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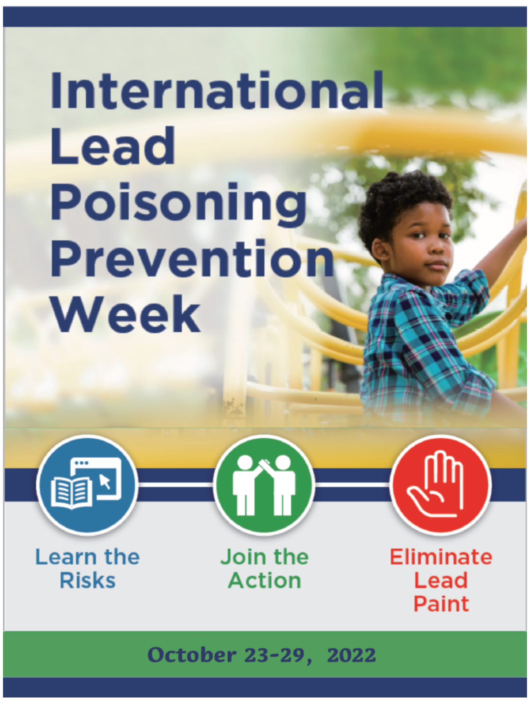

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Cover Image: adapted from the World Health Organization, https://www.who.int/news-room/events/detail/2022/10/23/default-calendar/international-lead-poisoning-prevention-week-2022---say-no-to-lead-poisoning.

Preplanned Studies

Declines in Blood Lead Levels Among General Population — China, 2000–2018

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Summary

What is already known about this topic?

Environmental and occupational lead exposure has generally declined in the past two decades. However, there is no large-scale monitoring of blood lead levels (BLLs) in the Chinese general population.

What is added by this report?

This nationally representative study showed declines of BLLs in all ages of participants; for children aged 3–5 years, down from 78.1 μg/L to 16.9 μg/L, corresponding to 78.4% decrease in the past two decades (2000–2018).

What are the implications for public health practice?

Recommendations for elevated BLLs on screening children at high risk now need to be revisited and updated from 100 μg/L to 50 μg/L in guidelines to conform with the substantial declines in China.

High exposure to lead is associated with numerous adverse health outcomes, particularly impairment of neural development in children (*1*). Large-scale biomonitoring is necessary to quantify risk assessments in public health. The United States carries out the National Health and Nutrition Examination Surveys (NHANES) to monitor changes in environmental chemicals. Monitoring of blood lead levels (BLLs) in children led to action on the reduction of exposure from for example leaded gasoline and leaded paint (*2*). Following the recent BLL decline, the US CDC updated the blood lead reference value (BLRV) to 35 μg/L based on the latest two rounds of the NHANES and reported in Morbidity and Mortality Weekly Report (*3*). In China, the latest national recommendations for BLLs in children, issued in 2006, established a BLRV of 100 μg/L for hyperleademia (*4*). Recent studies indicated that BLLs in Chinese children have been declining over the past two decades (*5*). However, China does not have a suitable definition of elevated BLLs. To this end, the China CDC initiated the China National Human Biomonitoring (CNHBM) in 2017.

The distribution and temporal trends of BLLs during the past two decades in the Chinese population were from the data of a nationally representative study and two previous regional-scale surveys. The 2017/18 survey based on CNHBM, a nationally representative study for tracing the dynamic change of environmental chemicals, included 21,746 samples recruited from 152 counties in 31 provincial-level administrative divisions (PLADs) of China (Supplementary Figure S1, available in http://weekly.chinacdc.cn). Due to 45 participants without available BLLs information, 21,701 participants aged 3–79 years were included in this study. The CNHBM used an advanced computer-assisted personal interviewing (CAPI) online system to conduct a household interview and Epidata (version 3.2, EpiData Association, Odense, Denmark) for data entry and management, collecting the data of age, gender, residence, districts, and so on. Details of covariate definition are shown in Supplementary Methods (available in http://weekly.chinacdc.cn). Details about the study design have been previously reported (*6*). Approval was obtained from National Institute of Environmental Health ethics committee, Chinese Center for Disease Control and Prevention (No.201701). All participants signed written informed consent. The 2000 survey included 6,085 children aged 3–5 years randomly selected from 19 cities (*7*). The 2009/10 survey a included 11,090 participants of the general population aged 6–59 years (*8*). In 2000, 2009/10, and 2017/18 surveys, venous blood specimens were collected in the morning after an overnight fast for all persons in the local community health centers, frozen, and shipped to China CDC (Beijing) for analysis. Inductively coupled plasma mass spectrometry (ICP-MS) was used to measure lead concentrations in blood samples in the three surveys (Supplementary Methods). The lead measurement in the 2017/18 survey was finished in 2019. The BLLs in each of the three surveys were calibrated using standards prepared from lead nitrate Standard Reference Material obtained from the National Institute of Standards and Technology.

Characteristics of participants in the 2017/18 survey were stratified by quartiles of BLLs. Geometric means and distributions of BLLs and the number of participants with elevated BLLs were calculated by incorporating the weights for the entire Chinese population. The spatial distribution of BLLs in the Chinese population was mapped. The 97.5th percentile of the BLLs in participants of all age groups from CNHBM was chosen as the BLRV (*3*). Description of the method adopted to estimate the disease burden for children aged 3–5 years and participants aged 6–59 years are presented in Supplementary Methods, respectively. Analyses were done with SAS (version 9.4, SAS Institute Inc., Cary, USA), R (version 3.4.1, R Development Core Team, Vienna, Austria), and ArcGIS (version 3.6.1, Environmental Systems Research Institute Inc., California, USA). All *P* values were two-sided, and a *P* value of less than 0.05 was considered significant.

The geometric mean of BLLs of all 21,701 participants aged 3–79 years in the 2017/18 survey was 20.66 μg/L, and the proportions of BLLs over 50 μg/L was 6.0% (Table 1). The spatial distribution of BLLs in the Chinese population in 2017/18 is shown in Figure 1. During the past two decades (2000–2018), the BLLs of children aged 3–5 years were down from 78.1 μg/L to 16.9 μg/L, dropping by 78.4%. For participants aged 6–59 years, the BLLs were 20.41 μg/L in 2017/18, down from 36.9 μg/L in 2009/10, dropping by 44.7%. The lead exposure-related burden of disease measured in DALYs showed clear downward trends over time (Table 2). Based on the BLLs in 2017/18, the BLRV for participants aged 3–5 years was updated to 50 μg/L considering the 97.5th percentile of the BLLs in this population (Table 1). Characteristics of participants in surveys are shown in Supplementary Tables S1–S2 (available in http://weekly.chinacdc.cn). Supplementary Figure S2 (available in http://weekly.chinacdc.cn) compares the proportion of BLLs over 50 μg/L in participants from 2000 to 2018. More details of disease burden are shown in Supplementary Tables S3–S4 (available in http://weekly.chinacdc.cn).

DISCUSSION

Our study found that both the BLLs among the Chinese population aged 3–5 years and 6–59 years exhibited decreases of varying degrees in the past two decades. Our study demonstrated that the decline in BLLs in the Chinese population was akin to the decline in the USA. After the implementation to eliminate leaded gasoline, which preceded the observed decline in BLLs. Leaded paint, while a major source of indoor exposure in the United States, was not widely used in the Chinese housing stock, and most residents reside in dwellings built after the banning of leaded paint. Therefore, the BLLs in Chinese residents were closely related to the levels of environmental lead exposure and the formulation of policies related to lead. However, compared with the latest monitoring results of developed countries such as the United States and Canada, the internal exposure to lead in Chinese population was still at a relatively higher level, indicating a higher disease burden and limiting intellectual quotient attainment of children on a population scale (*9*–*10*). It has been observed that BLLs in Tibet are higher than in other regions, which may be due to this population's unique dietary and living habits.

The BLRV is 100 μg/L in China at present, higher than the American standard (35 μg/L) (*3*) and the World Health Organization (WHO) standard (50 μg/L) (*11*), and therefore needs updates based on our measurements in the decline of BLLs over the past two decades. However, setting standards is complicated by various literature using inconsistent criteria for BLRV definition. In this study, we established reference values based on blood lead concentrations stratified according to age. Although a lower BLRV increases the burden on the medical system, especially in pediatrics, we cannot deny that a more stringent BLRV would identify at-risk populations as much as possible and give caregivers, communities, and officials more opportunities to act earlier. Measures to improve lead exposure monitoring and prevention interventions for high-risk populations are priorities for future work. Government agencies, employers, and worker-affiliated organizations are responsible for carrying out education in the workplace and community in accordance with the latest guidelines and recommendations.

The strengths of this study include the CNHBM data obtained by the official organization, which firstly permits the characterization of BLLs in a nationally representative sample of the general Chinese

TABLE 1. Blood lead levels (BLLs) in different age, gender, residence and districts among Chinese population in 2017/18.

Sub group	<LOD* (%)	Geometric mean (95% CI), μg/L	Median (95% CI), μg/L	P_{90} (95% CI), μg/L	P_{95} (95% CI), μg/L	$P_{97.5}$ (95% CI), μg/L	Participants with BLLs ≥35 μg/L, n (%), million†	Participants with BLLs ≥50 μg/L, n (%), million§	Participants with BLLs ≥100 μg/L, n (%), million¶
Total	0.27	20.66 (19.90–21.46)	20.72 (20.03–21.42)	42.82 (40.73–44.91)	52.72 (50.03–55.41)	65.80 (60.93–70.67)	222.4 (16.7)	79.9 (6.0)	9.0 (0.7)
Age (years)									
3–5	0.36	16.87 (16.06–17.72)	17.01 (16.33–17.68)	33.87 (31.87–35.87)	41.67 (38.32–45.02)	50.95 (44.86–57.03)	11.8 (8.7)	3.7 (2.7)	0.7 (0.5)
6–11	0.24	16.84 (16.12–17.59)	17.01 (16.34–17.67)	31.27 (29.49–33.04)	38.65 (35.91–41.40)	45.87 (42.46–49.29)	11.6 (7.1)	3.0 (1.8)	0.1 (0.1)
12–18	0.36	15.21 (14.53–15.93)	15.27 (14.71–15.83)	29.30 (27.18–31.42)	37.66 (33.73–41.59)	46.28 (38.59–53.97)	9.7 (6.1)	3.2 (2.0)	0.6 (0.3)
19–39	0.36	21.32 (20.33–22.36)	21.65 (20.50–22.79)	41.79 (39.12–44.45)	51.15 (47.70–54.61)	62.64 (55.65–69.63)	47.9 (16.2)	15.2 (5.2)	1.2 (0.4)
40–59	0.30	24.78 (23.70–25.91)	25.02 (23.90–26.14)	49.47 (47.09–51.85)	58.68 (54.54–62.81)	71.33 (64.98–77.68)	84.6 (25.2)	32.2 (9.6)	3.3 (1.0)
60–79	0.06	24.40 (23.32–25.52)	23.70 (22.75–24.64)	49.37 (45.49–53.26)	63.92 (57.30–70.54)	85.72 (78.31–93.14)	56.8 (23.8)	22.6 (9.5)	3.1 (1.3)
Sex									
Men	0.24	24.41 (23.37–25.50)	24.43 (23.39–25.48)	47.34 (44.72–49.96)	57.34 (53.26–61.41)	71.38 (65.29–77.47)	154.1 (23.3)	54.5 (3.8)	5.2 (0.8)
Women	0.28	17.51 (16.86–18.18)	17.39 (16.90–17.89)	35.37 (33.31–37.44)	45.54 (42.46–48.62)	57.44 (52.24–62.64)	68.3 (10.2)	25.4 (8.2)	3.8 (0.6)
Residence									
Urban	0.26	20.50 (19.46–21.59)	20.70 (19.83–21.57)	42.61 (39.87–45.35)	52.25 (48.98–55.52)	63.10 (55.88–70.33)	132.8 (16.5)	46.6 (5.8)	5.0 (0.6)
Rural	0.29	20.92 (19.78–22.11)	20.81 (19.60–22.02)	43.09 (39.84–46.34)	53.35 (48.27–58.42)	67.48 (61.25–73.71)	89.6 (17.1)	33.3 (6.4)	4.0 (0.8)
Districts									
North China	0.28	19.34 (18.21–20.54)	19.45 (18.28–20.62)	38.57 (34.24–42.90)	49.10 (42.41–55.80)	55.93 (46.99–64.88)	25.8 (13.5)	8.3 (4.3)	1.0 (0.5)
Northeast China	0.11	19.39 (17.40–21.61)	18.93 (16.70–21.16)	44.14 (36.97–51.30)	56.15 (47.37–64.94)	72.30 (48.78–95.83)	18.2 (16.4)	7.3(7.1)	0.7 (0.6)
East China	0.18	19.39 (17.90–21.00)	20.03 (18.94–21.12)	38.11 (35.36–40.86)	45.53 (42.22–48.84)	54.52 (49.59–59.45)	55.2 (13.4)	13.8 (3.3)	1.4 (0.4)
South-Central China	0.09	22.22 (20.34–24.28)	21.63 (19.36–23.89)	46.97 (41.79–52.14)	56.06 (48.65–63.47)	67.70 (56.18–79.22)	65.0 (20.2)	26.3 (8.1)	2.5 (0.8)
Southwest China	0.66	23.95 (21.95–26.14)	23.69 (21.91–25.48)	51.88 (45.02–58.74)	70.76 (62.21–79.32)	89.66 (78.16–101.15)	40.7 (24.6)	18.8 (11.2)	3.1 (1.8)
Northwest China	0.36	20.36 (18.70–22.15)	20.30 (18.85–21.75)	38.13 (32.54–43.72)	47.78 (36.45–59.11)	60.89 (41.25–80.53)	17.5 (13.9)	5.4 (4.3)	0.3 (0.3)

Abbreviation: LOD=limit of detection.

* The LOD of blood lead was 0.035 μg/L; <LOD (%) was the proportion below LOD.

† Participants with BLLs ≥35 μg/L, n (%) were calculated incorporating the sample weights.

§ Participants with BLLs ≥50 μg/L, n (%) were calculated incorporating the sample weights.

¶ Participants with BLLs ≥100 μg/L, n (%) were calculated incorporating the sample weights.

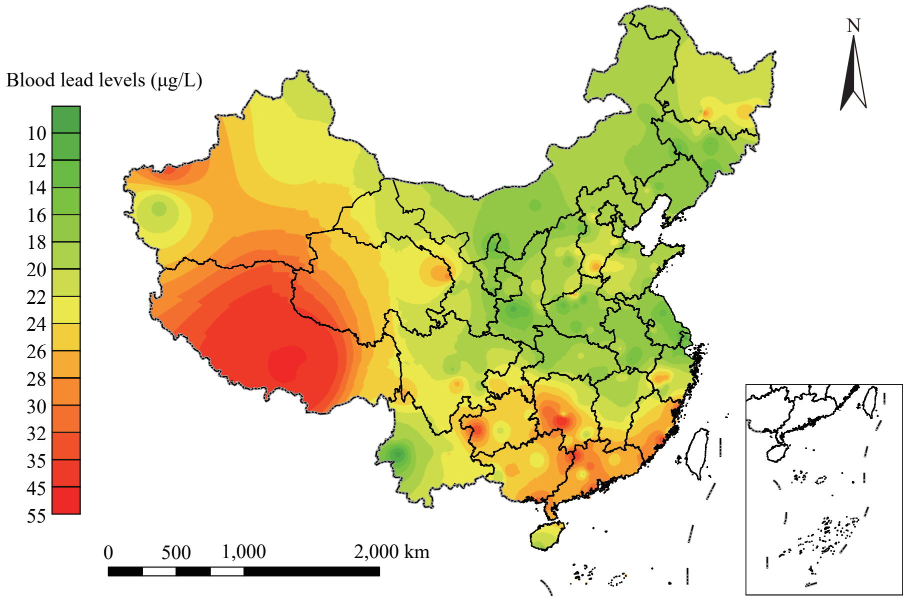

FIGURE 1. The spatial distribution of blood lead levels in Chinese population aged 3 to 79 years in 2017–2018 (*N*=21,701).

TABLE 2. Declines in blood lead levels (BLLs) for Chinese population aged 3–59 years during the past two decades.

