tianjin Municipality (purple); Kashgar Prefecture (yellow); Urumchi City (blue); Beijing Municipality Xinfadi Wholesale Market (green); northeastern China including Heilongjiang Province (pink) and Shulan (orange) related to imported cases; Dalian City (brown); Wuhan City in December 2019 (dark gray); and the Russian strain that has high nucleotide sequence homology with the Manzhouli strains (navy). The S(A)- or L(B)-lineage and sublineages of the COVID-19 virus were marked and colored on the right.

## Commentary

## Highly Effective Stratified Hub-and-Spoke Non-Pharmaceutical Intervention Provides New Insight into the Prevention of COVID-19 Transmission

Hao Li<sup>1,\*</sup>; George F. Gao<sup>1</sup>

As of November 20, 2020, there have been 56,982,476 confirmed cases of coronavirus disease 2019 (COVID-19) globally, with the death toll reaching 1,361,847, as reported to the World Health Organization (WHO) (1). Given the multiple epicenters of the pandemic and mounting death toll, it is imperative to seek optimal alternative non-pharmaceutical interventions (NPIs) strategies from a broader, more integrated perspective to fully project the subsequent waves of the pandemic, as no specific viral inhibitors or vaccines are available at the moment.

Many studies have implicated the role of community-based transmission and case importation in modulating the transmission dynamics of COVID-19 virus (2–3). There are now many modeling analyses focusing on the optimization of NPIs to control COVID-19. Among these interventions, mask-wearing, social distancing, and lockdown suppression seem to be the most effective (4–8). So far, by implementing strict NPIs, China has been extremely successful. What should we do globally?

In a recent PNAS paper, Li et al. test an effective framework of global coordination to contain pandemic outbreaks by developing a mathematical model that incorporates two factors of COVID-19 transmission, i.e. climate seasonality and human movement into various NPIs scenarios and proposes a hub-and-spoke [Global Intervention Hub (GIH) and secondary high-risk areas] organization mode for intervention strategies (9). A total of 2,485,256 confirmed cases, accounting for 92.75% of the world's total, were selected from 59 high-risk areas in countries with distinct climates where more than 10,000 cumulative cases had been reported as of April 24, 2020. Two mechanisms, i.e. the climate-driven community transmissions and movement-modulated spatial diffusions, that were likely to shape the post-pandemic trajectory of COVID-19 were incorporated. In addition, a variety of scenarios featuring different strategies, intensities,

and durations of intervention in community-based transmission and international travel were applied to the model. As shown from the pandemic data, the transmission risk and spread of infections could be modulated by local climate conditions and the flow of flights. Wintertime and the airline flow are positively correlated with the onset of the COVID-19 pandemic. In this study, five intervention strategies based on the mathematical model were applied and their effectiveness was evaluated. Impact was evaluated in terms of the proportion of clinical cases averted and the number of areas where the goal of effectively reducing the incidence to less than 10 cases per day could be achieved in advance as compared with the projection in the absence of interventions.

In this model, the hub-and-spoke NPIs, specifically 8-week intensive intervention in the initial period among GIHs and subsequent 8-week intensive intervention among the secondary areas, resulted in a median of 88.02% (23.18% to 98.25%) fewer cases, with 46 areas achieving control of transmission in advance. This scenario was deemed to be the most promising strategy when compared with other strategies, such as the 2-week mild intervention that reduces community-based transmission and international travel by 20%. This model projected that a median of 15.11% (90% CI: 2.02%–20.92%) of clinical cases could be averted, and when coupled with the accelerated reduction of incidence to less than 10 cases (taken as “the effective control”) in 15 areas, the 12-week mild intervention could avert a median of 52.44% (9.69% to 70.12%) cases and lead to effective control of transmission in 26 areas. Lifting to a moderate intensity for 12 weeks would lead to a median of 79.95% (19.89% to 93.94%) cases averted, accelerating the process of effective control in 42 areas. Based on this research, the 8-week intensive NPIs targeting the reduction of local transmissibility and international travel were efficient and effective.

This result showed three key points. First, the theory

that seasonality of climate and international travel contributed significantly to the global transmission of COVID-19 was validated. Second, given that the hub-and-spoke organization of interventions, particularly 8-week intensive intervention in GIHs or secondary high-risk areas, had resulted in a median of 87.02% (13.41% to 98.23%) averted cases, it was proposed that such kind of collaboration should be launched in areas with a high density of population and international travel, followed by other high-risk areas. Third, considering both climate seasonality and the changes of human behaviors, the author demonstrated that global collaborations on prompt and intensive interventions were fundamental to flatten out the curves of COVID-19 cases. Against the background of the COVID-19 pandemic, taking a tiered intervention strategy of hub-and-spoke organization, where interventions were first implemented at GIHs followed by timely interventions in secondary high-risk areas, was believed to be able to integrate global efforts and effectively improve the global emergency response to COVID-19 and many other infectious diseases.

