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Foreword

Foreword from Editor-in-Chief George F. Gao — China's Outreach to the World：Public Health Goes Global

China CDC Weekly is a national public health bulletin published by the Chinese Center for Disease Control and Prevention (China CDC). It will serve as the primary communications channel of China CDC for disseminating timely, reliable, authoritative, accurate, objective and useful public health information as well as recommendations to health professionals and the public. *China CDC Weekly* is indexed and archived as a scientific journal, and its contents can therefore be searched and referenced.

China CDC Weekly also includes analyses of surveillance and survey data on communicable diseases, non-communicable diseases, and risk behaviors. It prioritizes important information for the practice of preventive medicine and public health, and each document undergoes thorough scientific vetting and is cleared for publication by China CDC as consistent with its plans and policies. In addition, as a professional scientific journal, it will also publish manuscripts (both basic and applicable science) of disease control and public health from all over the world.

China has about one fifth of the world's population, and ensuring the health of Chinese population is critical to the security of global health. As global economies rapidly expand, new geographical linkages appear through new trade partnerships, and infectious disease outbreaks and epidemics emerge and transmit without warning, unified platforms are urgently required to share our experiences, failures, and successes as a global community. *China CDC Weekly* will contribute significantly to this great need.

In the last few decades, China has made tremendous strides in improving public health. From 1949 to 2018, the life expectancy for Chinese residents has increased from 35 years to 77 years, the maternal mortality rate has decreased from 1,500/100,000 to 18.3/100,000, and infant mortality has decreased from 200/1,000 to 6.1/1,000. China's success in these three internationally-accepted indicators has resulted from intensive research, meticulous planning, and strategic implementation, and these efforts continue to receive strong support from the government through commitments such as Healthy China 2030 (*1*). *China CDC Weekly's* mission, therefore, is to share China's experiences, history, and perspectives to provide invaluable information for the improvement of global health.

China has much to share with the world based on great achievements from decades of effort in public health and disease control. For instance, All-People's Patriotic Health Campaign is a well-organized and well-coordinated program implemented in China with five major lessons: first, government political will was key for "no-profit" public health programs; second, societal involvement and active participation with proper knowledge was prioritized as professionals alone could not solve every public health issue; third, good stakeholder coordination reinforced every efforts; fourth, the National Immunization Program (NIP) provided a strong foundation for public health work; fifth, expanding the program's influence to underdeveloped areas helped innovate new techniques for increasing accessibility and reach.

China CDC Weekly will follow a path initially set forth by the United States Centers for Disease Control's (US CDC) *Morbidity and Mortality Weekly Report* (MMWR) (*2*). Over its history, MMWR has provided some of the most significant contributions to public and global health and is one of the primary resources for researchers, practitioners, policymakers, the public, and mass media worldwide.

On June 5, 1981, MMWR published the first report to describe what would later become known as acquired immunodeficiency syndrome (AIDS) (*3*). During the first eight years, almost 50 recommendations and guidelines were published in MMWR (*3*). Reflecting on these publications, we can see the trajectory of the AIDS epidemic and the evolving complexity of the resulting countermeasures. Most notably, the weekly format of MMWR allows for new information to quickly be released, absorbed and revised as progress moved forward. US CDC is able to garner media attention, draw forth political willpower, and alert the national community of health workers and researchers largely through the reach of MMWR. Today, MMWR continues to play a vital role in communicating new findings and developments in the fight against global epidemics (*3*), as evidenced in the report of the last Ebola disease cluster in Sierra Leone in 2016 (*4*).

Just as MMWR acts as a major lever for US CDC's influence on public and global health, we hope *China CDC Weekly* will help cement China CDC's influence in the global community. Following this legacy, we report in the first issue on the recent plague event in China in 2019, calling for awareness for a devastating but almost-forgotten infectious disease. Nothing can be neglected in regards to public health.

As the Belt and Road Initiative (BRI) continues to develop, over 65 countries containing 70% of the world's population and 30% of the world's GDP will be connected. Meanwhile, China CDC will have more opportunities to share, cooperate, and learn from our global counterparts (*5*). In September, 2018, heads of State and dignitaries from 53 African countries congregated in Beijing for the seventh triennial Summit of the Forum on China-Africa Cooperation (FOCAC). While some major initiatives promoted trade, industry, and cultural exchange, public health emerged as the top priority for the cooperative plans (*6*). China has become a pivotal partner for global health as the China CDC collaborates with Africa CDC to build a unified, well-trained public health entity that is equipped to promote the health of Africa and to ensure global health security. On November 1, 2018, in collaboration with other leading influenza specialists and all five WHO Collaborating Centers for Influenza, we initiated the first World Flu Day, supported by the WHO and Dr. Tedros Adhanom Ghebreyesus, the WHO Director-General (*7*). Launching the World Flu Day in China provided an important opportunity to strengthen global collaborations in the research and control of influenza and other diseases (*8*).

Outbreaks, epidemics, and chronic diseases have repeatedly shown to permeate every layer of human society and transcend national borders without discretion (*9*). Furthermore, occupational, nutritional, environmental, radiation safety, and many other types of public health issues represent enormous challenges for the world. Thus, public health should be our top priority for our increasingly integrated global community.

The establishment of *China CDC Weekly* represents a major step forward for global health. China CDC has dedicated substantial resources towards this public health bulletin, and with the advice and expertise of many international partners, *China CDC Weekly* will act as a model for other developing countries to disseminate their public health experiences, findings, and progress.