Sub-population	Year	Geometric mean (95% *CI*), μg/L	BLLs ≥50 μg/L, %	Rate of decline, %	Disease burden, DALYs (million person-years)
Aged 3–5 years					
Total				78.4	
	2000	78.1 (77.0–79.0)	84.8		16.66
	2017–2018	16.9 (16.1–17.7)	2.7		0.41
Sex					
Men				77.7	
	2000	80.0 (78.5–81.5)	88.3		8.83
	2017–2018	17.8 (16.4–19.4)	2.6		0.21
Women				78.1	
	2000	75.9 (74.3–77.5)	81.2		7.83
	2017–2018	16.6 (15.8–17.5)	2.7		0.20
Aged 6–59 years					
Total				44.7	
	2009–2010	36.9 (32.1–14.6)	29.8		9.33
	2017–2018	20.4 (20.0–20.8)	4.9		6.46
Sex					
Men				43.1	
	2009–2010	44.3 (37.8–50.8)	34.6		6.65
	2017–2018	24.2 (23.2–25.3)	7.7		4.95
Women				44.6	
	2009–2010	30.3 (24.6–36.0)	19.5		2.70
	2017–2018	16.8 (16.1–17.4)	3.2		1.50

TABLE 2. (Continued)

Sub-population	Year	Geometric mean (95% *CI*), μg/L	BLLs ≥50 μg/L, %	Rate of decline, %	Disease burden, DALYs (million person-years)
Age (years)					
6–11				52.4	
	2009– 2010	35.3 (30.0–41.6)	23.7		0.21
	2017–2018	16.8 (16.1–17.6)	1.8		0.12
12–18				54.4	
	2009–2010	33.3 (26.1–42.6)	22.5		0.47
	2017–2018	15.2 (14.5–15.9)	2.0		0.25
19–39				40.5	
	2009–2010	35.8 (28.4–45.2)	28.9		1.90
	2017–2018	21.3 (20.3–22.4)	5.2		1.23
40–59				37.5	
	2009–2010	39.6 (33.1–47.6)	32.5		6.74
	2017–2018	24.8 (23.7–25.9)	9.6		4.71

Abbreviation: DALYs=disability-adjusted life years.

population aged 3–79 years. We updated the BLRV based on the current blood lead levels from the results of the nationally representative study with the largest sample size and scope so far. Our study conducted a longitudinal comparison of BLLs among Chinese population through three surveys, focusing on the general population rather than specific groups such as those with high occupational exposure.

This study was subject to some limitations. First, surveys in 2000 and 2009/10 were only regional-scale, though being the largest study of BLLs monitoring in China at the time, and the study samples only covered part of the age group, limiting the comparison of the changing trend of BLLs. Second, our study involved three different cross-sectional studies, with the result that different people were sampled with iterations of the study, so that determination of within-individual temporal trends in BLLs cannot be obtained.

The study demonstrated a substantial decline in BLLs and the disease burden of the entire Chinese population in the past two decades, which provided evidence that China has made significant achievements in controlling lead pollution. Furthermore, there is an urgent need to update a lower BLRV based on the significant reductions in current blood lead levels that are more sensitive to monitor and screen people with high BLLs with significant public health value for prevention of hazards of lead exposure. The study added needed evidence on behalf of populous developing countries. There is no known safe blood lead concentration, and even as BLL declines, governments and public health institutions need to protect future generations if continued efforts to preemptively control or even eliminate lead sources and provide timely interventions for persons at the highest risk for exposure.

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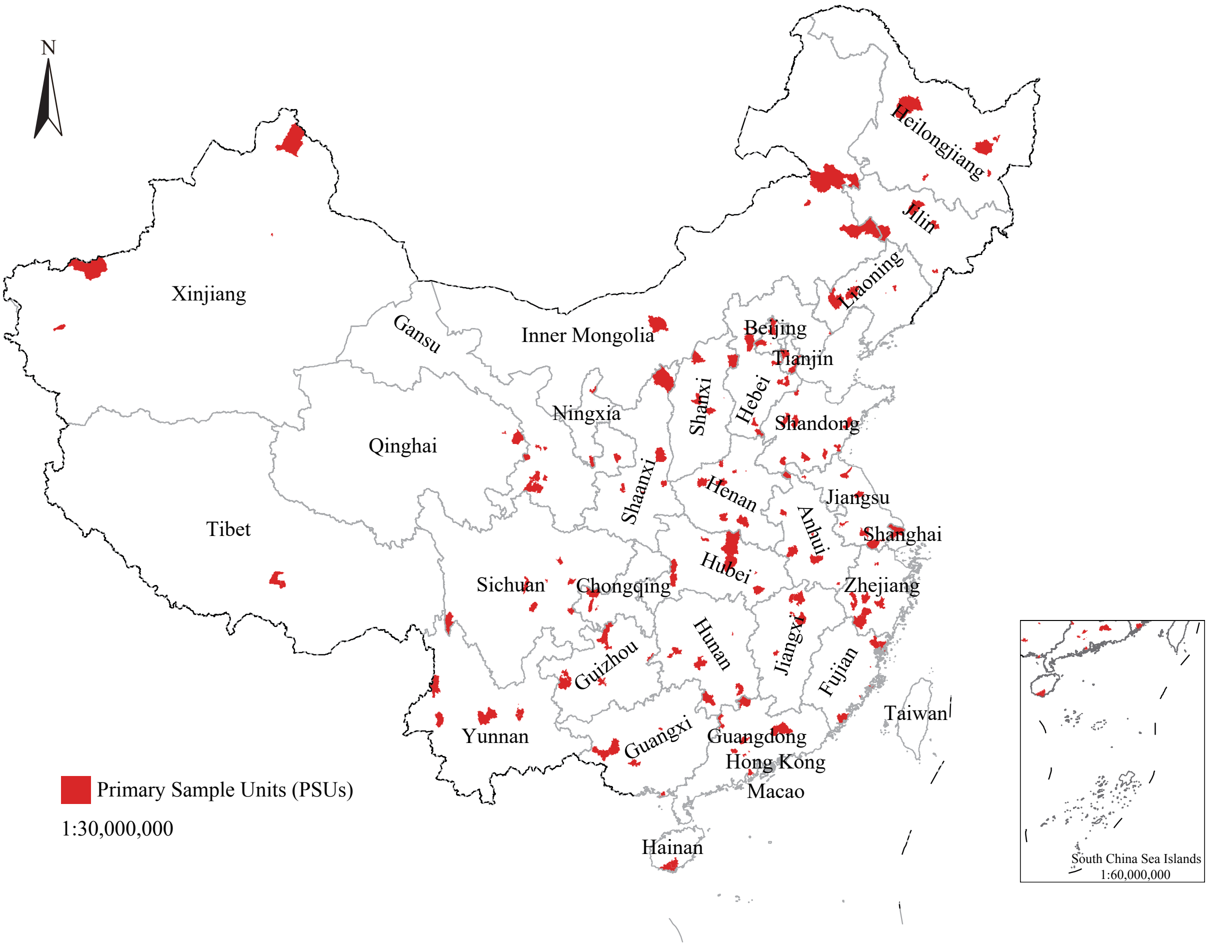
SUPPLEMENTARY MATERIALS

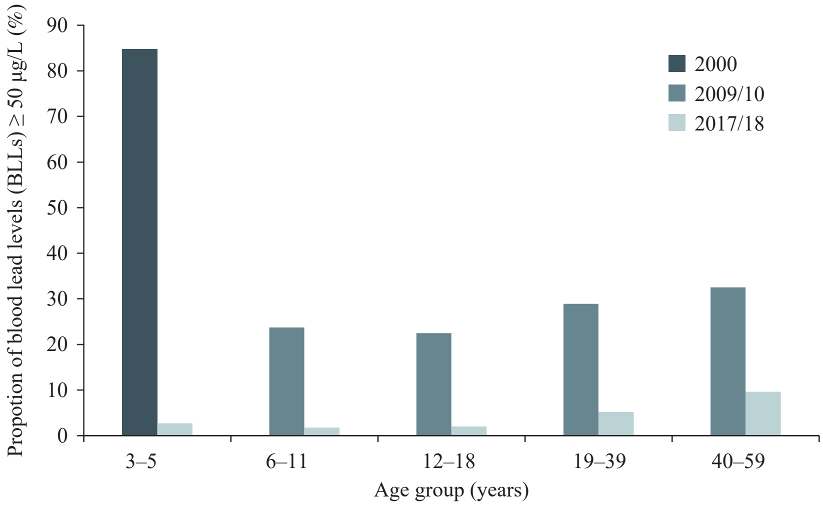
Supplementary Methods

Variable Definition

Residences were categorized as rural and urban. Districts were defined as northern, northeastern, eastern, central south, southwest, and northeast. Occupation was defined as the first, secondary and tertiary industries. House type was categorized as cottage, simple building, villa, and other types. Lifestyle variables were cigarette smoking, tea drinking, and alcohol drinking. Cigarette smoking was defined as never, <70 cigarettes/week, 71–105 cigarettes/week, 106–140 cigarettes/week, ≥141 cigarettes/week. Alcohol drinking was defined as never, <2 times/month, 2–4 times/month, 2–3 times/week, and ≥4 times/week. Tea drinking was defined as <once/month, once/month–6 times/week, 7–20 times/week, ≥21 times/week. Dietary habits were constructed as described previously based on food groups including sea fish (never, <once/month, 1–7 times/month, 2 times/week, 3 times/week, ≥4 times/week, missing), sea shell (once/month, 1–7 times/month, 2 times/week, ≥3 times/week, missing), freshwater fish (once/month, 1–3 times/month, once/week, 2 times/week, ≥3 times/week, missing), rice (<4 times/week, 4–6 times/week, 7–13 times/week, 14–20 times/week, ≥21 times/week, missing), meat (<once/month, 1–2 times/month, 3–6 times/week, 7–13 times/week, 14–20 times/week, ≥21 times/week, missing), milk (<once/month, 1–3 times/month, 1–6 times/week, ≥7 times/week, missing), fruits (<once/month, 1–3 times/month, 1–6 times/week, 7–13 times/week, ≥14 times/week, missing), flour (<once/month, 1–3 times/month, 1–6 times/week, 7–13 times/week, ≥14 times/week, missing), tubers (<once/month, 1–3 times/month, 1–2



SUPPLEMENTARY FIGURE S1. Spatial locations of the monitoring units in China National Human Biomonitoring.



SUPPLEMENTARY FIGURE S2. Comparison of proportion of blood lead levels (BLLs) over 50 μg/L in 2000–2018.

times/week, ≥3 times/week, missing), beans (<once/month, 1–3 times/month, once/week, 2 times/week, ≥3 times/week, missing), nuts (<once/month, 1–3 times/month, 1–2 times/week, 3–6 times/week, ≥7 times/week, missing).

Blood Lead Measurements

The methods for determining lead in blood (1 μg/L = 0.00483 μmol/L), including quality control and assurance procedures, have been described for each survey. Comparability has been established for the method used in five laboratories. The limits of determination (LOD) for blood lead were 0.8, 0.28, and 0.03 μg/L in the 2000, 2009/10, and 2017/18 surveys, respectively. 2.3% of samples were less than LOD in the 2017/18 surveys. For the calculation of mean lead levels, the LOD/2 was imputed for samples below the LOD. Although there is no safe blood lead level (BLL) for the population, using dichotomous BLL thresholds is advantageous for assessing trends over time. These cut points may be more easily understood than statistically derived cut points such as quartiles. An elevated BLL was defined a priori as 50 μg/L at or above selected values chosen in part because of their prior or potential use in public health policy. Given the multiple hazards of exposure to lead, during a May 2021 meeting of the Lead Exposure and Prevention Advisory Committee (LEPAC), the workgroup recommended that the blood lead reference value (BLRV) be updated from 50 μg/L to 35 μg/L using data derived from the two most recent National Health and Nutrition Examination Surveys (NHANES) cycles (2015–2016 and 2017–2018).

Quality Control in the Laboratory of Blood Lead

We used high-purity reagents for standard solutions and sample preparation. Before analysis and determination, the instrument was tuned with a mass spectrometry tuning solution, and the experiment was carried out after the main technical indicators (low, medium, and high-quality element sensitivity, oxide ratio, and double charge ratio) reached the standard. The nebulizer and sample cone were periodically soaked and cleaned with diluted nitric acid. Calibration curves, certified standard reference materials (external quality control), parallel samples, field blanks, and laboratory reagent blanks were determined for each batch of experiments. The linear correlation coefficient r of the calibration curve was required to be greater than 0.995. The certified reference material was measured once every 30 samples, and the measurement result was within the allowable error range of the reference value; one parallel sample (randomly selected) was measured for every 20 samples. The relative error of the parallel sample was less than 10%. The laboratory reagent blank determination was less than the method's detection limit. When the measured concentration of the sample exceeded the measurement range of the calibration curve, we reduced the sampling amount or increased the dilution factor and then re-measured.

Methods of Estimating the Burden of Disease Associated with Lead Exposure in Participants Aged 6–59 years

The burden of disease was assessed using the disability-adjusted life years (DALYs) developed by the Global Burden of Disease Study. This study assessed *YLLs* in the 6–59 age group.

YLLs calculation method: Firstly, based on the literature to find the dose-response relationship between lead and the risk of all-cause mortality, the *HR*(*Ci*) values under the exposure level *Ci* of different age groups and sex groups of Chinese residents were calculated by the hazard ratio (*HR*). Mortality *M* in different age and gender groups was collected and calculated according to formula (*1*) the mortality M' in the region if exposure levels were reduced to the theoretical minimum risk value across the region. According to formula (*2*), the number of premature deaths due to exposure to lead (*Mi*) can be calculated. This study estimated *YLLs* according to Equation (*3*). The *HR*(*Ci*) values involved in the formula were estimated by finding the *HR* values in the dose-response relationship between internal exposure and the risk of all-cause death in the relevant literature, combined with the actual exposure level of Chinese residents. The mortality data of each age group when calculating *YLLs* comes from the "2016 China Cause of Death Surveillance Dataset".

$$M' = M / HR(Ci) \tag{1}$$

$$Mi = Pi \times M' \times (HR(Ci) - 1) \tag{2}$$

$$YLLs = Mi \times (\text{Average life expectancy} - \text{The average life expectancy of the age group}) \tag{3}$$

Methods of Estimating the Burden of Disease Associated with Lead Exposure in Children Aged 3–5 Years

The burden of disease was calculated based on the method published in 2003 by World Health Organization (WHO). The method indicates that the loss of intelligence quotient (IQ) points can be calculated ideally based on the linear dose-response relationship between BLLs and IQ loss. When the BLL is between 50 and 200 μg/L, the IQ decreases by 1.3 points for every 50 μg/L increase; for BLLs over 200 μg/L, a loss of 3.5 IQ points is assumed. When IQ levels are above 50 points, intelligence in human populations generally approximates a normal distribution. According to the distribution of BLL of Chinese residents obtained from our investigation and the assessment method provided by WHO, the proportion of children aged 3–5 years with different BLLs and the proportion of children with IQ loss caused by lead exposure were calculated respectively on the premise that the IQ distribution in the population was a normal distribution.

The WHO guidelines use the incidence of mild mental retardation (MMR) as a quantified indicator of the health effects caused by lead exposure and assess the burden of MMR disease. MMR occurs when the IQ is below 70 points but above 50 points. Even if IQ points decrease due to various diseases or exposures, they can also remain above 70 because of the higher original IQ. Consequently, assessing the disease burden of MMR requires counting the number of people with an IQ slightly above the threshold of 70 who enter the MMR range through loss of IQ points due to lead exposure. Some infectious and parasitic diseases can also cause MMR, therefore, according to the prevalence of MMR caused by known non-congenital causes in different regions, WHO calculates the adjustment ratio (*AR*) of MMR. According to the method, the incidence of MMR in each age group was calculated by multiplying the proportion of children with the defined IQ point losses by the respective percentage of the population in that range of BLLs, based on the distributions of BLLs and IQ levels of children. The formula is as follows:

$$I_{MMR} = AR \times [(E1 \times P1) + (E2 \times P2) + (E3 \times P3) + (E4 \times P4)] \tag{4}$$

In formula (*1*), *E1*, *E2*, *E3*, and *E4* represent the proportion of children with BLLs of 50–100 μg/L, 100–150 μg/L, 150–200 μg/L, and >200 μg/L, respectively; *P1*, *P2*, *P3*, and *P4* represent the proportion of children with IQ points of 70–70.65, 70–71.95, 70–73.25, and 70–73.50, respectively; AR is the adjustment ratio and the value of China (WHO Western Pacific Region) is 3.03.3.