Regarding the negative impact of social and economic lockdowns (10), this research explored control approaches aimed at more rapidly and effectively controlling the pandemic spread in specific major international hubs, but failed to scientifically evaluate the negative impact of such approaches on the economy. The hub-and-spoke strategy provided an option for the decisionmakers of pandemic prevention and will be a functional one to alleviate the tremendous burden on public health and society. Based on the findings of this study, here we are calling for active community-level NPIs for the new wave of pandemic around the world. Though the pandemic is under effective control in China at the moment, the world still needs to act with better coordination.

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## Increasing Health Literacy in China to Combat Noncommunicable Diseases

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### Summary

Health literacy involves knowledge, motivation, and competence to access, understand, appraise, and apply health information to make judgments and make decisions every day to maintain or improve quality of life. It is of great importance to the health and wellbeing of individuals, families, and society and plays a crucial role in noncommunicable disease (NCD) prevention and control. Recognizing that health literacy is a public health challenge in China, the Chinese government has been making great effort to address this issue. This paper presented a general overview of health literacy status in China with a focus on NCDs, described China's challenges and practices in improving health literacy, and provided suggestions to decision makers, practitioners, and researchers to address the needs of health literacy in China.

### THE ROLE OF HEALTH LITERACY IN NCD PREVENTION AND CONTROL

Noncommunicable diseases (NCDs), including heart disease, stroke, cancer, diabetes, chronic lung disease, and other chronic conditions, are of long duration and demand continuous management and lifelong maintenance of healthy lifestyles, which requires people to grasp sophisticated concepts and possess self-management skills (1). Health literacy plays a crucial role in NCD prevention and control (1). It involves knowledge, motivation, and competence to access, understand, appraise, and apply health information to make judgements and make decisions every day to maintain or improve quality of life (2). Health literacy not only brings individual benefits, such as improved knowledge, self-management skills, compliance with prescribed actions, greater autonomy, and personal empowerment in health related decision-making, and better health outcomes, but also yields community and social benefits like increasing the

participation of the community in population health programs, improving community empowerment, and enhancing the capacity to address social and economic determinants of health (2).

### HEALTH LITERACY IS A PUBLIC HEALTH CHALLENGE IN CHINA

The health literacy among the Chinese population is still at a low level and has disparities between regions and groups (3–4). Results from the National Health Literacy Surveillance among Chinese residents aged 15–69 years old showed that the proportion of people with basic health literacy was 19.17% in 2019 and 22.73% for NCD health literacy was higher in urban areas than rural ones (24.81% vs. 15.67%), highest in the eastern region than central and western regions (24.60%, 16.31%, and 14.30%, respectively), and higher in younger people and people with higher levels of education (3–4). A survey among students in years 7–9 from secondary schools in Beijing in 2015 found that the proportion of students with low health literacy varied by health literacy assessment tools and ranged from 29.0% to 45.5% (5).

A survey among diabetic patients in Beijing Municipality, Ningbo City, and Xiamen City in 2012 showed that 73.7% of the patients were classified as having poor health literacy (6). A survey among acute ischemic stroke patients at time of discharge in Hubei in 2014 showed that about 31.2% of the patients did not know what ischemic stroke was; 20.3% did not realize they needed immediate medical attention after onset; 50% did not know the warning signs of stroke; over 40% were not aware of the risk factors of the condition such as hypertension, hyperlipidemia, diabetes, and smoking; and over 20% had no idea that they need long-term medication and strict control of blood pressure, blood lipids, and blood sugar (7).

Health literacy is influenced by a number of personal, societal, and environmental determinants like age, gender, socioeconomic status, education, culture,

and societal systems, and can be improved through education and health system improvement (2). Although the health literacy in China has been improving (4), there are many challenges that need to be addressed:

### **Low levels of education and unequal socioeconomic development**

About 30% of the Chinese population aged 6 years old and above had only primary school educations or no schooling in 2018, and the education level of females was lower than males (8). In rural and western regions of China, the economic level and education level were relatively low, health services and health education resources were insufficient, and access to health information was also deficient, leading to the significant disparities in health literacy compared with more developed areas (3).