Improving health for the welfare of the global population requires action, requires coordination, and requires communication. Therefore, it is my sincere pleasure to introduce the establishment of *China CDC Weekly*.

George F. Gao, DPhil
Editor-in-Chief, *China CDC Weekly*
Director-General, Chinese Center for Disease Control and Prevention

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Foreword

Letter of Congratulations from Dr. Gauden Galea, WHO Representative in China

On behalf of the WHO Representative Office in China, I would like to extend my sincere congratulations to the founding of *China CDC Weekly*.

Health is more than the absence of disease. It follows then that poor health is sometimes more than the result of an infection or infirmity, but also the result of a complex web of social, economic, and environmental conditions. As public health specialists, therefore, we rely heavily on evidence collected from the real world to help ensure that our strategies and interventions have the desired impact while also taking into account these inter-related factors that can affect our health.

This is why the weekly epidemiological update that *China CDC Weekly* will offer is much needed and appreciated. Working on the frontline to address every issue that concerns the health and wellbeing of the Chinese people, the Chinese Center for Disease Control and Prevention (China CDC), under the leadership of National Health Commission, is uniquely situated to assess and disseminate findings generated by surveillance data and research results from the field.

Employing the resources of China CDC, *China CDC Weekly's* influence can be expanded. The data it provides may help effectively direct resources to where it is most needed and guide public health stakeholders at all levels to better perform their duties. It can also be used to present China's public health experience—to facilitate global dialogue.

As future readers of *China CDC Weekly*, we at the WHO Representative Office in China also believe that the new publication will enlighten our work in China as we continue to deepen the cooperation with China CDC and strive for Healthy China 2030 together.

Congratulations again.

Dr Gauden Galea, MD, MSc (Lond)
WHO Representative in China

Announcements

The 32nd World AIDS Day — December 1, 2019

World AIDS Day is observed every December 1 to raise public awareness and recognize the impact of the human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS) epidemic worldwide.

In 2018, 37.9 million people globally were living with HIV, including 1.7 million people newly infected that year (*1*). According to a 2018 joint assessment by China CDC, UNAIDS, and WHO, 1.25 million people were living with HIV in China and 81,000 people were newly infected in 2018. Though serious challenges remain, significant progress has been made in HIV prevention and control in China as prevalence remained low at the national level (*2*).

UNAIDS has designated this year's World AIDS Day theme: "Communities make the difference" (*3*). In response to the global World AIDS Day theme for 2019 and the Healthy China Initiative (2019-2030), National Health Commission has announced China's 2019 national theme: "Mobilizing communities for AIDS prevention, Healthy China starts with my action."

These themes recognize the importance of community contributions in responding to the epidemic and emphasizes that personal responsibility for awareness, society-government cooperation, stakeholder agency, and other social forces will help curb the global AIDS epidemic and build a healthier China (*4*).

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Preplanned Studies

Progress Towards the 90-90-90 Targets for Controlling HIV — China, 2018

Yan Zhao[1]; Mengjie Han[1,#]; Ye Ma[1]; Dongmin Li[1]

Summary

What is already known about this topic?

Since the Joint United Nations Programme on HIV and AIDS (UNAIDS) announced the 90-90-90 targets to control the global HIV epidemic in 2014, many countries have undertaken innovative measures to achieve this goal. The National Center for AIDS/STD Control and Prevention (NCAIDS) of China CDC convenes experts annually to evaluate the national progress towards these indicators. The most recent progress of 90-90-90 targets in China has not been previously published.

What is added by this report?

At the end of 2018, the percentage of living with HIV (PLWH) who had received a confirmed HIV diagnosis in China was 68.9% (61.5%-78.3%). The antiretroviral treatment coverage of diagnosed PLWH was 83.4%, and among patients on treatment for at least 12 months, 94.2% achieved viral suppression. This provides most recent progress of 90-90-90 target in China.

What are the implications for public health practice?

China has made significant strides in curbing the HIV epidemic, but analysis on progress for the first 90 target for HIV testing remains out of reach. Innovative testing strategies may need to be developed to ensure that more PLWH can be identified.

In 2014, the Joint United Nations Programme on HIV and AIDS (UNAIDS) established the 90-90-90 targets, which sets the goal that by 2020, 90% of all people living with HIV (PLWH) should be aware of their HIV status, 90% of all diagnosed PLWH should be accessing antiretroviral therapy (ART), and 90% of all patients receiving ART should have suppressed viral loads (*1*). Correspondingly, the Chinese government developed an action plan for 2016-2020 to meet the 90-90-90 targets and to control the national HIV epidemic. As part of this effort, the Chinese National

Free Antiretroviral Treatment Program eliminated the CD4 cell count eligibility threshold and began offering free treatment to all PLWH starting in 2016 (*2*).

Every year, the National Center for AIDS/STD Control and Prevention (NCAIDS) of Chinese Center for Disease Control and Prevention, compiles data from the nationwide HIV/AIDS Comprehensive Response Information Management System (CRIMS) (*3*) and convenes experts to evaluate the state of the epidemic and the national response (Table 1). Data on China's progress towards the 90-90-90 targets are shared with international organizations, including UNAIDS and the World Health Organization (WHO). As of the end of 2018, estimates for the three target indicators stand at 68.9% (61.5%-78.3%), 83.4%, 94.2%, respectively. Progress towards the first 90% target lags behind the second and third targets. Testing strategies need to be tailored and strengthened so that more PLWH can be screened and diagnosed in a timely manner.