Disability adjusted life years (DALYs) were used to quantitatively measure the burden of MMR in children caused by lead exposure. The DALYs are the sum of years of life lost due to premature death [years of life lost (*YLLs*)] and years lived with disability including permanent disability and temporary incapacity [years lived with disability (*YLDs*)]. Because MMR due to lead exposure in children rarely leads to death, only *YLDs* were estimated. So we performed the calculation based on the simplified formula for DALYs recommended in the approach of The Global Burden of Diseases, Injuries, and Risk Factors enterprise (GBD 2010):

$$YLD = I \times DW \times L \tag{5}$$

In formula (*2*), I is the number of prevalent cases, it can be obtained by multiplying IMMR by the number of children in that age group; DW is the disability weight; L is the duration of disability. It is generally assumed that intellectual impairment exists early in life and remains throughout life, life expectancy is therefore calculated as the duration of disability. The incidence of MMR, the number of children in 3–5 age group in the sixth national census of China, the average life expectancy data (77.0 years) in the 2018 Statistical Bulletin of China's Health Development and the disability weight of MMR (0.361) were substituted into the formula for calculation.

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SUPPLEMENTARY TABLE S1. The blood lead levels of Chinese children aged 3–5 years in 2000.

Sub group	Frequency	Geometric mean (95% *CI*), μg/L	P_{10} (95% *CI*), μg/L	P_{25} (95% *CI*), μg/L	Median (95% *CI*), μg/L	P_{75} (95% *CI*), μg/L	P_{90} (95% *CI*), μg/L	P_{95} (95% *CI*), μg/L	P_{99} (95% *CI*), μg/L
Total	6,085	78.1 (77.0–79.2)	38.5 (36.5–40.4)	62.0 (60.8–63.0)	81.4 (80.5–82.1)	110.9 (109.0–112.5)	150.5 (147.0–153.0)	175.0 (171.0–178.5)	228.0 (219.5–241.5)
Gender									
Male	3,260	80.0 (78.5–81.5)	41.5 (38.5–43.5)	63.0 (61.6–64.0)	82.5 (81.5–83.6)	114.5 (111.0–117.5)	152.4 (149.5–156.0)	176.9 (170.7–183.0)	226.6 (216.0–238.5)
Female	2,825	75.9 (74.3–77.5)	35.5 (33.0–38.0)	60.7 (59.1–62.2)	80.2 (79.0–81.3)	106.5 (103.8–109.2)	146.2 (143.0–152.1)	173.0 (167.0–178.2)	234.0 (218.0–260.0)
PLADs									
Anhui	837	70.5 (68.9–72.1)	52.0 (49.2–53.6)	61.0 (59.5–62.5)	70.0 (68.9–70.9)	82.0 (79.8–85.0)	102.5 (98.5–110.1)	124.5 (114.5–142.0)	175.2 (168.3–204.5)
Gansu	248	116.0 (109.6–122.7)	65.5 (56.5–74.0)	85.6 (79.9–93.8)	118.3 (107.6–125.0)	156.4 (147.5–176.5)	211.1 (197.8–229.0)	241.5 (226.6–266.0)	268.0 (266.0–299.0)
Hainan	526	103.7 (99.6–107.9)	52.5 (45.1–60.4)	78.61 (72.7–82.8)	115.0 (105.8–123.0)	151.9 (147.0–156.8)	176.4 (169.1–180.0)	185.5 (182.7–189.8)	197.7 (193.0–210.9)
Henan	543	128.6 (124.9–132.3)	83.3 (78.6–88.0)	107.9 (102.5–111.0)	134.0 (129.6–139.5)	160.0 (155.5–163.0)	190.0 (183.0–202.0)	215.0 (203.6–222.9)	259.50 (241.0–283.0)
Heilongjiang	1,105	76.9 (75.0–78.8)	52.2 (48.4–55.7)	70.7 (67.9–72.7)	82.0 (81.0–82.6)	90.7 (88.8–92.1)	113.5 (108.6–120.0)	136.0 (128.0–143.6)	190.30 (176.0–214.5)
Hubei	495	55.3 (52.0–58.9)	17.5 (15.0–20.0)	40.5 (32.5–49.5)	66.5 (64.5–68.5)	86.0 (80.0–90.0)	116.0 (107.5–125.5)	135.0 (126.0–149.5)	228.0 (167.0–328.5)
Hunan	443	37.3 (35.1–39.6)	17.5 (15.5–19.0)	24.0 (23.0–26.0)	35.0 (32.5–37.0)	52.0 (47.5–56.5)	99.0 (83.0–124.5)	134.0 (124.5–146.0)	199.5 (163.0–319.0)
Jilin	893	93.7 (91.0–96.6)	62.0 (58.2–64.4)	76.5 (74.6–78.2)	93.5 (90.5–96.0)	121.0 (117.5–125.0)	155.8 (146.7–165.4)	182.0 (172.0–195.5)	270.0 (234.0–443.4)
Ningxia	995	71.9 (70.0–73.8)	41.0 (38.5–43.5)	55.5 (53.5–57.5)	71.5 (69.5–74.1)	97.0 (93.4–100.0)	121.5 (118.0–128.0)	141.5 (134.5–150.5)	194.0 (170.5–231.0)

Abbreviation: PLADs=provencial level administrative divisions.

SUPPLEMENTARY TABLE S2. The blood lead levels of Chinese population in 2009/10.

Sub group	Frequency	Geometric mean (95% *CI*), μg/L	P_{10} (95% *CI*), μg/L	P_{25} (95% *CI*), μg/L	Median (95% *CI*), μg/L	P_{75} (95% *CI*), μg/L	P_{90} (95% *CI*), μg/L	P_{95} (95% *CI*), μg/L	P_{99} (95% *CI*), μg/L
Total	11,090	36.9 (30.3–44.9)	17.6 (14.7–20.5)	25.7 (22.3–29.1)	37.3 (31.0–43.5)	55.9 (40.0–71.9)	83.9 (38.6–129.2)	109.7 (46.4–173.0)	211.6 (.–.)*
Age, years									
6–11	1,525	35.4 (30.0–41.6)	19.96 (17.1–22.8)	26.8 (23.0–30.6)	35.6 (30.6–40.6)	49.1 (34.8–63.4)	67.6 (36.8–98.5)	81.96 (.–.)*	112.6 (91.0–134.3)
12–18	3,573	33.3 (26.1–42.6)	16.8 (13.0–20.6)	23.6 (19.2–28.0)	33.8 (26.2–41.4)	47.8 (26.8–68.8)	70.7 (.–.)*	89.6 (.–.)*	151.5 (.–.)*
19–39	3,533	35.9 (28.5–45.2)	17.2 (13.2–21.2)	25.3 (21.3–29.3)	36.9 (29.9–44.0)	55.0 (36.6–73.5)	84.1 (34.2–134.1)	109.2 (67.0–151.3)	176.3 (.–.)*
40–60	2,459	39.7 (33.1–47.6)	17.8 (15.2–20.4)	26.7 (23.8–29.5)	39.7 (34.1–45.3)	60.4 (45.2–75.7)	92.0 (32.2–151.7)	126.2 (.–.)[a]	262.4 (.–.)*
Gender									
Female	5,616	29.9 (23.6–38.0)	14.6 (11.4–17.8)	21.5 (18.1–25.0)	30.3 (24.6–36.0)	45.1 (28.5–61.6)	69.1 (.– .)[a]	88.8 (.–.)*	166.8 (.–.)*
Male	5,474	45.0 (38.0–53.3)	22.7 (18.9–26.5)	31.5 (28.0–35.0)	44.3 (37.8–50.8)	65.5 (47.1–83.8)	96.3 (58.8–133.9)	124.2 (70.0–178.5)	225.9 (.–.)*
Region									
Eastern China	8,010	31.9 (26.6–38.3)	21.0 (.–.)*	27.7 (13.6–41.8)	43.1 (20.7–65.5)	65.0 (19.4–110.7)	92.2 (16.6–167.9)	114.1 (64.4–163.8)	208.5 (.–.)*
Central China	1,376	43.4 (29.2–64.3)	15.7 (12.5–19.0)	23.6 (20.4–26.9)	33.6 (29.4–37.7)	47.0 (40.3–53.7)	65.95 (44.6–87.4)	83.2 (.–.)*	200.1 (.–.)*
Western China	1,704	63.8 (38.5–105.9)	30.3 (.–.)*	43.8 (.–.)*	66.3 (20.2–112.3)	93.0 (55.3–130.7)	125.4 (94.9–155.9)	147.8 (112.0–183.6)	227.0 (.–.)*
City									
Beijing	568	33.9 (32.1– 35.9)	18.4 (16.2– 20.6)	26.1 (24.5– 27.6)	36.2 (34.7–37.8)	49.8 (47.4–52.2)	66.3 (61.2–71.5)	75.9 (70.2–81.7)	100.2 (81.1–119.2)
Chaozhou	699	47.5 (45.5–49.6)	26.8 (24.7–28.8)	35.3 (33.5–37.2)	45.97 (44.1–47.8)	63.8 (60.0–67.6)	83.9 (78.2–89.5)	100.3 (85.97– 114.7)	269.7 (165.0–374.5)
Chengde	554	29.9 (28.4–31.5)	15.8 (14.4–17.3)	21.1 (19.9–22.3)	30.4 (27.7–33.1)	44.3 (41.1–47.5)	54.7 (50.7–58.7)	60.1 (51.4–68.8)	81.8 (.–.)*
Dandong	492	33.0 (31.3–34.8)	19.4 (18.1–20.7)	25.8 (24.4–27.2)	33.8 (32.5–35.2)	44.0 (40.7–47.2)	56.2 (50.2–62.2)	66.1 (56.5–75.6)	83.9 (.–.)*
Haidong	560	44.7 (42.3–47.3)	22.4 (20.7–24.0)	30.8 (28.6–33.0)	42.9 (40.4–45.4)	62.4 (56.9–67.9)	95.5 (77.0–114.0)	130.4 (114.5–146.3)	177.9 (.–.)*
Heze	313	9.8 (8.2–11.8)	2.3 (0.9–3.6)	5.9 (4.3–7.6)	13.9 (11.9–15.8)	23.5 (20.1–26.8)	33.1 (28.2–38.0)	41.3 (29.6–53.0)	66.4 (.–.)*

Continued

Sub group	Frequency	Geometric mean (95% *CI*), μg/L	P_{10} (95% *CI*), μg/L	P_{25} (95% *CI*), μg/L	Median (95% *CI*), μg/L	P_{75} (95% *CI*), μg/L	P_{90} (95% *CI*), μg/L	P_{95} (95% *CI*), μg/L	P_{99} (95% *CI*), μg/L
Jiaozuo	463	60.3 (56.9–64.1)	32.8 (30.1–35.5)	40.6 (37.3–43.9)	57.5 (53.2–61.8)	82.5 (76.8–88.3)	108.3 (98.9–117.7)	135.7 (93.3–178.1)	311.1 (.–.)*
Jinan	465	22.7 (20.9–24.7)	8.6 (6.5–10.7)	16.6 (14.7–18.4)	25.8 (23.6–27.9)	36.4 (34.4–38.4)	47.0 (43.4–50.5)	56.8 (50.2–63.3)	71.0 (30.9–111.2)
Jinzhou	566	31.3 (29.9–32.8)	17.8 (16.7–19.0)	23.6 (22.1–25.1)	30.1 (28.7–31.5)	42.2 (39.3–45.2)	55.3 (51.3–59.4)	63.9 (55.2–72.7)	81.9 (.–.)*
Langfang	549	36.8 (34.6–39.2)	19.9 (17.9–22.0)	27.9 (26.3–29.5)	37.6 (35.3–40.0)	51.8 (47.7–55.9)	68.1 (64.2–72.0)	75.9 (70.6–81.2)	110.9 (.–.)*
Lianyungang	455	34.5 (33.1–36.0)	22.0 (20.7–23.3)	27.6 (26.4–28.8)	34.9 (33.5–36.3)	43.95 (40.9–47.0)	55.4 (52.5–58.3)	60.5 (55.9–65.0)	76.6 (.–.)*
Pingdingshan	467	32.4 (30.5–34.4)	18.4 (17.0–19.8)	22.6 (21.4–23.8)	30.8 (28.4–33.1)	44.5 (41.4–47.6)	54.1 (48.1–60.1)	72.7 (43.9–101.5)	151.9 (.–.)*
Puyang	446	39.96 (37.4–42.7)	19.4 (18.3–20.5)	25.1 (23.4–26.9)	39.1 (34.4–43.8)	62.8 (57.3–68.2)	83.6 (75.1–92.1)	109.1 (92.7–25.5)	144.8 (.–.)*
Qingdao	313	20.4 (18.1–23.0)	7.1 (5.3–9.0)	13.2 (11.2–5.2)	21.9 (18.4–25.4)	35.4 (29.2–41.6)	56.1 (50.1–62.1)	61.3 (52.7–69.9)	97.0 (.–.)*
Qingyuan	530	83.1 (76.3– 90.6)	34.7 (32.1–37.3)	47.0 (43.4–50.6)	76.9 (67.8–86.0)	136.7 (113.5–159.8)	227.6 (188.1–267.0)	298.6 (161.3–435.8)	604.7 (.–.)*
Shenyang	247	25.9 (24.3–27.5)	14.9 (13.4–16.4)	19.3 (17.2–21.4)	27.4 (25.0–29.7)	33.7 (30.5–36.9)	44.1 (41.3– 46.9)	47.8 (43.8–51.2)	66.1 (.–.)*
Shijiazhuang	543	32.1 (30.8–33.3)	19.4 (18.0–20.7)	25.1 (23.5–26.6)	31.3 (29.5–33.1)	41.6 (39.8–43.4)	52.9 (48.5– 57.2)	58.9 (54.3–63.6)	80.1 (.–.)*
Suzhou	522	33.3 (31.7–35.1)	18.9 (17.1–20.6)	25.2 (23.7–26.6)	33.5 (31.7–35.4)	45.4 (43.5–47.2)	57.1 (50.8– 63.3)	68.8 (61.8–75.8)	85.2 (68.1–102.3)
Taizhou	549	35.7 (34.4–37.0)	23.2 (21.7–24.8)	28.2 (27.1–29.4)	35.6 (34.1–37.0)	44.2 (42.5–46.0)	55.1 (51.4– 58.8)	62.7 (56.6–68.9)	84.3 (.–.)*
Xining	1,144	76.0 (73.4–78.6)	41.6 (38.8–44.4)	57.4 (54.8–60.0)	76.3 (73.5–79.1)	100.4 (96.4–104.4)	131.7 (122.8– 140.6)	157.1 (139.7–174. 6)	261.2 (182.8–339.7)
Zhanjiang	645	22.9 (21.1–24.9)	10.6 (9.0–12.3)	17.7 (16.5–18.9)	26.1 (24.8–27.5)	36.9 (34.4–39.4)	48.8 (42.7– 55.0)	60.7 (54.9–66.5)	91.5 (32.5–150.5)

* The frequency is too low for bootstrap to resample.

SUPPLEMENTARY TABLE S3. Burden of disease from lead exposure in Chinese population aged 6–59 years measured in 2000 and 2017/18.

Age group, years	HR	Weighted mortality, %	Adjusted weighted mortality, %	Population, million	Population of premature deaths	DALYs
6–11						
2009–2010						
Male	1.23	0.024	0.019	45.83	2,028	139,530
Female	1.23	0.015	0.012	38.71	1,097	75,453
Total	–	–	–	–	–	214,984
2017–2018						
Male	1.12	0.024	0.021	45.83	1,131	77,794
Female	1.11	0.015	0.014	38.71	564	38,785
Total	–	–	–	–	–	116,579
12–18						
2009–2010						
Male	1.22	0.036	0.030	65.74	4,257	265,231
Female	1.22	0.019	0.015	99.89	3,306	205,934
Total	–	–	–	–	–	471,166
2017–2018						
Male	1.11	0.036	0.033	65.74	2,436	151,745
Female	1.09	0.019	0.017	99.89	1,581	98,491
Total	–	–	–	–	–	250,236
19–39						
2009–2010						
Male	1.23	0.093	0.075	136.50	23,913	1,155,014
Female	1.23	0.038	0.030	218.83	15,492	748,246
Total	–	–	–	–	–	1,903,260
2017–2018						
Male	1.16	0.093	0.080	136.50	17,318	836,466
Female	1.11	0.038	0.034	218.83	8,196	395,878
Total	–	–	–	–	–	1,232,344
40–59						
2009–2010						
Male	1.26	0.450	0.358	198.83	183,229	5,093,771
Female	1.26	0.151	0.120	191.58	59,334	1,649,472
Total	–	–	–	–	–	6,743,243
2017–2018						
Male	1.18	0.450	0.381	198.83	136,697	3,800,183
Female	1.13	0.151	0.134	191.58	32,919	915,159
Total	–	–	–	–	–	4,715,342
60–79						
2009–2010						
Male	–	–	–	–	–	–
Female	–	–	–	–	–	–
Total	–	–	–	–	–	–

TABLE S3. (Continued)

Age group, years	HR	Weighted mortality, %	Adjusted weighted mortality, %	Population, million	Population of premature deaths	DALYs
2017–2018						
Male	1.17	2.929	2.493	78.27	341,216	2,661,485
Female	1.14	1.408	1.233	78.34	136,747	1,066,628
Total	–	–	–	–	–	3,728,114
Total						
2009–2010						
Male	–	–	–	–	–	6,653,547
Female	–	–	–	–	–	2,679,105
Total	–	–	–	–	–	9,332,652
2017–2018						
Male	–	–	–	–	–	7,615,225
Female	–	–	–	–	–	2,568,477
Total	–	–	–	–	–	10,183,702

Abbreviation: HR=hazard ratio; DALYs=disability-adjusted life years.