### **Inadequate education service at clinical settings**

Healthcare institutions are an important setting for people to acquire health knowledge and develop health literacy. Delivering free health education service to all residents by primary healthcare institutions composed an important part in the national essential public health services since 2009 (9). However, compared with abundant health education campaigns aimed towards the public, education services at clinical settings were inadequate. Barriers to health education delivery included defects in health education design, inadequate capacity in primary healthcare sectors to provide health education, residents' poor cooperation, weak health system, etc. (9). Another concern is poor health literacy of healthcare providers themselves. Results from the national health literacy survey in 2012 showed that only about 30% of the healthcare providers possessed basic health literacy and was lower in males (27.34%), rural areas (22.42%), and western regions (27.70%) (10).

### **Unreliable health information disseminated through the internet**

The rise of internet based technologies has facilitated the dissemination of and easy access to health information. However, the quality of health information disseminated through the internet has been a concern as a lot of distorted health information exists on the internet, which imposes a challenge to

individuals that need to scrutinize health information. This ability to properly discern accurate information is fairly difficult for most people, and disinformation also presents a challenge to the government and the industry on how to regulate the dissemination of health information through the internet.

### **Insufficient research in health literacy**

Research on health literacy started late in China and is still in its infancy. Current research mainly focuses on the description of health literacy status and analysis of influencing factors from a public health perspective. Research on health literacy theory, development of assessment instruments, high quality intervention and evaluation, and research in clinical settings are still insufficient (11).

## **STRATEGIES AND MEASURES**

Recognizing health literacy is a public health challenge in China. The Chinese government has made great effort in improving the health literacy of the people by developing and implementing a series of specific policies and actions, especially since the late 2000s, such as defining and disseminating the basic health knowledge and skills, monitoring the health literacy status of the people, and implementing national action plans for promoting health literacy. Improving health literacy has been positioned as a strategic goal in the Healthy China 2030 blueprint and is a special initiative in the Healthy China Initiative (2019–2030) (12) where it is integrated into almost every other initiative.

The major outcome indices and initiatives relevant to healthy literacy proposed in the Healthy China Initiative (2019–2030) are listed in Table 1 and Table 2, respectively. Generally, the initiatives present an integrated and comprehensive strategy for improving health literacy by covering a variety of contexts (communities, healthcare institutions, and schools), populations (general people, NCD patients, healthcare workers, children, and the elderly), and content including NCDs and related risk factors. In addition, they provide strategies for individuals, families, governments, and the overall society to develop a linked, multi-sectoral effort to improve health literacy. Some strategies and measures are outlined here that the governments and the society need to do to improve health literacy:

- 1) Strengthen health information development,

TABLE 1. Major outcome indices relevant to healthy literacy proposed in Healthy China Initiative (2019–2030).

Indices	Target date	
	2022	2030
1. Overall health literacy level (%) (proportion of people with basic health literacy)	≥22	≥30
2. NCDs health literacy level (%)	≥20	≥30
3. Nutrition knowledge awareness rate (%)	10% higher than 2019	10% higher than 2022
4. Mental health literacy level (%)	20	30
5. Environmental health literacy level (%)	≥15	≥25

TABLE 2. Examples of strategies and measures to improve health literacy in Healthy China Initiative (2019–2030).