The number of HIV tests performed annually has increased from 128 million in 2014 to 241 million in 2018 (Figure 1). For this same period, CRIMS data report that the total survival number of PLWH with a confirmed diagnosis increased from 500,679 to 861,042 (Table 2), and the number of newly diagnosed cases per calendar year rose from 103,501 in 2014 to 148,589 in 2018 (Figure 1). CRIMS data on the care continuum are presented in Table 2. A joint assessment by NCAIDS, UNAIDS and WHO used Spectrum modelling to estimate that at the end of 2018, the total number of PLWH in China was 1,250,000 (1,100,000-1,400,000). The percentage of PLWH with a confirmed HIV diagnosis at the end of 2018 in China was 68.9% (61.5%-78.3%). There were an estimated 81,000 (60,000-105,000) new infections in 2018 and the estimated national prevalence in 2018 is 0.090% (0.079%-0.101%).

The number of people receiving ART increased from 295,358 in 2014 to 718,499 in 2018 (Table 2), corresponding to treatment coverage of 59.0% in 2014 and 83.4% in 2018 (Figure 2). Over 90% of patients on ART for over 12 months have suppressed viral loads, and this percentage rose to 94.2% in 2018.

Discussion

In 2018, UNAIDS presented an update on the

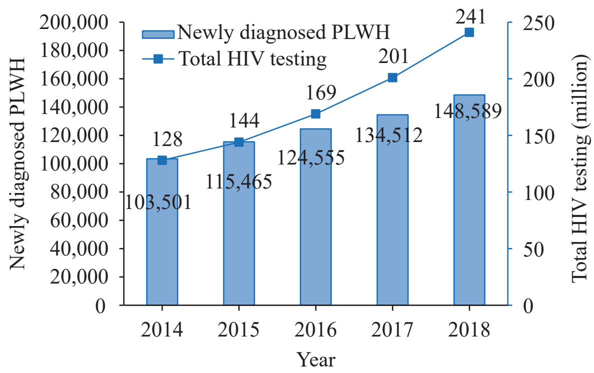

FIGURE 1. Number of total HIV tests performed and number of newly diagnosed PLWH from 2014 to 2018.

TABLE 1. Definitions of the 90-90-90 targets, calculated each calendar year using CRIMS data.

	Numerator	Denominator
First 90%: Diagnosis	Number of surviving PLWH with a confirmed HIV diagnosis, taken from CRIMS.	Number of PLWH estimated through Spectrum modelling, figures were taken from the joint estimation group.
Second 90%: Treatment	Number of PLWH on ART, taken from CRIMS.	Number of surviving PLWH with a confirmed HIV diagnosis, taken from CRIMS.
Third 90%: Viral Suppression	Number of PLWH with viral load ≤1,000 copies/mL, taken from CRIMS.	Number of PLWH on ART for at least 12 months and at least one viral load test result*, taken from CRIMS.

* The calculation of the third 90% is different from the UNAIDS recommendation. The Chinese National Free Antiretroviral Treatment Program provides free viral load testing once a year. Patients newly initiated on ART may not have received a viral load test by the end of the reporting period (*4*).

TABLE 2. China's continuum of HIV care, 2014–2018.

Items	2014	2015	2016	2017	2018
Total survival number of PLWH	500,679	577,423	664,751	758,610	861,042
PLWH on ART	295,358	386,756	494,657	609,829	718,499
Patients on ART eligible for viral load testing	216,576	285,237	359,337	447,720	573,992
Patients on ART with ≥1 viral load test result	197,735	263,712	255,924	362,970	512,499
Patients with suppressed viral load	179,807	241,003	237,696	339,510	482,954

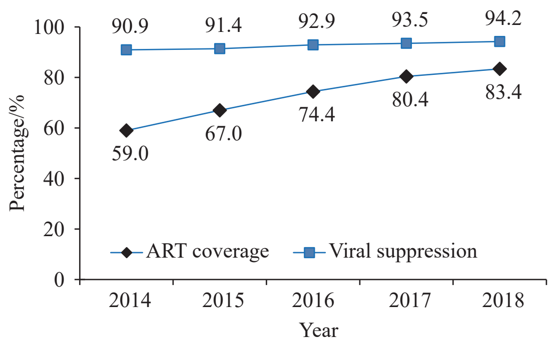

FIGURE 2. ART coverage and viral suppression from 2014 to 2018.

global progress towards the 90-90-90 targets: 79% (67%-92%) of all PLWH globally knew their HIV status. Among those who knew their HIV status, 78% (69%-82%) were accessing antiretroviral therapy, and 86% (72%-92%) of PLWH on ART had suppressed viral loads. Fifteen countries reported meeting the targets in 2018 (*5*).

Although China can be credited for substantial recent progress, the challenges remain in achieving 90-90-90 targets. Data show that there is a large gap to meeting the first 90% target. This indicates that there is insufficient access to testing for those who already infected with HIV. New approaches to testing should be investigated and implemented, including additional focus on self-testing, partner testing, and promoting testing-seeking behavior strategies. National HIV testing outreach campaigns will also be intensified to increase awareness and uptake of HIV testing among key populations at risk. Through investing in new policies and programs, earlier HIV detection and prevention of further transmission can be achieved.

While China's ART coverage is relatively favorable among low- and middle-income countries (*6*), improvements are necessary in the treatment and care services system (*7*). A major priority is to reduce the time between HIV diagnosis and ART initiation (*8*). Patients who are diagnosed late at low CD4 cell counts and advanced disease progression should be offered immediate and/or accelerated ART initiation (*2*). Previous research has shown that structural interventions to simplify the algorithm between screening and treatment initiation can reduce mortality, and the implementation of such interventions should continue to be expanded nationally (*9*). Maintaining timely linkage to care and high treatment retention rates is crucial to improving overall health outcomes (*9*).