SUPPLEMENTARY TABLE S4. Burden of disease from lead exposure in Chinese population aged 3–5 years old measured in 2000 and 2017/18.

Year	No. of participants	Blood lead geometric mean, μg/L	Incidence of mild mental retardation (‰)	DALYs (Person-year/1,000 children)	DALYs (Person-year)
2000	46,612,176	78.1	13.87	357.4	16,659,509
2017–2018	45,202,983	16.9	0.33	9.0	408,780

Abbreviation: DALYs=disability-adjusted life years.

Preplanned Studies

Incidence and Risk Factors of the Upper-Limb Musculoskeletal Disorders Among Occupational Groups in Key Industries — China, 2018–2021

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Summary

What is already known about this topic?

The burden of illness and economic losses due to upper-limb work-related musculoskeletal disorders (UL-WMSDs) is high; thus, they have become a major global public health problem. At present, the epidemiological characteristics of UL-WMSDs in China's occupational population are still unknown.

What is added by this report?

The incidence of UL-WMSDs among key occupational groups in China is 22.5%, with distinct occupational characteristics.

What are the implications for public health practice?

This study has primarily determined the occurrence and potential risk factors of UL-WMSDs in key industries in China and provided data support for recommending prevention and control of the occurrence of such diseases in key industries in China, and in facilitating the addition into the China's List of Legal Occupational Diseases.

Upper limb work-related musculoskeletal disorders (UL-WMSDs) are the most common after lower back pain and have been included in the list of occupational diseases by the International Labor Organization (ILO). In recent years, WMSDs have been widespread among the Chinese occupational populations, leading to job replacement and long-term sick leave. It is difficult to add UL-WMSDs to China's List of Legal Occupational Diseases because data on the occurrence of UL-WMSDs and their relationship with specific works are lacking. Therefore, this study included a large sample to conduct an epidemiological investigation and research into the occurrence of UL-WMSDs in key industry populations in different regions of China. The results showed the standardized incidence of UL-WMSDs in crucial industries or occupational groups in China is 22.5%. The risk of UL-WMSDs changes with the length of service, type of work, work posture, work organization, and other factors. The results may provide data support for recommending the prevention and control of such diseases and their inclusion in China's List of Legal Occupational Diseases.

The research data included in this study were obtained from seven China regions (North, East, Central, South, Southwest, Northwest, and Northeast China), and included data from 21 industries or operations, such as automobile manufacturing, furniture manufacturing, and the footwear industry. In this study, we used a stratified cluster sampling method; the workers on duty were the study participants. The inclusion criteria for subjects were employed for more than a year. The exclusion criteria were as follows: patients with congenital spinal deformity and those with non-WMSDs due to trauma, infectious diseases, and malignant tumors. This study has been reviewed by the Medical Ethical Review Committee of the Occupational Health and Poison Control at the Chinese Center for Disease Control and Prevention.

To conduct this survey, experts used the Ergonomic Evaluation and Analysis System of WMSDs provided by the Department of Occupational Protection and Ergonomics of the National Institute of Occupational Health and Poison Control of the Chinese Center for Disease Control and Prevention was used to investigate the incidence of WMSDs and its influencing factors in participants from key industries or occupational groups in different regions of China. The system includes four other sub-systems: an electronic ergonomics survey and evaluation tool for remote operation site, a real-time data monitoring system, a data transmission network, and a background data terminal. This study's survey tool (the Chinese electronic version of the musculoskeletal disorders questionnaire) was one of the built-in questionnaires in the system, namely. This electronic questionnaire system was based on the Nordic Musculoskeletal Disorders Questionnaire (NMQ) and Dutch Musculoskeletal Questionnaire (DMQ) (*1–2*). After appropriate modification, it was shown to have good reliability and validity, and can be used for Chinese occupational populations. After the survey data were exported from the backend database, they were statistically processed using SPSS 20.0 statistical software (version 20.0, SPSS Inc, Chicago, IL, USA). Based on China's population composition data, the standardized incidence rate of upper-limb musculoskeletal disorders was calculated using the direct method. The single-factor analysis of WMSDs adopts the χ^2 test method, multivariate analysis was performed using an unconditional logistic regression model.

Till date, 72,029 valid questionnaires have been received. Table 1 shows that the standardized rate of UL-WMSDs in key industries or occupational groups in China was 22.5%, and the standardized rates differed significantly between different industries (P<0.05). The standardized incidence rates (ranked from the highest to the lowest) in the top five industries were animal husbandry (40.8%), biopharmaceutical product manufacturing (36.8%), civil aviation (32.5%), healthcare industry (31.5%), ferrous metal smelting and rolling processing industry (29.9%).

TABLE 1. Prevalence of upper-limb musculoskeletal disorders in key industries or occupational groups in China, 2018–2021 (*n*=72,029).

Industry/working group	Number	Upper-limb musculoskeletal disorders		
		n	p_i (%)	p' (%)
Total	72,029	18,193	25.3	22.5
Animal husbandry	246	62	25.2	40.8
Biopharmaceutical manufacturing	285	115	40.4	36.8
Civil aviation	1,356	420	31.0	32.5
Healthcare industry	6,961	2,520	36.2	31.5
Ferrous metal smelting and rolling	1,921	444	23.1	29.9
Cement, lime, and gypsum manufacturing	193	22	11.4	25.4
Nonferrous metal smelting and rolling processing industry	2,364	696	29.4	25.0
Computer, communication industry, and other electronic equipment manufacturing	8,910	2,229	25.0	23.3
Automobile manufacturing	21,598	5,730	26.5	22.0
Toy manufacturing	333	141	42.3	20.4
Automobile repair and maintenance	802	145	18.1	19.2
Footwear industry	7,123	1,844	25.9	18.2
Coal mining, and washing	3,461	804	23.2	17.3
Shipping and related device manufacturing	3,493	886	25.4	16.7
Railway transportation equipment manufacturing	965	186	19.3	16.7
Agriculture	243	52	21.4	16.5
Road transportation	1,317	228	17.3	16.1
Construction	1,476	206	14.0	15.2
Power, heat, gas, water production, and supply	591	82	13.9	13.5
Furniture manufacturing	8,241	1,371	16.6	12.0
Petrochemical industry	150	10	6.7	4.0
Chi-square test			1203.6	
P value			0	

Note: p_i: actual age-specific prevalence rate, p': standardized prevalence rate.

The influencing factors of UL-WMSDs were divided into individual, work type, and work organization factors. The univariate analysis results (Table 2) show that gender, age, length of service, educational level, smoking status, sports, and other individual-level factors were significantly associated with the occurrence of UL-WMSDs (P<0.05). The incidence of UL-WMSDs in women was higher than that in men. The risk of UL-WMSDs increased with the length of service and educational level. The risk of UL-WMSDs in smoking and physical exercise groups was significantly lower than in the control group. Maintaining the same posture at a high frequency, always making the same movement with the trunk, always pinching/grasping some objects/tools, wrist is in a bent posture for a prolonged time, and other factors such as work type correlated significantly with the occurrence of UL-WMSDs (P<0.05). Frequent overtime work, staff shortages, and doing the same job nearly every day are positively correlated with the occurrence of UL-WMSDs, and the difference is statistically significant (P<0.05).

TABLE 2. Univariate analysis of factors of upper-limb musculoskeletal disorders among occupational groups in key industries in China, 2018–2021.

Variable	Upper-limb musculoskeletal disorders			
	Number of workers	**Case**	**Percentage (%)**	***OR* (95% *CI*)**
Individual risk factors				
Gender				
Men	49,079	11,050	22.5	1
Women	22,950	7,143	31.1	1.555 (1.502–1.611)*
Age (years)				
<25	7,909	1,858	23.5	1
25–	29,582	7,495	25.3	1.105 (1.043–1.171)*
35–	19,768	5,269	26.7	1.184 (1.114–1.258)*
45–	11,385	2,857	25.1	1.091 (1.020–1.167)*
55–	3,385	714	21.1	0.871 (0.790–0.960)*
Length of service (years)				
<2	19,138	4,143	21.6	1
2–	14,549	3,617	24.9	1.198 (1.138–1.260)*
4–	9,179	2,332	25.4	1.233 (1.163–1.307)*
6–	6,790	1,781	26.2	1.287 (1.207–1.372)*
8–	22,373	6,320	28.2	1.425 (1.362–1.491)*
Educational level				
Junior high school	21,365	4,810	22.5	1
Senior high school	26,632	6,586	24.7	1.131 (1.084–1.180)*
University degree	14,365	3,776	26.3	1.227 (1.169–1.289)*
Graduate degree	9,667	3,021	31.3	1.564 (1.483–1.651)*
Body mass index (BMI)				
<18.5	6,681	1,725	25.8	1
18.5–	48,323	12,284	25.4	0.979 (0.924–1.038)
25–	17,025	4,184	24.6	0.936 (0.877–0.999)
Smoking				
No	43,743	11,600	26.5	1
Occasionally	13,034	2,800	21.5	0.758 (0.723–0.795)*
Frequently	15,252	3,793	24.9	0.917 (0.879–0.957)*

TABLE 2. (Continued)

Variable	Upper-limb musculoskeletal disorders			
	Number of workers	Case	Percentage (%)	*OR* (95% *CI*)
Physical exercise				
No	21,619	5,877	27.2	1
Occasionally	38,073	9,443	24.8	0.883 (0.851–0.918)*
Frequently	12,337	2,873	23.3	0.813 (0.772–0.856)*
Workplace risk factor				
Standing often at work				
No	11,038	2,816	25.5	1
Yes	60,991	15,377	25.2	0.984 (0.940–1.031)
Sitting often at work				
No	30,850	7,792	25.3	1
Yes	41,179	10,401	25.3	1 (0.967–1.035)
Squatting or kneeling often at work				
No	41,776	9,828	23.5	1
Yes	30,253	8,365	27.7	1.242 (1.201–1.285)*
Lifting heavy loads (more than 5 kg)				
No	25,091	5,764	23.0	1
Yes	46,938	12,429	26.5	1.208 (1.165–1.252)*
Lifting heavy loads (more than 20 kg)				
No	38,885	9,189	23.6	1
Yes	33,144	9,004	27.2	1.205 (1.165–1.247)*
Exerting great force on the upper limbs or hands				
No	11,908	2,186	18.4	1
Yes	60,121	16,007	26.6	1.614 (1.535–1.696)*
Use of vibration tools at work				
No	43,855	10,087	23.0	1
Yes	28,174	8,106	28.8	1.352 (1.307–1.399)*
Maintaining the same posture at a high frequency				
No	13,728	1,927	14.0	1
Yes	58,301	16,266	27.9	2.370 (2.251–2.495)*
Trunk posture				
Trunk straight	24,051	4,441	18.5	1
Bending slightly at the trunk	38,398	10,502	27.4	1.662 (1.598–1.729)*
Bending heavily at the trunk	9,580	3,250	33.9	2.267 (2.149–2.391)*
Always turning around with the trunk				
No	25,512	5,327	20.9	1
Yes	46,517	12,866	27.7	1.449 (1.397–1.502)*
Always bending and twisting with the trunk				
No	40,670	8,313	20.4	1
Yes	31,359	9,880	31.5	1.790 (1.731–1.852)*
Always making the same movement with the trunk				
No	28,488	5,031	17.7	1
Yes	43,541	13,162	30.2	2.020 (1.947–2.096)*

TABLE 2. (Continued)

Variable	Upper-limb musculoskeletal disorders			
	Number of workers	Case	Percentage (%)	*OR* (95% *CI*)
Always bending the wrist up and down				
No	25,344	4,431	17.5	1
Yes	46,685	13,762	29.5	1.973 (1.899–2.049)*
Wrist is in a bent posture for a prolonged time				
No	40,455	7,503	18.5	1
Yes	31,574	10,690	33.9	2.248 (2.172–2.326)*
Wrist is often placed on the edge of hard and angular objects				
No	45,945	9,733	21.2	1
Yes	26,084	8,460	32.4	1.786 (1.726–1.848)*
Always pinching/grasping some objects/tools				
No	16,396	2,643	16.1	1
Yes	55,633	15,550	28.0	2.019 (1.929–2.113)*
Working above the shoulder level				
No	59,211	14,804	25.0	1
Yes	12,818	3,389	26.4	1.078 (1.032–1.126)*
Work organization factors				
Often working overtime	34,078	7,492	22.0	1
No	37,951	10,701	28.2	1.394 (1.347–1.442)*
Yes				
Abundant resting time				
No	38,303	12,579	32.8	1
Yes	33,726	5,614	16.6	0.408 (0.394–0.423)*
Deciding on an independent rest time				
No	57,741	15,346	26.6	1
Yes	14,288	2,847	19.9	0.687 (0.657–0.719)*
Staff shortage				
No	38,967	8,003	20.5	1
Yes	33,062	10,190	30.8	1.724 (1.666–1.783)*
Doing the same job nearly every day				
No	8,579	1,415	16.5	1
Yes	63,450	16,778	26.4	1.820 (1.715–1.932)*
Job rotation				
No	34,642	9,457	27.3	1
Yes	37,387	8,736	23.4	0.812 (0.785–0.840)*

Abbreviation: COR=Crude odds ratio; *CI*=confidence interval.
* $P<0.05$.

Abundant resting time, deciding on an independent rest time and job rotation are the protective factor of UL-WMSDs. The results of the multiple logistic regression showed that the influencing factors of UL-WMSDs were maintaining the same postures at a high frequency, use of vibration tools at work, working above shoulder level, length of service (in years), exerting great force on the upper limbs or hands, lifting of heavy loads (more than 20 kg) and job rotation, according to the odds ratio (*OR*). The last item, job rotation, is a protective factor (Table 3).

TABLE 3. Multivariate logistic regression model predicting the risk factors of upper-limb musculoskeletal disorders among occupational groups in key industries in China, 2018–2021.

Variable	Coefficient	Wald χ^2	a*OR*	95% *CI*	*P* value
Maintaining the same posture at a high frequency	0.270	418.798	1.310	1.277–1.345	0.000
Use of vibration tools at work	0.148	53.134	1.160	1.114–1.207	0.000
Working above the shoulder level	0.076	10.515	1.079	1.030–1.130	0.001
Length of service	0.071	117.284	1.073	1.060–1.087	0.000
Exerting great force on the upper limbs or hands	0.066	4.675	1.068	1.006–1.134	0.031
Lifting heavy loads (more than 20 kg)	0.056	7.430	1.058	1.016–1.102	0.006
Job rotation	−0.105	17.066	0.900	0.857–0.946	0.000

Note: North China: Beijing, Tianjin; East China: Shanghai, Jiangsu, Zhejiang, Fujian, Shandong, Jiangxi; Central China: Hubei; South China: Guangdong; Southwest China: Sichuan, Chongqing, Guizhou, Yunnan, Northwest China: Shanxi, Ningxia; Northeast China: Liaoning.
Abbreviation: a*OR*=adjusted odds ratio; *CI*=confidence interval.

DISCUSSION

This study was an occupational health risk assessment investigation established by the Chinese Center for Disease Control and Prevention from January 2018 to December 2023. It is the largest population survey on WMSDs in China so far. It aimed to include a large sample to conduct an epidemiological survey and research into the occurrence of UL-WMSDs in critical industries or occupational groups in different regions of China. This aim was to determine the occurrence and distribution characteristics of WMSDs in key sectors in China. Furthermore, we explored the epidemic rule and identified the influencing factors of WMSDs.

Moreover, our study provided big data to support the inclusion of WMSDs in crucial industries in China's List of Legal Occupational Diseases. The study published relevant reports in *China CDC Weekly* in 2020 and 2021, respectively (*3*–*4*). The data reported in this paper were those collected until 2021. Hence, they only described the occurrence of UL-WMSDs and analyzed the relevant influencing factors.