Initiative	Strategies and measures
<b>Health Literacy Initiative</b>	
Health information development, dissemination, and supervision	<ol style="list-style-type: none"> <li>1) Establish national and provincial expert libraries and resource libraries on health literacy improvement and conduct activities.</li> <li>2) Build multimedia mechanisms for the release and dissemination of health information and strengthen guidance and supervision.</li> <li>3) Apply new media such as WeChat, Weibo, and short videos and promote internet-technology-based precision delivery of health information.</li> </ol>
Health education in healthcare services	<ol style="list-style-type: none"> <li>1) Health professionals should have a good understanding about the health information that needs to be delivered to the patients, and actively provide health guidance to the patients.</li> <li>2) Healthcare institutions should provide lectures and consultation services for community residents and patients.</li> <li>3) Develop health education prescriptions and other materials.</li> <li>4) Improve the contents of training courses and teaching materials for general practitioners and specialists and significantly improve family doctors' knowledge and skills necessary for health promotion and education.</li> <li>5) Establish incentive and evaluation mechanisms to encourage health institutions and healthcare providers to engage in health promotion and education.</li> </ol>
Engagement of social forces	<ol style="list-style-type: none"> <li>1) Mobilize social forces to join health literacy improvement by encouraging them to organize various forms of health education activities for the public and provide training to organizations.</li> <li>2) All communities and workplaces should organize health communication activities such as health lectures for the residents and employees.</li> <li>3) Improve health literacy for people living in poor areas.</li> </ol>
Technologies and tools	Develop and promote technologies and tools, especially encouraging the application of artificial intelligence and wearable devices in health management to improve self-management ability of the public.
Health promotion programs/campaigns	Establish Health Promotion County (or districts), carry out the Healthy China Campaign and the National Healthy Lifestyle Initiative.
<b>Health literacy in other initiatives</b>	
Healthy diet initiatives	<ol style="list-style-type: none"> <li>1) Strengthen guidance to food enterprises about nutrition label knowledge and guide consumers to read nutrition labels correctly.</li> <li>2) Add mandatory labeling of sugar, encourage enterprises to become “low sugar” or “no sugar”, and actively promote the use of “front of package labeling (FOP)” information on food packaging to help consumers quickly choose healthy food.</li> </ol>
Tobacco control initiatives	<ol style="list-style-type: none"> <li>1) Promote a smoke-free culture, e.g. smoke-free weddings and smoke-free families.</li> <li>2) Improve the content and form of health warnings on cigarette packaging.</li> </ol>
Health promotion initiatives in schools	<ol style="list-style-type: none"> <li>1) Set up health courses, teaching knowledge about health behavior and lifestyle, disease prevention and control, adolescent health, etc.</li> <li>2) Provide various forms of health education for students and parents.</li> <li>3) Train and cultivate health education teachers.</li> </ol>
Health promotion initiatives for the elderly	Provide educational activities and trainings for the elderly about fitness, disease prevention, treatment, rehabilitation, and health emergency skills for self-rescue and mutual aid etc.

dissemination, and supervision to ensure the quality and accessibility of health information, such as by establishing national and provincial expert libraries and resource libraries, applying multimedia to release and disseminate health information, and strengthening supervision of the quality of health information.

2) Mobilize social forces to join health literacy improvement, by encouraging them to organize health education activities and trainings, and requiring all communities and workplaces to organize health communication activities such as health lectures for residents and employees.

3) Develop and promote technologies and tools, especially encouraging the application of artificial intelligence and wearable devices in health management to improve the self-management ability of the public.

4) Strengthen health education in healthcare services by emphasizing the responsibility of healthcare institutions in providing health education to the patients and community residents. For example, health professionals should be trained to gain knowledge and skills necessary for health promotion and education and actively provide health guidance to the patients.

5) Strengthen health education in schools, such as by setting up health courses, providing various forms of health education for students and parents, and training and cultivating health education teachers.

6) Improve health literacy among particular populations, such as by providing educational activities and training for the elderly and strengthening the health literacy promotion for people living in poor areas.

7) Implement health promotion programs/campaigns, such as by establishing Health Promotion County work, conducting the Healthy China Campaign and the National Healthy Lifestyle Initiative, and promoting smoke-free culture.

8) Improve the content and form of health warnings on cigarette packages, teach consumers to read nutrition labels, add mandatory labeling of sugar, and promote the use of “front of package labeling (FOP)” information on food packaging to help consumers quickly choose healthy food.

## SUGGESTIONS FOR IMPROVING HEALTH LITERACY IN CHINA

“Healthy China 2030” has put forward goals and strategies to improve health literacy in China. Here are some suggestions for decision makers, practitioners, and researchers when pursuing this work:

1) It should be understood that improving health literacy is not only about improving skills of the patients or the public through education, but also improving health information and removing literacy-related barriers to health services, like reducing the complexity of health information, enhancing health professionals skills in health education, etc., about examining organizational and system-wide norms, policies, and regulations that influence the actions and resources of those seeking assistance and of those

providing services (13).

2) Special attention and effort should be given to people with lower health literacy that are vulnerable to serious health disparities, such as rural residents, migrants from rural areas, elderly people, and people with low socioeconomic status. Specific strategies, programs, and research should be developed to address their barriers and needs in improving health literacy that demand the development of cross-sectoral, cross-disciplinary collaboration and the engagement of the community.

3) For patient education at clinical settings, health professionals should be sensitive to the patient’s health literacy level, and a rapid health literacy assessment is necessary for delivering tailored health education with suitable communication strategies. Effective educational and support models, such as peer-to-peer education and group care programs for chronic disease management, could be integrated within daily practice (1).