Finally, the increased involvement of community-based organizations has led to greater HIV awareness, program participation, and improved HIV-related outcomes. Specifically, initiatives led by community-based organizations can increase HIV testing uptake and decrease HIV-related mortality and virologic failure (*10*). Additional investment in collaborations between health authorities and community-based organizations can yield significant benefits.

The findings in this report are subject to some limitations. First, the number of PLWH estimated through modelling methods may be affected by available parameters and complex circumstances. Second, China's national treatment program only provides free viral load testing on a once per year basis post-ART initiation. Thus, only the viral loads of patients who have been treated for more than one year and have successfully accessed viral load testing are capable of being observed. This introduces bias into the national viral suppression estimates because patients who failed treatment are also more likely to not receive a viral load test. However, CRIMS is a robust and comprehensive case reporting system with national coverage and up-to-date clinical information on all diagnosed PLWH in China (*3*), and we have confidence in the overall findings.

China has made significant strides in the fight against HIV. Yet, in light of the geographic diversity of the epidemic and the complexity in addressing disparate population needs, many challenges still exist. Tremendous efforts need to be sustained in order to curb transmission. Proportional budget allocations, healthcare system reform and expansion, reduction in HIV stigma, and additional emphasis on key populations are needed for China to achieve the 90-90-90 targets.

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Preplanned Studies

Short-term Exposure to Fine Particles and Risk of Cause-Specific Mortality — China, 2013-2018

Chen Chen[1]; Tiantian Li[1]; Lijun Wang[2]; Jinlei Qi[2]; Wangying Shi[1]; Mike Z He[3]; Qinghua Sun[1]; Jiaonan Wang[1]; Huanhuan Zhu[1]; Xiaoming Shi[1,#]

Summary

What is already known about this topic?

Short-term exposure to $PM_{2.5}$ has been associated with population excess death. This issue is of critical concern in China given its high level of exposure to $PM_{2.5}$ compared to that of the rest of the world.

What is added by this report?

Existing studies were conducted from 2013-2015 and have failed to capture the full effects of China's actions towards cleaner air in recent years, such as the first Action Plan for Air Pollution Prevention and Control issued in 2013. This study uses the longest time series data to date from 2013-2018, provides the latest evidence on $PM_{2.5}$ and cause-specific death nationwide, and identifies regional patterns of $PM_{2.5}$-related effects as well as $PM_{2.5}$-related susceptible populations.

What are the implications for public health practice?

This study suggests that the development of standards and the implementation of actions to clean the air and protect public health should be tailored to $PM_{2.5}$-related sensitive diseases, susceptible populations, and regional patterns.

Fine particulate matter (particles with aerodynamic diameter ≤2.5 μm; $PM_{2.5}$), a non-threshold pollutant, has been associated with excess death at low levels of short-term exposure in a several epidemiological studies in developed countries (*1–3*). However, few studies on national $PM_{2.5}$ exposure and population death have been done in China because pertinent data started becoming available in January 2013, and existing studies performed on three-year time series data from 2013–2015 might fail to capture health impacts under recent initiatives for air quality improvement (*4–5*). Ambient $PM_{2.5}$ might exhibit similar risk patterns in China, and the excess death toll could be larger and more immediate given higher population densities and pollution levels. To assess the association between $PM_{2.5}$ and cause-specific death nationwide, National Institute of Environmental Health (NIEH) of China CDC analyzed daily mortality cases during a six-year study period from January 1, 2013 to December 31, 2018 provided by China CDC's Disease Surveillance Point System (DSPS). A 0.14% (95% CI[*]: 0.06-0.21) increase in non-accidental mortality and a 0.12% (95% CI: 0.02-0.21) increase in cardio-cerebrovascular mortality were associated with 10 μg/m^3 increases in a three-day moving average of $PM_{2.5}$. Males and individuals over 75 years old were found to be more susceptible to increases in $PM_{2.5}$, and China's northern and southern regions were found to have differing cause-specific mortalities associated with $PM_{2.5}$. National plans for regulating $PM_{2.5}$ need to be prioritized with consideration for variability across regions, for susceptible populations, and for highly associated diseases.

This study used daily mortality cases from January 1, 2013 to December 31, 2018 provided by the DSPS of China CDC and involved a study population of 81.02 million from 130 Chinese counties, 88 of which are in the northern region and 42 in the southern region. Twelve specific causes of deaths were classified according to the International Statistical Classification of Disease, 10th Revision (ICD-10; World Health Organization 2007), by sex (male and female), and by age (<65 years, 65–74 years, and >74 years)(Figure 1). Daily $PM_{2.5}$ 24-hour mean concentrations were obtained from the National Urban Air Quality Real-Time Release Platform, and to adjust for the confounding effects of meteorological factors, data on 24-hour mean temperature and relative humidity of study sites were obtained from the National Meteorological Information Center.

This study applied a two-stage statistical analysis of a multi-county time series design. In the first stage, a generalized additive model (GAM) with quasi-Poisson regression was used to estimate the county-specific associations of daily mortality and $PM_{2.5}$ for each

[*] CI=Confidence Interval.