The survey results show that the standardized rate of UL-WMSDs in key industries or occupational groups in China was 22.5%. A survey (*5*) on musculoskeletal diseases related to work during the second industrial revolution in the 21st century in Europe shows a prevalence of upper limb musculoskeletal diseases between 4% and 26%, similar to our survey results. The survey found a significantly different incidence of WMSDs among different industries and showed that WMSDs were related to the work type and work organization factors, with prominent occupational characteristics. This study found that animal husbandry and biopharmaceutical product manufacturing had the highest upper limb musculoskeletal diseases among the industries, with an incidence of more than 35%. The survey found that the operation mode in the above two industries occurred during the assembly line operation, and workers' hands, wrists, and elbows needed quick and repetitive activity. At the end of each operation cycle, there was little or very short rest time. Research shows that (*6*) prolonged, repeated exertion may lead to local muscle fatigue and, if left unrecovered for a long time, causes musculoskeletal disorders easily. The risk factors of UL-WMSDs can be divided into individual-level, work type, and work organization factors. The results of this study showed that, in terms of individual-level factors, gender, age, length of service, educational level, smoking status, and sports were all related to the occurrence of UL-WMSDs (P<0.05). Of these, length of service remained a significant variable in univariate and multivariate logistic regression analyses. In terms of the work type factors, repetitive work in the same posture at a high frequency, use of vibration tools at work, working above shoulder level, exerting great force on the upper limbs or hands, lifting of heavy loads (more than 20 kg) are all risk factors of UL-WMSDs. A large number of scholarly articles have confirmed the above results. A population-based case-control study found (*7*) a dose-response relationship between the cumulative duration of work with highly elevated arms (positioned above shoulder level) and ruptures of the supraspinatus tendon.

The results of this study show that the risk of UL-WMSDs will increase when handling objects that weigh over 20 kg. Some studies have also confirmed (*8*) that the occurrence of UL-WMSDs is positively correlated with the weight of the object being carried (load mass). This may be related to manual handling without the use of auxiliary tools. The heavier the load of moving objects, the harder it is for workers to carry them, resulting in increased hand pain. In terms of work organization factors, the results of this study show that job rotation is a protective factor of UL-WMSDs. Previous studies also support this view. A study showed that (*9*) the implementation of job rotation can help increase the variability of muscle activities, particularly in upper extreme muscles and can reduce the burden of occupational injury.

Although this study is a population survey with a large sample used to clarify the epidemiological characteristics and risk factors of UL-WMSDs in critical sectors or occupational groups in China, the following limitations still exist. First, the current study's design makes it difficult to determine the temporal relationship between the antecedents and consequences and infer the causal relationship between the risk factors and the occurrence of UL-WMSDs. Second, this study used questionnaires to obtain information about the respondents' illnesses in the past year. Since it is easy to forget the past, report and recall bias could have occurred.

In conclusion, the standardized incidence of UL-WMSDs in key industries or occupational groups in China is 22.5%. UL-WMSDs have recognized occupation-related characteristics, and their risk factors change with the length of service, type of work, work posture, work organization, and other factors. Given this, it is suggested to continue to carry out special epidemiological investigation and research on a large sample of the occupational population in key industries nationwideand establish a database of factors related to musculoskeletal disorders among occupational population in key industries in China, to provide extensive data support for listing UL-WMSDs to relevant regions in China's List of Legal Occupational Diseases.

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Preplanned Studies

Characteristics and Containment of 74 Imported COVID-19 Outbreaks: Experiences, Lessons, and Implications — China, 2020–2021

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Summary

What is already known about this topic?

After the initial coronavirus disease 2019 (COVID-19) outbreak in Wuhan, China, the outbreaks during the dynamic-zero policy period in the mainland of China have not been systematically documented.

What is added by this report?

We summarized the characteristics of 74 imported COVID-19 outbreaks between March 19, 2020 and December 31, 2021. All outbreaks of early severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) variants were successfully contained with the aid of nucleic acid testing, modern communication technologies, and non-pharmacological interventions.

What are the implications for public health practice?

These findings provide us with confidence for the containment of future emerging infectious diseases alike at early stages to prevent pandemics or to win time to gain experience, develop vaccines and drugs, vaccinate people, and wait for the possible lessening of the virus' pathogenicity.

After the successful containment of the initial coronavirus disease 2019 (COVID-19) outbreak in Wuhan, China adopted a dynamic-zero policy in March 2020 aimed at eradicating all imported outbreaks. In this report, we provided a comprehensive documentation and analyses of all the imported outbreaks before 2022. Data on daily COVID-19 infections were retrieved from the website of the National Health Commission of China. Results of epidemiological investigations of the outbreaks were retrieved from 1,504 publications by local governments or mainstream social media. Seventy-four outbreaks were identified consisting of 10,082 symptomatic cases and all were successfully contained. Characteristics of the outbreaks were summarized including source of the first case(s), time, place, scale, and duration. These data were then analyzed to identify potential problems and plan for future emerging infectious diseases alike. China's experience in successfully containing 74 consecutive outbreaks provides important evidence that COVID-19 or newly emerging infectious diseases alike can be contained at their early stage to prevent the occurrence of pandemics, or at least gain experiences and win time for the development of vaccines and drugs.

Data on daily number of imported cases, domestic cases, symptomatic domestic cases, and close contacts from March 19, 2020 to December 31, 2021 were retrieved from the official reports of Daily Briefing on Novel Coronavirus Cases. Our analyses of outbreaks only included symptomatic domestic cases from all the outbreaks; cases found in quarantined inbound cross-border travelers were excluded. For each symptomatic case, epidemiological investigations were traced via official reports from local governments. A total of 1,504 reports were retrieved and scrutinized. The definitions for outbreaks are presented in Supplementary Figure S1, available in https://weekly.chinacdc.cn/.

The national daily numbers of cases, which included data on location and magnitude of these outbreaks, were described chronologically and geographically. Characteristics of the outbreaks were compared among 3 study periods divided according to the announcement dates of the 7th and 8th editions of the Protocol on Prevention and Control of COVID-19 and the source of the first case (*1–2*). All statistical analyses were performed by using R software version 3.6.2. A full description of methods is in Supplementary Materials, available in https://weekly.chinacdc.cn/.

Overall, the study identified 74 outbreaks with a total of 10,082 symptomatic cases between March 19, 2020 and December 31, 2021 (Figure 1). The median

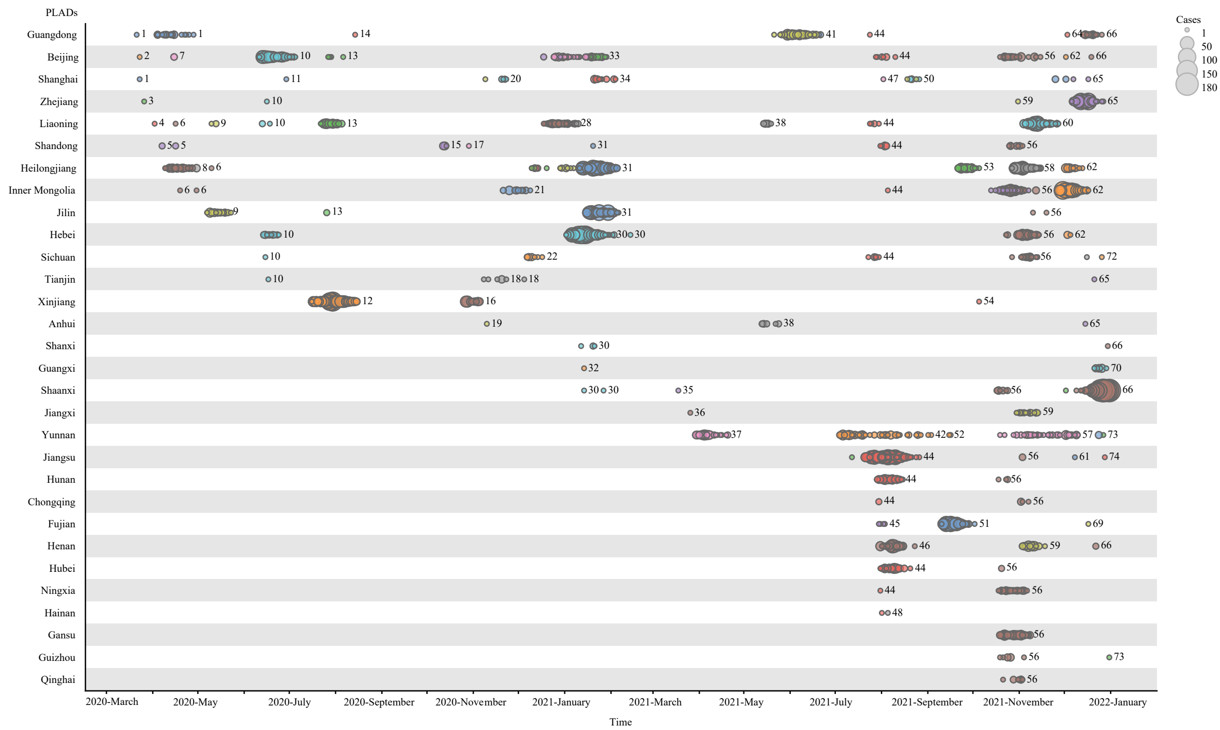

FIGURE 1. Occurrence and size of outbreaks by region and time in the mainland of China between March 19, 2020 and December 31, 2021.
Note: The number next to each outbreak refers to the unique ID number assigned for each outbreak in Supplementary Table S1 (available in http://weekly.chinacdc.cn). Cases with the same numbers belong to the same outbreak.
Abbreviation: PLADs=provincial-level administrative divisions.

number of cases in an outbreak was 10, ranging from 1 to 1,506. Out of the 74 outbreaks, 43 (58.1%) were detected via proactive surveillance, and 57 (77.0%) were contained at their origin within the provincial-level administrative divisions (PLADs) (Table 1). The outbreaks on average lasted for 10 days, ranging from 1 to 62 days. The ratio of daily number of close contacts over daily number of cases, an approximate indicator of people quarantined per case, was 60, ranging from 4 to 2,830. Detailed characteristics for each outbreak were presented in Supplementary Table S1 available in https://weekly.chinacdc.cn/.

Due to heavy international air traffic, it was anticipated that the earliest imported outbreaks occurred in Guangdong, Beijing, Shanghai, and PLADs near them. These outbreaks were generally small and quickly contained. However, as outbreaks continued to spread, an increasing trend emerged including a higher frequency of outbreaks and higher number of PLADs involved (Figure 1). By December 31, 2021, all PLADs in the mainland of China had been involved in at least one outbreak except Xizang (Tibet). No seasonal trends were observed.

Geographically, PLADs including Beijing, Shanghai, Guangdong, and their neighboring regions had the highest frequency of outbreak attacks (Supplementary Table S2, available in https://weekly.chinacdc.cn/). Five PLADs with the highest number of outbreaks included Beijing (11), Shanghai (10), Liaoning (10), Guangdong (9), and Heilongjiang (9). The 5 regions with the largest number of cases accumulated were Shaanxi (1,494 cases), Heilongjiang (1,145 cases), Hebei (1,103 cases), Xinjiang (906 cases) and Jiangsu (826 cases), totally accounting for 54.3% (5,474/10,082) of all cases.

Chronologically, the daily number of imported cases that were diagnosed during quarantine and did not cause community outbreaks considerably fluctuated during the study period. Although there was no clear increasing trend with time, there was a slight elevation after June 2021 (Supplementary Figure S2, available in https://weekly.chinacdc.cn/). The daily number of symptomatic domestic cases and close contacts showed a similar pattern.

In addition, the average size and duration of outbreaks and the average number of PLADs involved in each outbreak are shown in Table 1. Although the number of outbreaks and that of cases accumulated

TABLE 1. Characteristics of the 74 outbreaks according to the three periods of study.

Study period	Length of period (days)	Number of outbreaks (*n*, %)	Number of outbreaks involving ≥2 PLADs (*n*, %)	Number of outbreaks detected via proactive surveillance (*n*, %)	Average number of cases per outbreak (median, range)	Total number of cases (*n*, %)	Duration of outbreaks (days) (median, range)	Ratio of daily number of close contacts over that of cases (median, range)
Period 1: 2020/3/19–2020/9/30	196	14 (18.9)	5 (35.7)	2 (14.3)	7 (1, 827)	1,457 (14.5)	11.5 (1, 39)	29 (4, 2,807)
Period 2: 2020/10/1–2021/5/31	242	25 (33.8)	4 (16.0)	14 (56.0)	13 (1, 1,055)	2,632 (26.1)	12.0 (1, 44)	116 (8, 2,830)
Period 3: 2021/6/1–2021/12/31	213	35 (47.3)	8 (22.9)	27 (77.1)	6 (1, 1,506)	5,993 (59.4)	7.0 (1, 62)	68 (8, 1,737)
*P**	–	–	0.386	*P*<0.001	0.805	–	0.668	*P*<0.001
P for trend	–	–	0.610	0.030	0.392	–	0.717	0.300
Entire period	650	74 (100.0)	17 (23.0)	43 (58.1)	10 (1, 1,506)	10,082 (100.0)	10.0 (1, 62)	60 (4, 2,830)

Abbreviation: PLADs=provincial-level administrative divisions.
* *P* value for comparisons among the three study periods. Kruskal-Wallis test was used for comparisons in skewed continuous variables, Fisher's exact Chi-square test for categorical variables, and linear regression and Cochran-Armitage trend test for assessing trend for the two types of variables, respectively.

TABLE 2. Characteristics of the 74 outbreaks according to the source of the first case(s).

Source of the first case (s)	Number of outbreaks (*n*, %)	Number of outbreaks involving ≥2 PLADs (*n*, %)	Number of outbreaks detected via proactive surveillance (*n*, %)	Average number of cases per outbreak (median, range)	Total number of cases (*n*, %)	Duration of outbreaks (days) (median, range)
First frontier: cross border entrances	35 (47.3)	9 (25.7)	23 (65.7)	8 (1, 1,056)	5,654 (56.1)	8 (1, 62)
Land borders	15 (20.3)	3 (20.0)	11 (73.3)	20 (1, 636)	1,702 (16.9)	11 (1, 62)
Airports	14 (18.9)	5 (35.7)	8 (57.1)	5 (1, 1,506)	3,551 (35.2)	5 (1, 44)
Ports	6 (8.1)	1 (16.7)	4 (66.7)	19 (1, 308)	401 (4.0)	8 (1, 24)
Second frontier: Quarantine related	23 (31.1)	1 (4.3)	15 (65.2)	2 (1, 468)	805 (8.0)	1 (1, 32)
Possibly via quarantined inbound visitors	13 (17.6)	1 (7.7)	7 (53.8)	3 (1, 468)	595 (5.9)	1 (1, 32)
Designated care hospitals	5 (6.8)	0 (0.0)	4 (80.0)	2 (1, 167)	193 (1.9)	7 (1, 24)
Quarantine places	5 (6.8)	0 (0.0)	4 (80.0)	1 (1, 13)	17 (0.2)	1 (1, 11)
Local community (eg, markets & malls)	16 (21.6)	7 (43.8)	5 (31.3)	92 (1, 1,055)	3,623 (35.9)	21 (1, 39)
Possibly via cold chain	5 (6.8)	2 (40.0)	2 (40.0)	99 (10, 826)	1,333 (13.2)	25 (16, 31)
Uncertain	11 (14.9)	5 (45.5)	3 (27.3)	89 (1, 1,055)	2,290 (22.7)	20 (1, 39)
*P**	–	0.008	0.055	<0.001	–	*P*<0.001
All	74 (100.0)	17 (23.0)	43 (58.1)	10 (1, 1,056)	10,082 (100.0)	10 (1,62)

Abbreviations: PLADs=provincial-level administrative divisions.
* *P* value for comparisons among the three categories of sources of first cases. Kruskal-Wallis test was used for comparisons in skewed continuous variables, Fisher's exact Chi-square test for categorical variables.

were chronologically increasing during the 3 periods of study, the last period had the highest proportion of outbreaks detected via active surveillance (77.1%), the smallest number of patients per outbreak (6 cases), shortest duration of outbreaks (7 days), the largest proportion of outbreaks involving only one PLAD (77.1%), and an average number of 68 close contacts quarantined per patient. These findings showed that the number of outbreaks and thus prevention and control intensity increased over time, but the effect and efficiency of response actions also increased. As a result, the situation remained largely controllable.