4) To support evidence-based health literacy practices, the joint development of a research plan on health literacy by public health workers, clinicians, and health literacy/education experts should be performed to identify the current gaps and outline the most needed areas of research in China.

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## Recommendations

## Protocol for the Management of Asymptomatic Persons Infected with COVID-19 Virus

Joint Taskforce on COVID-19 Prevention and Control, China State Council

**Article 1** This Protocol is formulated in accordance with the *Law of the People's Republic of China on the Prevention and Control of Infectious Diseases* and the *Law of the People's Republic of China on Frontier Health and Quarantine* in order to strengthen the detection, reporting, and management of asymptomatic persons infected with COVID-19 virus.

**Article 2** The asymptomatic persons infected with COVID-19 virus (hereafter referred to as asymptomatic persons) refers to those who have no relevant clinical manifestations including clinically detectable signs or self-perceived symptoms such as fever, cough, or sore throat, but who have tested positive for COVID-19 virus in respiratory specimens or other specimens. There are two types of asymptomatic persons: 1) those who have no self-perceived symptoms or clinically detectable signs throughout the 14-day quarantine; and 2) those who are "asymptomatic" during the incubation period.

**Article 3** Asymptomatic persons are contagious with risks of transmission.

**Article 4** Strengthen the monitoring and detection of asymptomatic persons by: 1) actively testing close contacts of COVID-19 cases during their medical observation period; 2) actively testing during cluster investigations; 3) actively testing people with exposure during tracing the infection source; 4) actively testing people with travel or residential history in areas abroad with sustained COVID-19 transmission; and 5) detecting during epidemiological investigation and opportunistic screening.

**Article 5** Standardize reporting of asymptomatic persons. Healthcare facilities of all types and at all levels, having detected asymptomatic persons, should report the case within 2 hours through direct online reporting. After receiving the report of asymptomatic persons, the county-level CDC should complete the case investigation within 24 hours, promptly register close contacts, and submit the case questionnaire form or investigation report through National Notifiable Infectious Diseases Reporting System in a timely manner. After the asymptomatic infected person is

lifted from the centralized medical observation, the healthcare facility should fill in the completion date of medical observation in National Notifiable Infectious Diseases Reporting System in a timely manner.

**Article 6** Strengthen information transparency. The national health authority of the State Council shall publicize the information of reporting, outcome, and management of asymptomatic persons on a daily basis. The provincial authority shall publish the relevant information about their own jurisdiction. Local transmission and importation of COVID-19 cases shall be calculated and reported separately.

**Article 7** Strengthen the management of asymptomatic infected persons. Asymptomatic infected persons should be placed under medical observation for 14 days. During this period, those who develop clinical symptoms and signs of COVID-19 should be reclassified as confirmed cases. Those who have negative nucleic acid test results twice consecutively during the 14-day centralized medical observation (at least 24 hours apart between sampling) can be lifted from medical observation; those who have no clinical symptoms but have still tested positive during the medical observation period should continue to be under centralized medical observation.

**Article 8** If asymptomatic persons manifest clinical symptoms during the period of centralized medical observation, they should be immediately transferred to a designated health care facility for standard treatment and reclassified in a timely manner after the diagnosis has been confirmed.

**Article 9** Close contacts of asymptomatic infected persons should be put under 14-day centralized medical observation.

**Article 10** An expert panel should be organized to provide consultation tours for asymptomatic persons under concentrated medical observation to promptly detect potential confirmed cases.

**Article 11** Asymptomatic persons who have been lifted from centralized medical observation should be placed under another 14-day medical observation and follow-up, and they should have a follow up visit to the

designated hospital for health check up in the second and fourth week after the lifting of centralized medical observation.

**Article 12** Targeted screening efforts should be scaled up by testing close contacts of detected cases and asymptomatic persons. Enhance surveillance in key areas and settings and among key population groups. Identified asymptomatic persons should be put under centralized medical observation.

**Article 13** Asymptomatic infected persons have the characteristics of silent transmission, subjective symptoms, and limitations in being detected. The national government supports scientific research on infectivity, transmission, and epidemiology of asymptomatic infected persons.

**Article 14** Strengthen information communication, exchange and cooperation with relevant countries and international organizations such as the World Health Organization, and revise the diagnosis and treatment protocol and prevention and control protocol as

required.

**Article 15** Public education and communication on COVID-19 should be enhanced in all localities to provide evidence-based guidance on protection for the public; and extensive training should be conducted to improve the capacity of grassroots health care workers and community workers in prevention and control.

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