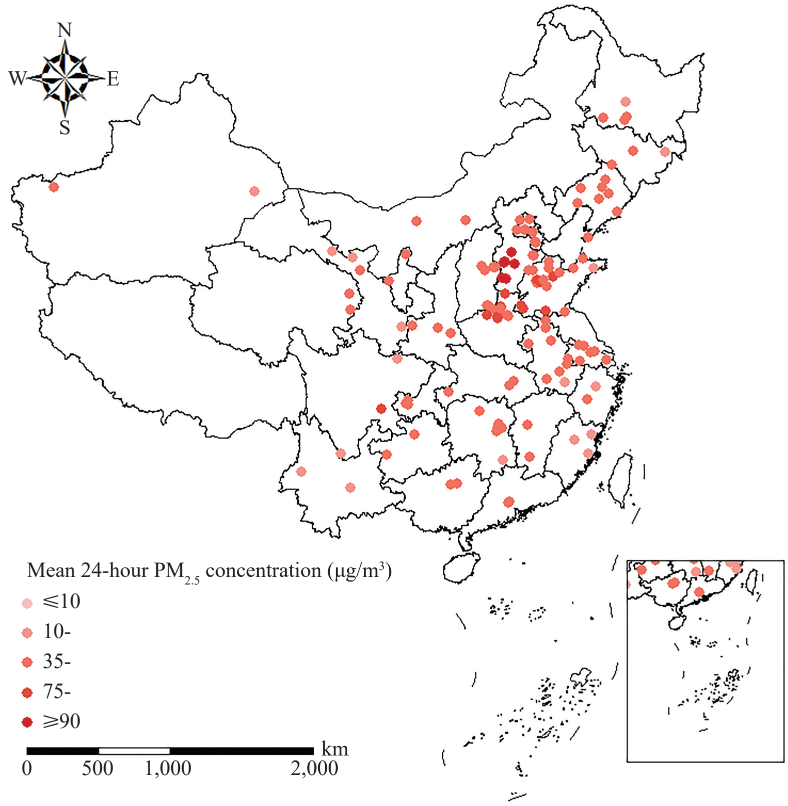

FIGURE 1. Map of 130 Chinese counties included in the study (color represents mean $PM_{2.5}$ concentration at county-scale).

cause.[†] In the second stage, a random effects meta-analysis was conducted to calculate effect estimates for both nationwide and north-south regional associations between cause-specific mortality and short-term $PM_{2.5}$ exposure. Stratified analyses of sub-populations by sex and age were also conducted to explore the potential vulnerable groups to $PM_{2.5}$. Given relatively strong associations between mortality and $PM_{2.5}$ with lagged cumulative exposure over several days (*2–4*), a 3-day moving average of the current and previous 2 days (lag 02) exposure to $PM_{2.5}$ was used for the core model.[§] Data analyses were conducted with the statistical software R(version 3.6.0) using the mgcv and meta for packages. Excess risks (ER) were expressed as the percentage increase in daily mortality associated with a per 10 μg/m³ increase in $PM_{2.5}$ in the study.

From 2013 to 2018, the population residing in study site areas was exposed to an mean daily $PM_{2.5}$ concentration of 58 μg/m³ (range from 3 to 807 μg/m³)(Table 1). A total of 2,411,410 deaths occurred from non-accidental causes, of which 1,181,292 were related to cerebrocardiovascular disease (CCVD) and 266,623 to respiratory diseases. On average, approximately 10 non-accidental deaths per day per county were recorded.

Positive associations (Figure 2A) with all analyzed causes of death and $PM_{2.5}$ were found in pooled estimates nationwide. Strongly significant effects were found for acute myocardial infarction (ER=0.21%, 95% CI: 0.05-0.37) and acute ischemic heart disease (ER=0.19%, 95% CI: 0.04-0.35), followed by non-accidental mortality (ER=0.14%, 95% CI: 0.06-0.21) and CCVD (ER=0.192%, 95% CI: 0.02-0.21).[¶]

Estimated CCVD values (Figure 2B) for males

[†] Time trend and meteorological factors (temperature and relative humidity) were controlled with a natural cubic regression spline with the degrees of freedom (*df*) that minimize the QAIC value of GAM. This analysis chose 6 *df* per year for time trend, with 3 *df* for meteorological factors. A dummy variable for the day of the week was also included for potential confounding.

[§] This study also summarizes the association between mortality and $PM_{2.5}$ current day (lag 0), a single-day lag of 1 (lag 1), 2 (lag 2), and 3 days (lag 3), and 2-day moving average of the current- and previous- day (lag 01) exposures (Figure S1). When examining the patterns of lag effects for short-term $PM_{2.5}$ exposure on non-accidental, cardio-cerebrovascular and respiratory death, associations at the single-lag exposures were estimated to be significant on lag 1 and 2 days, and insignificant on lag 3 days. Significance peaked at lag 02. Sensitivity analysis methods and results are presented in the supplementary materials (http://weekly.chinacdc.cn).

[¶] Although non-significant effects for respiratory and cerebrovascular causes were found, the lower limits of the confidence interval for respiratory causes were very close to zero.

TABLE 1. Summary of daily fine particulate, meteorological data and mortality counts across 130 counties in China (2013-2018).