Regarding the source of the first case(s) or the origin of an outbreak, 35 (47.3%) of the 74 outbreaks occurred at areas labeled as the first frontier, i.e., land borders, airports, and ports (Table 2). These outbreaks contributed 5,654 (56.1%) cases to the total number of cases from the 74 outbreaks (Supplementary Figure S3 available in https://weekly.chinacdc.cn/).

Surprisingly, 23 (31.1%) outbreaks occurred at the second frontier, including those at designated care hospitals, quarantine places, and among inbound travelers whose incubation time might be longer than the quarantine time or who got infected during quarantine (Table 2). However, these outbreaks were relatively small in size, quickly contained, and accounted for only 8.0% of the total number of symptomatic cases from the 74 outbreaks.

Lastly, 16 (21.6%) outbreaks were identified in communities such as shopping malls and food markets. Some were possibly caused via cold-chain logistics, while the rest had no clearly identifiable source of infection (Table 2). These outbreaks were most difficult to control when detected as well as difficult to detect once occurred, as only 31.3% (5 out of 16) were detected by proactive surveillance. As a result, they were most likely (43.8%) to involve 2 or more PLADs, resulting in more cases and longer durations per outbreak.

DISCUSSION

Under the dynamic-zero policy after the Wuhan outbreak, a total of 74 imported outbreaks were observed and successfully contained in the mainland of China before 2022. The success made in China, which was also demonstrated in economically less developed PLADs, proved that outbreaks of such highly infectious diseases could be rapidly contained by non-pharmacological interventions with the aid of nucleic acid testing and modern communication technologies.

The first and most important lesson is to put prevention first. Second, effective surveillance and early detection of domestic cases are keys to controlling outbreaks. On the technical front, prevention and control tactics are nothing more than the three conventional methods in the control of infectious diseases, namely controlling infection sources, blocking transmission routes, and protecting susceptible populations (*3*–*4*).

For controlling infection sources, quarantining inbound cross-border travelers is the first step (*5*). Due to limited quarantine facilities, international traveling also needs to be reduced. Routine nucleic acid testing in high-risk groups and general populations when deemed necessary is crucial for identifying new domestic cases. For blocking transmission routes, fast epidemiological investigations are possible with the aid of modern technologies and are important for the quick isolation of close contacts (*4*). For protecting susceptible populations, vaccination plays an important role but is far from enough due to fast waning of the protective effect of vaccines (*6*). When a community outbreak occurred, some restrictions on people's movability could be implemented on top of all the above measures. In addition, social distancing and mask-wearing are always part of the policy (*4*).

Another important lesson is to keep finding and closing the loopholes in current measures, which have been embodied in the 7th and 8th revisions of Chinese national guides for the prevention and control of COVID-19 (*1*–*2*). For instance, imported frozen goods from key areas were put under surveillance after outbreaks potentially related to cold chain logistics occurred in June 2020 (*7*). Another example is the complete separation of international and domestic passengers within the airport after a large outbreak that started in Nanjing Airport in July 2021 (*8*). The increasing number of proactively detected outbreaks over time reflected improvements in surveillance. The effects of these experiences were further confirmed in the recent large Omicron outbreak in Shanghai which caused over 626,000 cases but was eventually contained (*9*).

The limitations of this study were discussed in Supplementary Materials.

Although the strategy was overall effective, outbreaks and PLADs involved both increased over time. This may be partly because of 1) the increasing transmissibility of the new variants; 2) the efforts to resume work and life orders, which inevitably increased people's movability, cross-border traveling, and imported goods, and caused shortening of quarantine time; and 3) the "pandemic fatigue" since people are becoming tired of the sustained pressure of the pandemic. After all, the strategy has successfully won time for China to gain experiences, develop vaccines and drugs, vaccinate people, and wait for the possible lessening of pathogenicity of the virus so that a massive number of hospitalizations and deaths from COVID-19 can be avoided, even if large outbreaks inevitably occur in the future.

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SUPPLEMENTARY MATERIAL

Full Description of Methods and Definitions

Data collection and statistical analysis: Daily reports on coronavirus disease 2019 (COVID-19) infections from March 19, 2020 to December 31, 2021 were retrieved from the official website of Daily Briefing on Novel Coronavirus Cases of the National Health Commission of China, the most authoritative source of COVID-19 data in the country. Data reported on this website were collected through the Direct Reporting System for Infectious Diseases that covers the entire country (*1*). We extracted data on the daily number of imported cases, symptomatic domestic cases, all domestic cases either symptomatic or asymptomatic, and close contacts of both imported and domestic cases. Imported cases were the inbound travelers whose nucleic acid testing was positive at entrance or during quarantine, being either symptomatic or asymptomatic. Thirty cases related to the initial Wuhan outbreak at the beginning of our study period were excluded.

Our detailed analyses of outbreaks included all the 10,082 symptomatic domestic cases from all the outbreaks; cases found in quarantined inbound cross-border travelers were excluded. Those who stayed asymptomatic throughout the entire course of disease were not included in the detailed analyses because the numbers of such cases were often inconsistent between reports from the National Health Commission and local governments. Furthermore, the reporting of epidemiological investigations on asymptomatic cases at local levels was often incomprehensive. For each of the domestic symptomatic cases, details of epidemiological investigations were traced and retrieved mostly from official reports and publications by local governments and, for a small fraction (896/10,082) supplemented by reports from other mainstream media. In total, 1,504 reports were retrieved and scanned to obtain relevant data.

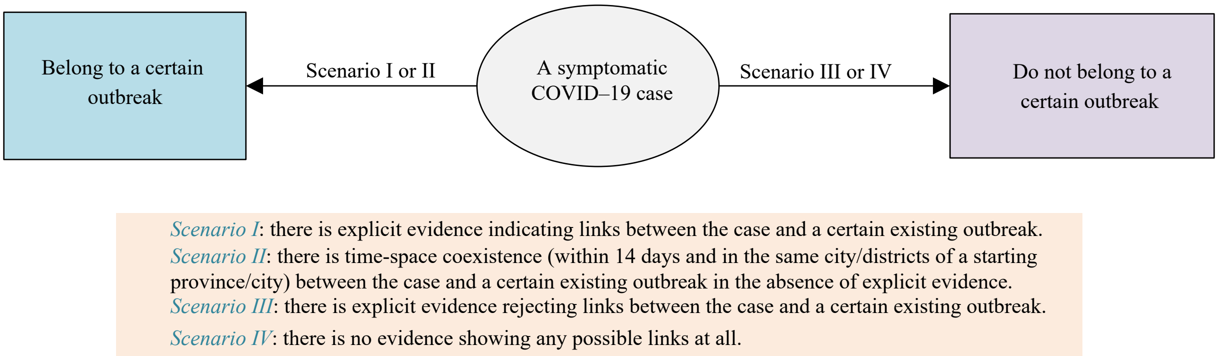
The national daily numbers of inbound cases, symptomatic domestic cases, all domestic cases, and close contacts were described chronologically in a line chart. The place and size of outbreaks were described chronologically in a bubble plot. The place and size of outbreaks were also demonstrated geographically on the map of the mainland of China. The characteristics of the outbreaks were summarized in tables according to the source of outbreak and the three periods of study which were defined based on the announcement dates of the 7th and 8th editions of Protocol on Prevention and Control of COVID-19 (*2*–*3*). All statistical analyses were performed using R software version 3.6.2. Kruskal-Wallis test was used for comparisons in skewed continuous variables, Fisher's exact Chi-square test for categorical variables, linear regression, and Cochran-Armitage trend test for assessing trend for the two types of variables, respectively. Two-tailed testing was used and P value ≤0.05 was considered statistically significant for all tests.

Definitions: An outbreak is defined as a cluster of domestic symptomatic COVID-19 cases that occurred within a period of time and could be linked to the same first case regardless of where they occurred in the country, although the majority of cases of an outbreak often occurred in the same city or nearby. Those who stayed asymptomatic throughout the entire course of disease were not included in the detailed analyses because the numbers of such cases were often inconsistent between reports of the National Health Commission and local governments. Furthermore, the reporting of epidemiological investigations on asymptomatic cases at local levels was often incomprehensive.

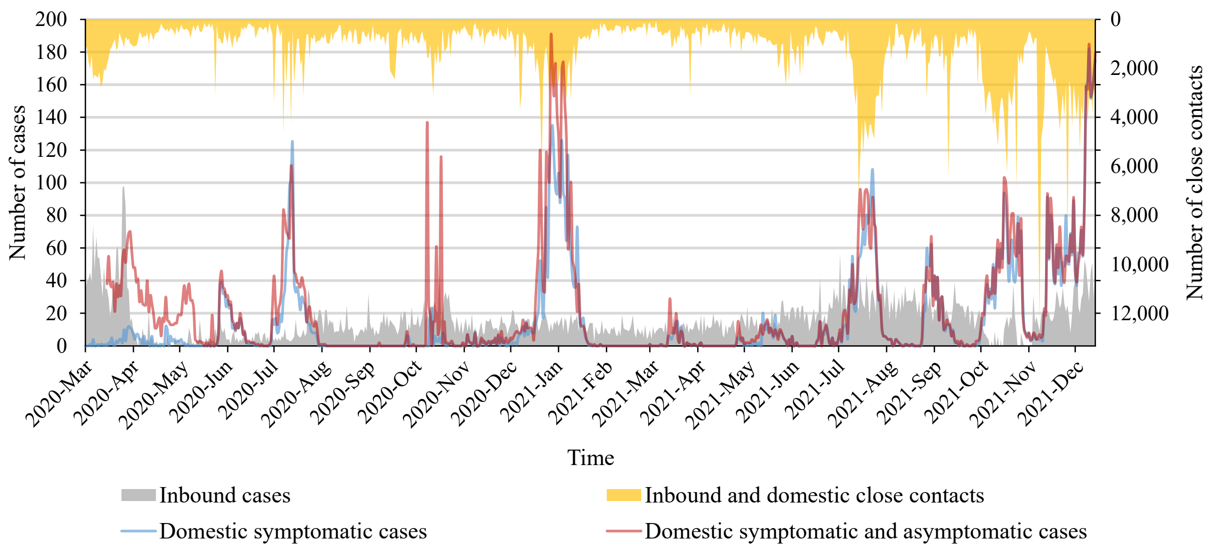
The first case of an outbreak was the one that occurred earliest in the outbreak, which was epidemiologically traced via the index case. The index case was the one that was first discovered in an outbreak and judged according to official epidemiological investigations unlinked to any other outbreaks.

The rules for judging whether a case belonged to a certain outbreak are presented in a flowchart in the supplementary materials (Supplementary Figure S1). The conclusion was made based on the 1,504 reports first by two researchers (CW& BLL) and then double-checked by a third one (FXL). Disagreement was in less than 1% of the cases. Despite excellent epidemiological investigations, 8.96% (896/10,082) of cases from the outbreaks were still uncertain in their links and were then included in major outbreaks nearest in place and time. In addition, two or more independent outbreaks could partly overlap in time and place. Although uncommon, cases of unidentified links in such overlapping outbreaks have not been found.

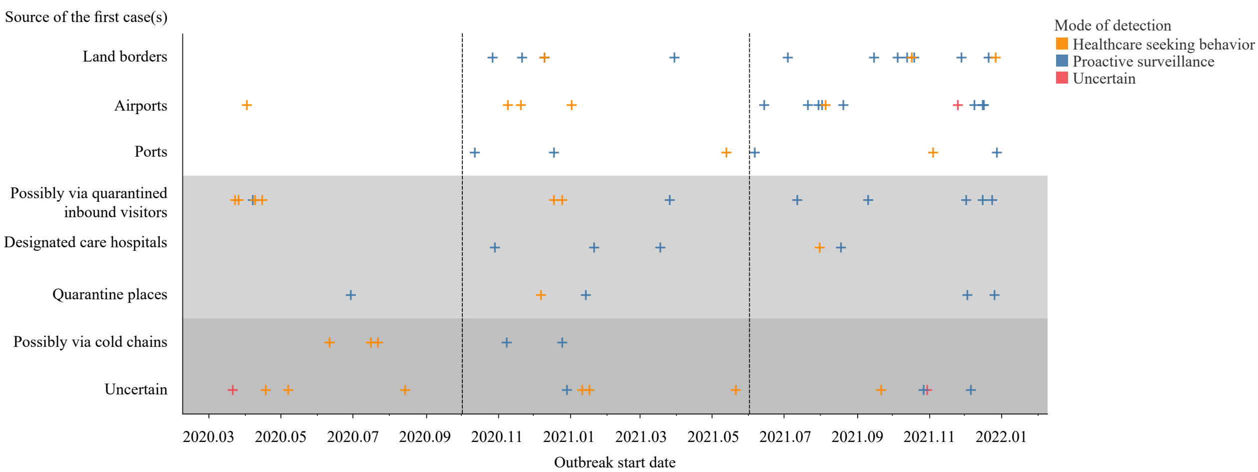
For each outbreak, the following information was recorded or estimated: 1) the place where it started; 2) the date when it was discovered; 3) the number of cases involved; 4) the number of PLADs involved; 5) duration or how long it lasted; 6) detection mode of the index case or how an outbreak was initially discovered; 7) the source of the outbreak or where or how the first case was infected.



SUPPLEMENTARY FIGURE S1. The rules for judging whether a symptomatic case belonged to a certain outbreak.



SUPPLEMENTARY FIGURE S2. Daily number of inbound cases, domestic symptomatic cases, domestic symptomatic and asymptomatic cases, and both inbound and domestic close contacts over time in the mainland of China between March 19, 2020 and December 31, 2021.



SUPPLEMENTARY FIGURE S3. The detection mode in each outbreak stratified by the source of the first case.

The duration of an outbreak was approximated by the time period from the date the index case was detected to the detection date of the last case, after which no more cases could be identified linked to the outbreak. In theory, the first case should be used but its detection date was normally unavailable. The mode of detection was classified into three categories: 1) patients' healthcare seeking behavior (as people were required to undergo nucleic acid testing for SARS-COV-2 before visiting healthcare facilities regardless of whether or not they had COVID-19 related symptoms); 2) proactive surveillance, mostly through mandated nucleic acid testing among high-risk populations such as those working at quarantine places, designated treatment hospitals, airports and customs; and 3) uncertain. The source of outbreak was the place or route most likely via which the first case of an outbreak got infected, including the entire environments of these places and people working there. The source of outbreak was classified into 3 categories and 8 sub-categories according to the results of official epidemiological investigations: border entrances (land borders, airports and ports); quarantine and care places (possibly via quarantined inbound travelers who might have had an incubation time longer than the quarantine time or caught infection during quarantine, designated care hospitals and quarantine facilities); and uncertain (possibly via cold chain and truly uncertain).

Limitations

The study has some limitations. First, a small fraction (about 8.9%) of data for epidemiological investigations was based on non-government-official sources. But we considered information from these sources reliable because the Chinese government has been cracking down on rumors or fake data regarding the COVID-19 epidemic with legal actions. Second, those who were asymptomatic throughout the entire study period were not included as their detailed individual data were generally not publicly reported. However, exclusion of these cases would affect or underrate only the estimates of the size and duration of outbreaks. Given that the proportion of asymptomatic infections is generally low in Asian regions (6.91%) before the Omicron variant period, we think the bias is unlikely to be large if any (*4*). Third, there may be difficulties in generalizing China's experiences to populations of different cultures and social systems.

SUPPLEMENTARY TABLE S1. Characteristics for all the imported COVID-19 outbreaks in China from March 19, 2020 to December 31, 2021.

ID	Starting place	Number of PLADs involved	Starting date	Duration (days)	Number of cases	Source of the first cases	Detection mode
1	Guangdong	2	2020/3/21	39	32	Uncertain	Uncertain
2	Beijing	1	2020/3/23	1	1	Possibly via quarantined inbound visitors	Passive self-monitoring
3	Zhejiang	1	2020/3/26	1	1	Possibly via quarantined inbound visitors	Passive self-monitoring
4	Liaoning	1	2020/4/2	1	1	Airports	Passive self-monitoring
5	Shandong	1	2020/4/7	10	4	Possibly via quarantined inbound visitors	Active organized surveillance
6	Heilongjiang	3	2020/4/9	32	70	Possibly via quarantined inbound visitors	Passive self-monitoring
7	Beijing	1	2020/4/15	1	3	Possibly via quarantined inbound visitors	Passive self-monitoring
8	Heilongjiang	1	2020/4/18	13	10	Land borders	Passive self-monitoring
9	Jilin	2	2020/5/7	17	45	Uncertain	Passive self-monitoring
10	Beijing	6	2020/6/11	25	362	Possibly via cold chain	Passive self-monitoring
11	Shanghai	1	2020/6/29	1	1	Quarantine places	Active organized surveillance
12	Xinjiang	1	2020/7/16	31	827	Possibly via cold chain	Passive self-monitoring
13	Liaoning	3	2020/7/22	16	99	Possibly via cold chain	Passive self-monitoring
14	Guangdong	1	2020/8/14	1	1	Uncertain	Passive self-monitoring
15	Shandong	1	2020/10/12	3	13	Ports	Active organized surveillance
16	Xinjiang	1	2020/10/27	10	78	Land borders	Active organized surveillance
17	Shandong	1	2020/10/29	1	1	Designated care hospitals	Active organized surveillance
18	Tianjin	1	2020/11/8	28	10	Possibly via cold chain	Active organized surveillance

TABLE S1. (Continued)

ID	Starting place	Number of PLADs involved	Starting date	Duration (days)	Number of cases	Source of the first cases	Detection mode
19	Shanghai	2	2020/11/9	2	2	Airports	Passive self-monitoring
20	Shanghai	1	2020/11/20	4	6	Airports	Passive self-monitoring
21	Inner Mongolia	1	2020/11/21	19	28	Land borders	Active organized surveillance
22	Sichuan	1	2020/12/7	11	13	Quarantine places	Passive self-monitoring
23	Heilongjiang	1	2020/12/10	11	3	Land borders	Active organized surveillance
24	Heilongjiang	1	2020/12/10	5	8	Land borders	Passive self-monitoring
25	Beijing	1	2020/12/18	12	3	Possibly via quarantined inbound visitors	Passive self-monitoring
26	Liaoning	1	2020/12/18	19	51	Ports	Active organized surveillance
27	Beijing	1	2020/12/25	23	35	Possibly via cold chain	Active organized surveillance
28	Liaoning	1	2020/12/25	17	36	Possibly via quarantined inbound visitors	Passive self-monitoring
29	Heilongjiang	1	2020/12/29	10	10	Uncertain	Active organized surveillance
30	Hebei	3	2021/1/2	44	948	Airports	Passive self-monitoring
31	Heilongjiang	3	2021/1/11	27	1,055	Uncertain	Passive self-monitoring
32	Guangxi	1	2021/1/14	1	1	Quarantine places	Active organized surveillance
33	Beijing	1	2021/1/17	13	31	Uncertain	Passive self-monitoring
34	Shanghai	1	2021/1/21	15	22	Designated care hospitals	Active organized surveillance
35	Shaanxi	1	2021/3/18	1	1	Designated care hospitals	Active organized surveillance
36	Jiangxi	1	2021/3/26	1	1	Possibly via quarantined inbound visitors	Active organized surveillance
37	Yunnan	1	2021/3/30	22	93	Land borders	Active organized surveillance
38	Anhui	2	2021/5/13	12	24	Ports	Passive self-monitoring
39	Guangdong	1	2021/5/21	29	159	Uncertain	Passive self-monitoring
40	Guangdong	1	2021/6/6	2	4	Ports	Active organized surveillance
41	Guangdong	1	2021/6/14	8	7	Airports	Active organized surveillance
42	Yunnan	1	2021/7/4	62	125	Land borders	Active organized surveillance
43	Jiangsu	1	2021/7/12	1	1	Possibly via quarantined inbound visitors	Active organized surveillance
44	Jiangsu	12	2021/7/21	37	1,060	Airports	Active organized surveillance
45	Fujian	1	2021/7/30	5	4	Airports	Active organized surveillance
46	Henan	1	2021/7/31	24	167	Designated care hospitals	Passive self-monitoring
47	Shanghai	1	2021/8/2	1	1	Airports	Active organized surveillance
48	Hainan	1	2021/8/5	1	1	Airports	Passive self-monitoring
49	Shanghai	1	2021/8/18	7	2	Designated care hospitals	Active organized surveillance
50	Shanghai	1	2021/8/20	7	7	Airports	Active organized surveillance
51	Fujian	1	2021/9/10	23	468	Possibly via quarantined inbound visitors	Active organized surveillance
52	Yunnan	1	2021/9/15	2	2	Land borders	Active organized surveillance
53	Heilongjiang	1	2021/9/21	15	89	Uncertain	Passive self-monitoring
54	Xinjiang	1	2021/10/5	1	1	Land borders	Active organized surveillance

TABLE S1. (Continued)

ID	Starting place	Number of PLADs involved	Starting date	Duration (days)	Number of cases	Source of the first cases	Detection mode
55	Inner Mongolia	1	2021/10/13	26	20	Land borders	Active organized surveillance
56	Shaanxi	15	2021/10/17	34	636	Land borders	Passive self-monitoring
57	Yunnan	1	2021/10/19	8	67	Land borders	Active organized surveillance
58	Heilongjiang	1	2021/10/27	20	277	Uncertain	Active organized surveillance
59	Jiangxi	3	2021/10/30	20	95	Uncertain	Uncertain
60	Liaoning	1	2021/11/4	24	308	Ports	Passive self-monitoring
61	Shanghai	2	2021/11/25	14	6	Airports	Uncertain
62	Inner Mongolia	4	2021/11/28	20	609	Land borders	Active organized surveillance
63	Shaanxi	1	2021/12/2	1	1	Possibly via quarantined inbound visitors	Active organized surveillance
64	Guangdong	1	2021/12/3	1	1	Quarantine places	Active organized surveillance
65	Zhejiang	4	2021/12/6	22	496	Uncertain	Active organized surveillance
66	Shaanxi	5	2021/12/9	23	1,506	Airports	Active organized surveillance
67	Guangdong	1	2021/12/16	3	2	Possibly via quarantined inbound visitors	Active organized surveillance
68	Sichuan	1	2021/12/16	1	1	Airports	Active organized surveillance
69	Fujian	1	2021/12/17	1	1	Airports	Active organized surveillance
70	Guangxi	1	2021/12/21	9	20	Land borders	Active organized surveillance
71	Yunnan	1	2021/12/24	1	4	Possibly via quarantined inbound visitors	Active organized surveillance
72	Sichuan	1	2021/12/26	1	1	Quarantine places	Active organized surveillance
73	Yunnan	2	2021/12/27	5	2	Land borders	Passive self-monitoring
74	Jiangsu	1	2021/12/28	1	1	Ports	Active organized surveillance

Abbreviation: COVID-19=coronavirus disease 2019; PLAD=provincial-level administrative division.

SUPPLEMENTARY TABLE S2. Distribution of the 74 outbreaks and symptomatic COVID-19 cases in the mainland of China by provinces in the order of the date for the first outbreak between March 19, 2020 and December 31, 2021.

PLAD	Number of total outbreaks*	Number of total symptomatic cases
Guangdong	9	232
Beijing	11	470
Shanghai	10	48
Zhejiang	4	495
Liaoning	10	515
Shandong	6	44
Heilongjiang	9	1,145
Inner Mongolia	6	780
Jilin	4	462
Hebei	4	1,103
Sichuan	6	51
Tianjin	3	12
Xinjiang	3	906
Anhui	3	12
Shanxi	2	5
Guangxi	2	21
Shaanxi	5	1,494
Jiangxi	2	23
Yunnan	6	292
Jiangsu	5	826
Hunan	2	114
Chongqing	2	8
Fujian	3	473
Henan	3	241
Hubei	2	93
Ningxia	2	46
Hainan	2	2
Gansu	1	144
Guizhou	2	13
Qinghai	1	12

Abbreviation: COVID-19=coronavirus disease 2019; PLAD=provincial-level administrative division.
*The sum of total outbreaks for all PLADs is more than 74 because one outbreak might involve more than one PLAD.

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Vital Surveillances

Surveillance and Analysis of SARS-CoV-2 Variant Importation — China, January–June 2022

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ABSTRACT

Introduction: The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) Omicron variant is the dominant circulating strain worldwide. To assess the importation of SARS-CoV-2 variants in the mainland of China during the Omicron epidemic, the genomic surveillance data of SARS-CoV-2 from imported coronavirus disease 2019 (COVID-19) cases in the mainland of China during the first half of 2022 were analyzed.

Methods: Sequences submitted from January to July 2022, with a collection date before June 30, 2022, were incorporated. The proportions of SARS-CoV-2 variants as well as the relationships between the origin and destination of each Omicron imported case were analyzed.

Results: 4,946 sequences of imported cases were submitted from 27 provincial-level administrative divisions (PLADs), and the median submission interval was within 1 month after collection. In 3,851 Omicron sequences with good quality, 1 recombinant (XU) and 4 subvariants under monitoring (BA.4, BA.5, BA.2.12.1, and BA.2.13) were recorded, and 3 of them (BA.4, BA.5, and BA.2.12.1) caused local transmissions in the mainland of China later than that recorded in the surveillance. Omicron subvariants dominated in the first half of 2022 and shifted from BA.1 to BA.2 then to BA.4 and BA.5. The percentage of BA.2 in the imported SARS-CoV-2 surveillance data was far higher than that in the Global Initiative on Sharing All Influenza Data (GISAID). The imported cases from Hong Kong Special Administrative Region, China, accounted for 32.30% of Omicron cases sampled, and 98.71% of them were BA.2.

Conclusions: The Omicron variant showed the intra-Omicron evolution in the first half of 2022, and all of the Omicron subvariants were introduced into the mainland of China multiple times from multiple different locations.

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) Omicron variant emerged in November 2021 (*1*). Within a month, Omicron subvariants were found in varying proportions in different regions worldwide and rapidly replaced the previous variants of concern (VOCs) (*2*–*3*). Studies have reported that the transmissibility and neutralization evasion capability of Omicron are enhanced in comparison to prior strains (*4*–*5*). The wide spread of the Omicron variant across the world has led to multiple recombinants emerging and significant intra-Omicron evolution. Since November 14, 2022, Omicron has evolved into 661 lineages, including recombinants (*6*). Some of them, designated as Omicron subvariants under monitoring by the World Health Organization (WHO) (*7*), have enhanced transmission advantages and have become more difficult to prevent and control than ever before.

In the mainland of China, several domestic transmissions associated with imported Omicron infections began to emerge in December 2021 (*8*–*11*), posing a significant challenge to the dynamic zero-coronavirus disease 2019 (COVID-19) policy. Under the current Omicron wave, genomic surveillance for SARS-CoV-2 from imported COVID-19 cases has had a crucial role in tracking the variant's international spread and inferencing the origin of domestic transmissions. According to the Protocol on Prevention and Control of COVID-19 (Edition 8), the laboratories of provincial CDCs were required to conduct SARS-CoV-2 whole-genome sequencing for samples from all imported COVID-19 cases and submit the genomic sequences to the China CDC. This study analyzed genomic surveillance data from January to June 2022 to understand the importation of SARS-CoV-2 variants in the mainland of China during the Omicron epidemic.

METHODS

The sequences of SARS-CoV-2 from imported cases were submitted from provincial CDC laboratories to the national China CDC for verification and further analyses. Sequences involved in the study were submitted from January to July 2022 — with a collection date before June 30, 2022. Data from Hong Kong Special Administrative Region (SAR), China; Macao SAR, China; and Taiwan, China were not included in this study. Global SARS-CoV-2 sequence surveillance data in the Global Initiative on Sharing All Influenza Data (GISAID) were extracted from the COV-spectrum platform on July 17, 2022 (*12*).

Consensus sequences were assessed for quality control by the Nextclade web tool (https://clades.nextstrain.org; version 2.4.1) with parameters for missing data, mixed sites, private mutations, mutation clusters, frameshifts, and stop codons. Sequences with good quality control status were typed using the Phylogenetic Assignment of Named Global Outbreak Lineages (PANGOLIN; version 4.0.5) web tool (*13*). The SARS-CoV-2 VOCs and Omicron subvariants under monitoring were classified according to the WHO's designation (*7*).

RESULTS

A total of 4,946 SARS-CoV-2 genomic sequences collected before June 30, 2022, from imported COVID-19 cases were submitted to the China CDC during the period of January to July, 2022. Except the Xizang (Tibet) Autonomous Region, Xinjiang Uygur Autonomous Region, Qinghai Province, and Anhui Province, the rest of the provincial-level administrative divisions (PLADs) had sequences submitted in various amounts (Figure 1A). To validate sequence submissions' timeliness, each sequence's deposition time was calculated according to the date of sample collection and the date of sequence submission. The results showed that Shanghai Municipality had the longest median time of sequence deposition, with a 28-day median time (IQR=21–38), followed by Liaoning Province with a 26-day median (IQR=11–44). The median time of sequence deposition of the remaining PLADs was within 3 weeks. However, 15, 10, and 6 sequences were submitted 90 days after sample collection in Yunnan Province, Henan Province, and Shanghai, respectively (Figure 1B).

Of the 4,946 sequences obtained, 4,742 were collected from January to June 2022. Among the 4,742 sequences, 3,893 (82.10%) had good quality control status, allowing for further lineage analysis (Figure 2A). Of them, the Omicron variant accounted for 98.92% (3,851/3,893), including 5 major lineages: BA.1, BA.2, BA.4, BA5, and recombinant. In January, the proportion of BA.1 was the highest: around 86.8%. Subsequently, BA.2 replaced BA.1, becoming dominant in February (79.9%) and overwhelmingly dominant from March to May (more than 90% per month). BA.4 and BA.5 were first detected in April, and their proportion gradually increased, accounting for 11.2% and 41.9% in June, respectively. In the lineages of Omicron, one recombinant XU, a hybrid of BA.1 and BA.2, and four subvariants under monitoring (BA.4, BA.5, BA.2.12.1, and BA.2.13) were recorded in the imported SARS-CoV-2 surveillance (Table 1). Three of them (BA.4, BA.5, and BA.2.12.1) had caused local transmissions in the mainland of China, and the time of causing local transmission was at least 26 days later than that recorded in the surveillance.

The distribution of dominant lineages for the sequences collected from imported cases in the mainland of China was in accordance with the worldwide sequencing data obtained from GISAID (Figure 2B). However, there were differences in the diversity and percentage of the lineages. The Alpha, Beta, Gamma, and Omicron BA.3 subvariants were recorded in the first half of 2022 in GISAID but were not detected in the imported SARS-CoV-2 surveillance in the mainland of China. The percentage of BA.2 in the imported SARS-CoV-2 surveillance was far more than that in GISAID (February: 79.9% *vs*. 30.2%; March: 93.3% *vs*. 77.4%). Notably, the number of sequences shared in GISAID decreased month by month in the first half of 2022.