Items	No. of counties	Mean ± SD	Median (P_{25}, P_{75})
Fine Particulate (24-h average, μg/m^3)			
Nationwide	130	58±51	44 (26, 73)
Northern	88	64±55	48 (28, 80)
Southern	42	46±35	37 (23, 58)
Meteorological Parameters			
Temperature (℃)	130	15±11	16 (6, 23)
Humidity (%)	130	64±19	66 (50, 79)
Cause of Mortality (daily counts per county)			
Non-Accidental Causes (A00-R99)	130	10±7	8 (5, 13)
Cardio-Cerebrovascular Diseases (I00-I99)	130	5±4	4 (2, 7)
Ischemic Heart Disease (I20-I25)	130	2±2	2 (1, 3)
Acute Ischemic Heart Disease (I20-I22, I24)	130	1±2	1 (0, 2)
Acute Myocardial Infarction (I21-I23)	130	1±1	1 (0, 2)
Cerebrovascular Disease (I60-I69)	130	2±2	2 (1, 3)
Stroke (I60-I64)	130	2±2	1 (0, 2)
Hemorrhagic Stroke (I60-I61)	130	1±1	1 (0, 1)
Intracranial Hemorrhagic Stroke (I61)	130	1±1	0 (0, 1)
Respiratory Diseases (J00-J99)	130	1±1	1 (0, 2)
Chronic Obstructive Pulmonary Disease (J41-J44)	130	1±1	0 (0, 1)
Chronic Lower Respiratory Disease (J40-J47)	130	1±1	0 (0, 1)

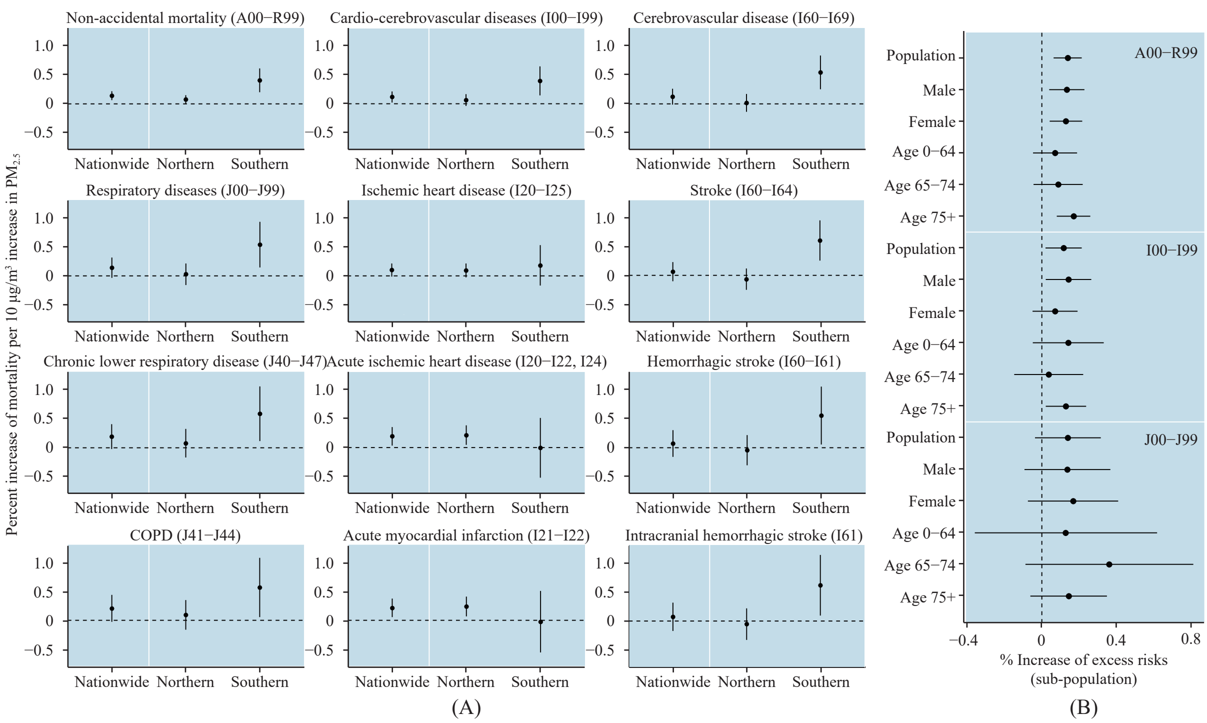

FIGURE 2. Percent increase of cause-specific mortality per 10 μg/m^3 increase in $PM_{2.5}$. Nationwide, north-south region-specific and subpopulation estimates for lag 02 exposure are presented (error bars represent 95% CIs of the estimates; ICD-10 codes of causes are shown in brackets).

(Error bars represent 95% CIs of the estimates. ICD-10 codes of causes are shown in brackets.)

(ER=0.14%, 95% CI: 0.02-0.26) were slightly stronger than those of females (ER = 0.07%, 95% CI: −0.05-0.19). Individuals over 75 years old also showed significantly higher susceptibility to $PM_{2.5}$ in two categories (non-accidental: ER=0.17%, 95% CI: 0.08-0.26; cardio-cerebrovascular: ER=0.13%, 95% CI: 0.02-0.24).

Cause-specific estimates of $PM_{2.5}$-mortality associations at lag 02 also varied from northern regions to southern regions (Figure 2A). Northern China had relatively weak associations with non-accidental and respiratory mortality, but stronger associations with acute myocardial infarction (ER=0.23%, 95% CI: 0.07-0.40) and acute ischemic heart disease (ER=0.21%, 95% CI: 0.05-0.38). For Southern China, risk estimates for non-accidental (ER=0.40%, 95% CI: 0.20-0.60), cerebrovascular (ER=0.54%, 95% CI: 0.25-0.82) and respiratory mortality (ER=0.53%, 95% CI: 0.15-0.93) tended to be much larger, especially stroke (ER=0.60%, 95% CI: 0.25-0.95) and intracranial hemorrhagic-stroke (ER=0.61%, 95% CI: 0.09-1.12).

Discussion

Stratified analyses by sex and age were used to reveal which populations were more vulnerable to $PM_{2.5}$, and the results reflected that males and people aged 75 years and older had higher ERs. Varying sex-specific acute effects of $PM_{2.5}$ could be attributed to smoking status (*6*–*7*), of which the rate of daily smoking among males is generally higher than that of females in China. Higher ER for individuals over 75 are consistent with previous epidemiological studies on acute effects of $PM_{2.5}$ and may be due to age-related deterioration of cardio-cerebrovascular and respiratory function in older adults and a much higher prevalence of age-related diseases than that of younger age groups (*1*,*8*).

The effect sizes of short-term $PM_{2.5}$ exposure nationwide reported here are smaller than that of comparable studies in Europe, the United States, and other WHO regions (*2*–*3*). A national time series study in the United States (*2*) with an average concentration of $PM_{2.5}$ less than 25 μg/m^3 from 1999–2005, estimated 0.98% (95% CI: 0.75, 1.22%), 0.85% (95% CI: 0.46, 1.24%) and 1.68% (95% CI: 1.04, 2.33%) increases per $PM_{2.5}$ 10 μg/m^3 increases in non-accidental, cardiovascular, and respiratory mortality, respectively. Moreover, a meta-analysis of related studies in other WHO regions** indicated that the association for cardio-cerebrovascular mortality (0.84%) was smaller than for respiratory mortality (1.51%) (*3*), while cardio-cerebrovascular mortality was more sensitive than respiratory mortality to acute $PM_{2.5}$ exposure in our study.

Variability in effect sizes across nations or regions, including differences between China's northern and southern regions, may be due to a combination of differences in population vulnerability, socioeconomic development, differing chemical composition of $PM_{2.5}$ and resulting toxicity to humans, and the nonlinear exposure-response relationship between $PM_{2.5}$ and mortality, i.e. the slope of this exposure-response curve might decline as exposure increases (*4*,*5*).

Although mean daily $PM_{2.5}$ concentrations have dropped in the 130 counties from 2013 (roughly 81.6 μg/m^3) to 2018 (roughly 44.0 μg/m^3), they still exceed the Interim Target-1 (35.0 μg/m^3) of WHO Air Quality guidelines. The estimates reported here consistently show that short-term $PM_{2.5}$ exposure has had a significant impact on population health in China, specifically increasing the risk of acute cardiovascular causes of death, such as acute ischemic heart disease and acute myocardial infarction.

These findings are subject to at least three limitations. First, as in most time-series studies, exposure misclassification was inevitable as related-$PM_{2.5}$ health effects were likely underestimated due to ambient concentrations from fixed-monitoring sites being used as proxies for true exposure levels (*9*). Secondly, study sites included in the study were limited by data accessibility, both on $PM_{2.5}$ monitoring data and death records. Some included study sites did not have complete data, which may reduce the statistical power of the analysis. Finally, this study only focused on $PM_{2.5}$ and did not involve PM_{10} and gaseous pollutants, which should be estimated in future research.

These findings suggest that policymakers should push forward the National Plan for Air Pollution Prevention and Control in China and suggest that additional consideration for susceptible populations and emission reduction measures be tailored towards local pollution circumstances.

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** China was excluded due to limited evidence.

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Outbreak Reports

Isolated Cases of Plague — Inner Mongolia-Beijing, 2019

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Summary

What is already known about this topic?

Plague is an acute infectious disease caused by *Yersinia pestis* (*Y. pestis*) and is primarily transmitted by rodents. Human can be infected by bites of bacterium-bearing fleas or direct contact with diseased or dead plague-infected animals. In 2004, the last human plague case was reported in Inner Mongolia Autonomous Region due to skinning a dead hare.

What is added by this report?

This is the first case of pneumonic plague imported into a major city since the founding of the People's Republic of China. Two primary pneumonic plague cases (Patients A and B) found in residents of Inner Mongolia were confirmed in Beijing on November 12, 2019. Another case (Patient C) of *Y. pestis* was identified as bubonic plague on November 14. Patient A most likely became infected from aerosol exposure to infective droplets while digging on his farm, located in an *Meriones unguiculatus* (*M. unguiculatus*) natural plague focus. Patient B became infected from contact with Patient A (her husband). Patient C became infected after skinning a dead hare. There was no epidemiological relationship between the Patient A/B and Patient C.

What are the implications for public health practice?

When epizootic plague is detected, local health-care providers and the public should be alerted about any possible risks. Public education efforts should focus on promoting personal protection measures.

On November 11, 2019, Beijing Center for Disease Control (Beijing CDC) identified two cases of *Yersinia pestis* (*Y. pestis*)-induced pneumonic plague in a husband and wife from the Sunitezuo Qi (County) of the Xilinguole League (Prefecture) in Inner Mongolia Autonomous Region. Three days later on November 14, 2019, another case of *Y. pestis* was identified in a patient from Huade County of Ulanchabu City in Inner Mongolia, 130 kilometers from the first two cases. China CDC established no epidemiological relationship between the two events (Figure 1).

A total of 447 persons with direct contact in Beijing and 46 in Inner Mongolia were quarantined for medical observation. As of November 21, 2019, all persons with direct contact were discharged from medical observation.

Investigation and Results

Patient A. The index case (Patient A) was a 43-year-old male herdsman. On October 25, the day after working the soil on his farm, he had sudden onset of fever (40 ºC), with chills, vomiting, chest pain, breathlessness, and cough with blood-tinged sputum. He reported no swollen lymph nodes. He sought treatment in a local county hospital, where he was admitted and stayed for two days. On October 27, his condition deteriorated and he was transferred to League Central Hospital (LCH) by ambulance and was admitted to the intensive care unit (ICU) where he stayed for seven days.