To gain insight into the introduction of Omicron into the mainland of China, this study generated a Sankey diagram to illustrate the relationships between the origin and destination of each Omicron imported case (Figure 3A). The results showed that 3,851 Omicron cases came from 118 countries or regions. The four major lineages, BA.1, BA.2, BA.4, and BA.5, were imported from 89, 81, 23, and 40 countries or regions, respectively. Hong Kong imported the most significant number of cases (32.30%, 1,244/3,851) and mainly introduced them to Guangdong Province (49.84%, 620/1,244) and Shanghai (32.56%, 405/1,244). Furthermore, almost all the imported cases from Hong Kong from January to June 2022 were the BA.2 strain (98.71%, 1,228/1,244). Finally, the sequences of the imported cases reported from Shanghai and Guangdong had the widest breadth of origin locations: sourcing from 73 and 65 countries or

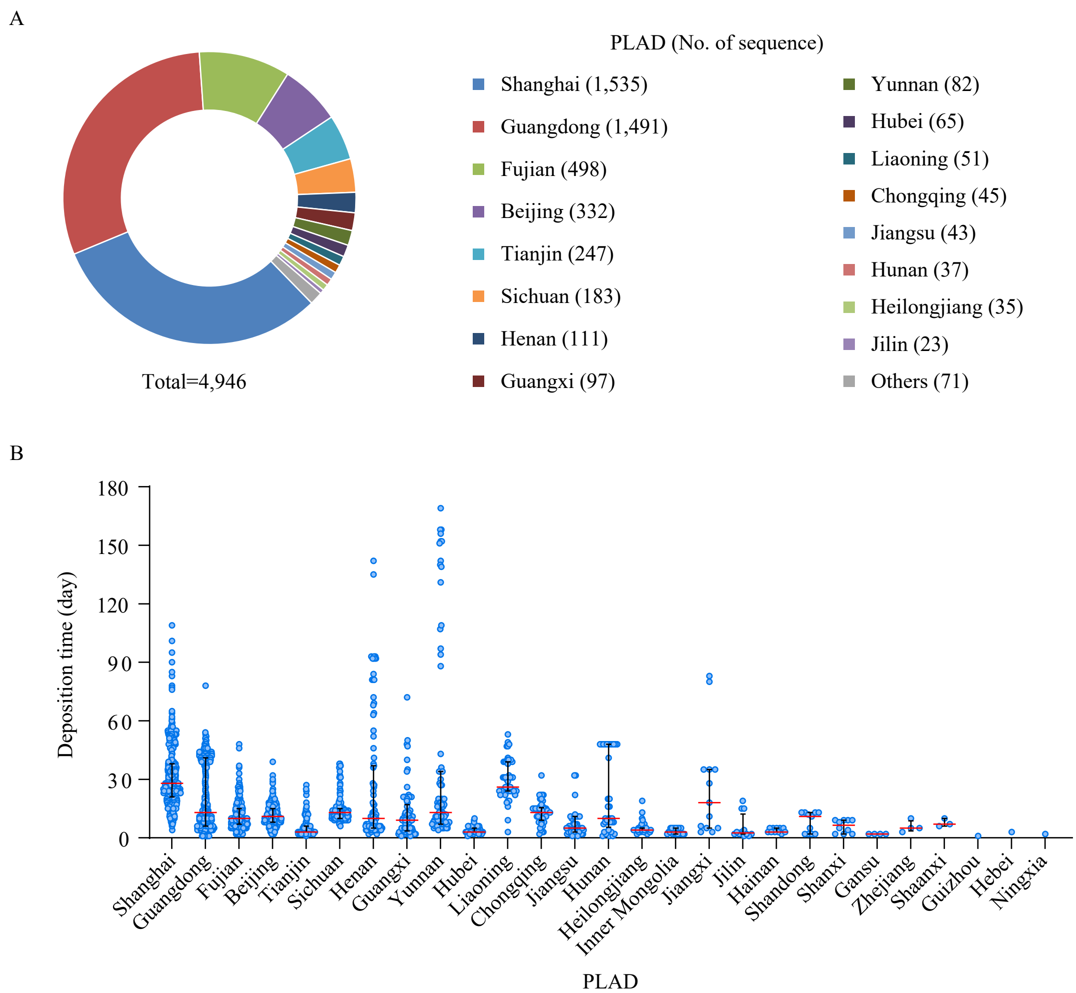

FIGURE 1. The surveillance of SARS-CoV-2 genomes in imported cases in the mainland of China from January to June 2022. (A) The number of genomic sequences of imported cases submitted by PLAD. (B) The sequence deposition time of each PLAD from sample collection to sequence submission.
Note: In panel A, the 11 PLADs with less than 10 sequence submissions were merged in the category "Others". In panel B, the PLADs were listed in order of the number of sequence submissions from most to least. Data was shown as median with interquartile range. Data as of July 31, 2022.
Abbreviation: SARS-CoV-2=severe acute respiratory syndrome coronavirus 2; PLAD=provincial-level administrative division.

regions, respectively.

As Hong Kong SAR had the largest number of cases recorded in the surveillance in the first half of 2022, this investigation compared the data of Hong Kong SAR in GISAID with that in the imported surveillance. In February and March, Hong Kong SAR submitted 1,153 and 770 sequences to GISAID, respectively — among which BA.2 accounted for 95.32% and 100.00%, respectively (Figure 3B). The proportions were similar to that in imported SARS-CoV-2 surveillance (February: 98.94%; March: 99.72%). Other months, except February and March, had fewer sequence records in the imported surveillance. The proportion of SARS-CoV-2 variants in the imported surveillance after the removal of Hong Kong was closer to that of GISAID data in February and March (Figure 2B and Figure 3B).

CONCLUSIONS

In the present study, genomic sequence surveillance data of SARS-CoV-2 from imported cases in the mainland of China from January to June 2022 were analyzed. The median deposition time in all PLADs submitting sequences was less than 1 month. However, some sequences were submitted 3 months after the sample collection date, which may blunt the surveillance sensitivity. Guangdong and Shanghai had the largest number of submission sequences and covered the widest range of origins, consistent with the

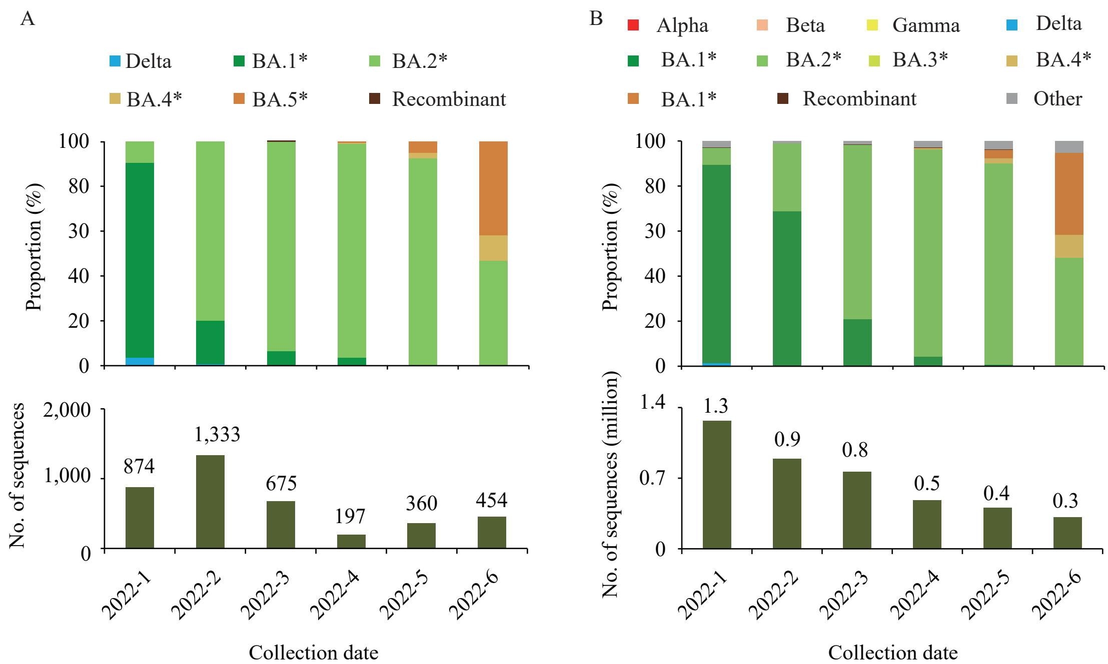

FIGURE 2. The proportion of SARS-CoV-2 VOCs in the imported SARS-CoV-2 surveillance and in GISAID from January to June 2022. (A) The imported SARS-CoV-2 surveillance in the mainland of China (Data as of July 31, 2022). (B) GISAID (Data as of July 17, 2022).

Note: Recombinant includes BA.1/BA.2 circulating recombinant forms such as XE. The catalogs BA.1*, BA.2*, BA.3*, BA.4*, BA.5* and Recombinant all belong to Omicron.

Abbreviation: SARS-CoV-2=severe acute respiratory syndrome coronavirus 2; VOC=variant of concern; GISAID=the Global Initiative on Sharing All Influenza Data.

* Includes the descendent lineages.

TABLE 1. The detection of SARS-CoV-2 Omicron recombinant and subvariants under monitoring in the mainland of China and the world.

Lineage*	Earliest recorded sequence in the imported SARS-CoV-2 surveillance			Date of first local transmission	Earliest documented samples in the world†
	Submitted PLAD	Submission date	Imported country		
XU§	Guangdong	2022-4-21 (Collection date: 2022-3-12)	United Arab Emirates	–	Japan, 2022-1
BA.4¶	Guangdong	2022-5-4 (Collection date: 2022-4-30)	Netherlands	Guangdong, 2022-6-25	South Africa, 2022-1
BA.5¶	Shanghai	2022-5-15 (Collection date: 2022-4-29)	Uganda	Chongqing, 2022-6-11	South Africa, 2022-1
BA.2.12.1¶	Sichuan	2022-4-29 (Collection date: 2022-4-15)	Canada	Sichuan, 2022-7-15	United States of America, 2021-12
BA.2.13¶	Guangdong	2022-6-24 (Collection date: 2022-6-20)	Canada	–	United States of America, 2021-12

Abbreviation: SARS-CoV-2=severe acute respiratory syndrome coronavirus 2; PLAD=provincial-level administrative division; WHO=World Health Organization.

* Includes the descendent lineages.

† According to the data published by the Pango lineages (*6*).

§ Recombinant lineage of BA.1 and BA.2.

¶ Omicron subvariants under monitoring designated by WHO (*7*).

results of surveillance data from 2021 (*2*). It is further suggested that international travel hubs such as Shanghai and Guangdong can be used as surveillance sites to strengthen the monitoring of SARS-CoV-2 global circulation.

From the surveillance data, Omicron dominated in the first half of 2022, shifting from BA.1 to BA.2, then to BA.4 and BA.5. The epidemic trend was in accordance with that in GISAID, while the proportions of each major lineage were quite different, especially in February and March. Based on further analyses of geographic origin, the discrepancy might be

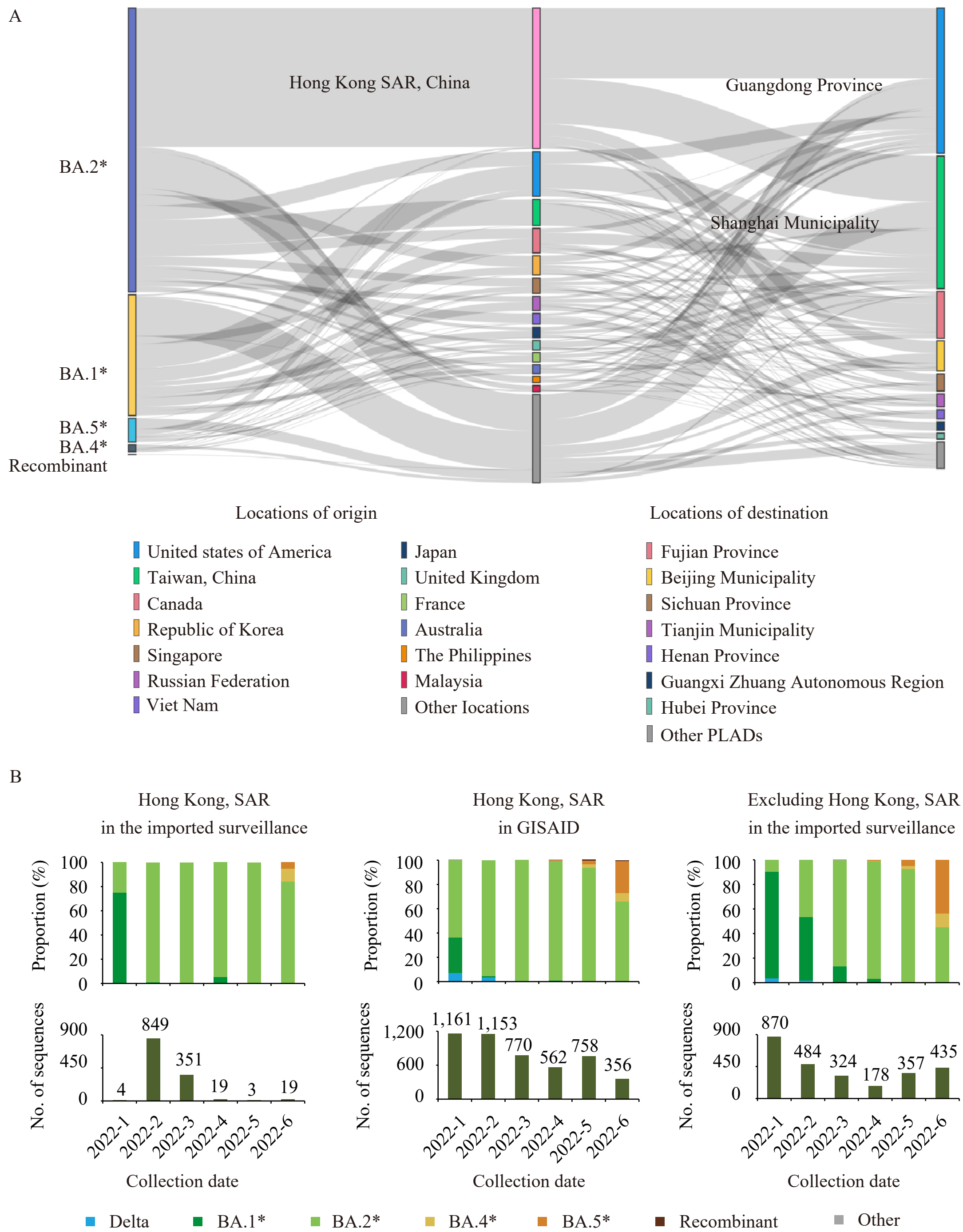

FIGURE 3. Specific source analysis of SARS-CoV-2 VOCs. (A) The relationships between the origin and destination of each SARS-CoV-2 Omicron imported case. (B) The proportion of SARS-CoV-2 VOCs from Hong Kong SAR in the imported SARS-CoV-2 surveillance and in GISAID, and the proportion of SARS-CoV-2 VOCs in the imported SARS-CoV-2 surveillance (excluding Hong Kong SAR) from January to June 2022.

Note: In panel A, the columns from left to right were the major lineages of Omicron, location of origin, and location of destination. Other locations: the other 104 locations with a number of sequences less than 50. Other PLADs: the other 15 PLADs with a number of sequences less than 50.

Data from the imported surveillance and GISAID was up to July 31, 2022 and July 17, 2022, respectively.

Abbreviation: SARS-CoV-2=severe acute respiratory syndrome coronavirus 2; VOC=variant of concern; PLAD=provincial-level administrative division; SAR=Special Administrative Region; GISAID=the Global Initiative on Sharing All Influenza Data.

* Includes the descendent lineages.

partially due to the surge of BA.2 imported cases from Hong Kong. Indeed, since January 2022, Hong Kong has experienced a large-scale COVID-19 epidemic caused by the sub-lineage of BA.2, with a cumulative number of over 1 million reported cases (*14*). Accordingly, findings from the imported surveillance are likely to be skewed by the case population. Optimizing the directing sequencing efforts toward travelers departing from targeted countries or regions might help overcome this limitation.

Notably, the Omicron recombinant XU imported from the United Arab Emirates was first documented in this imported SARS-CoV-2 surveillance. Only 17 sequences of XU were shared from Japan, India, Australia, the United States of America, the United Kingdom, and Malaysia in GISAID (*12*). The reasons for the absence of recombinant XU sequences from the United Arab Emirates in GISAID might be associated with genomic surveillance and data-sharing strategies conducted in the United Arab Emirates, indicating that the actual prevalence of some variants may be underestimated. So far, 33 Omicron recombinants have been designated as lineages in the Pango nomenclature system, named XD to XAR (*6*). With the exception of XE, which has been reported to be 9.8% more transmissible than BA.2 and spread to 28 countries in the first half of 2022 (*15*–*16*), the rest of the recombinants, including XU, have not been reported to cause rapid epidemic expansion and little is known about their transmissibility, severity, and neutralization evasion capability. Further surveillance and studies are needed for these recombinants.

There are 3 other limitations to these results. First, the data in GISAID may be affected by the differences in sequencing capacity and sampling strategies among countries, the lag of sequence uploading, or even the decreased number of shared sequences. Second, although PLADs in the mainland of China were required to conduct genome sequencing for all imported COVID-19 cases, the sequenced coverage of imported cases may be affected by sample quality, differences in sequencing capability, and differences in reporting timeliness by PLAD. During the study period, the sequence of imported cases from Xinjiang, Tibet, Qinghai, and Anhui was not received, which may cause bias in lineage proportion and geographic analysis. These aforementioned PLADs should strengthen the sequencing of imported cases and shorten the feedback time of sequences to improve overall national monitoring sensitivity. Third, a lack of information on regions passed through before imported case documentation may mask the true origin of imported cases.

This study's findings revealed that Omicron has been introduced into the mainland of China multiple times from multiple locations. Far more sequences were recorded in the first half of 2022 than in all of 2021 (*2*). The surge of imported cases increased the risk of triggering local outbreaks. Since February 2022, the sub-lineage of BA.2 that was circulating in Hong Kong SAR has caused an outbreak in Shanghai with over 600 thousand infections (*17*). In addition, of the 7 lineages designated as "the Omicron subvariants under monitoring" by WHO, BA.5 was the most dominant strain in June and caused local transmissions in the mainland of China more than once (*18*). Considering the rapid alternation of the dominant variant within Omicron in the first half of 2022 and the gradual slowing of global genomic sequence surveillance efforts, the long-term genomic surveillance of imported SARS-CoV-2 will continue to play a vital role in the early warning of new variants as well as tracing the source of local transmissions in the mainland of China.

Conflicts of interest: No conflicts of interest.

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