Patient B. On October 31, while Patient A was in the ICU, his wife (Patient B, 46 years old), who had accompanied and cared for him, had onset of cough with a low-grade fever (38 ºC). She was hospitalized in LCH. Over the next 24 hours her condition worsened with increasing cough, blood-tinged sputum production, nausea, vomiting, and diarrhea. Computerized tomography revealed pneumonia. Husband and wife were treated with antibiotics in the local hospital from October 25 to November 2 but did not show significant improvement. They were transferred by ambulance to a general hospital in Beijing on November 3 and were given Moxifloxacin and Cefoperazone sodium along with supportive treatment. There was no clinical improvement.

On November 12, blood and sputum specimens were tested by Beijing CDC and were found to be positive by RT-PCR and colloidal gold-immunochromatography assay targeting the F1 antigen

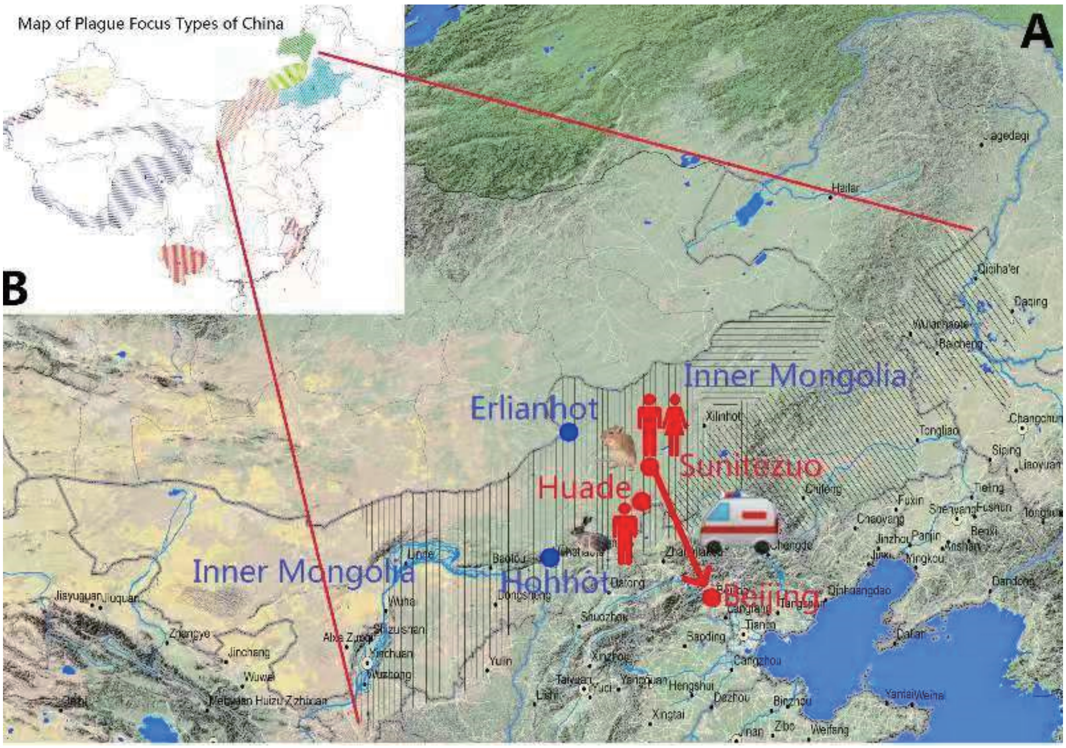

FIGURE 1. Geographic distribution and relation of the three human plague cases in Inner Mongolia and Beijing.

Part A: vertical line area: *Meriones unguiculatus* plague focus; horizontal line area: *Microtus brandti* focus; slant line area: *Spermophilus Dauricus* focus; cross line area: overlap area between *Meriones unguiculatus* and *Spermophilus Dauricus*. Part B: map of plague focus types in China.

and by reverse indirect hemagglutination assay (RIHA). Although *Y. pestis* was not able to be isolated by culture, NGS sequencing was weakly positive for *Y. pestis* genetic material. Beijing CDC and Inner Mongolia CDC immediately initiated a coordinated investigation, including evaluation of potential exposures to the patient and an environmental assessment to determine risk of further transmission. The Inner Mongolia Plateau is home to *Meriones unguiculatus* (*M. unguiculatus*), a primary mammalian host of *Y. pestis*, with cases of intense wild rodent epizootic disease in 2019.

Patient C. On November 11, 2019, Patient C (55-year-old male) sought treatment in a local hospital in Huade County for swollen lymph nodes and fever. Patient C had eaten a dead hare he found in the field. A clinician noted this exposure and suspected *Y. pestis* infection. The Inner Mongolia CDC laboratory identified *Y. pestis* by culture with the phage lysis test and with RT-PCR from lymph nodes aspirates. Blood cultures were negative for *Y. pestis*. On November 13, the patient was reported to Huade County CDC as having bubonic plague. An epidemiological investigation indicated no relation between Patients A/B and Patient C. However, Patient C lives in a county that is known to be a natural focus of *Y. pestis*.

Public Health Response

When epizootic plague is detected, local health-care providers and the public should be alerted to potential risks of plague. Educational efforts should promote personal protection measures, including: 1) educating the public to avoid direct contact with sick or dead animals (e.g., rodents and rabbits in Inner Mongolia); 2) wearing long pants and applying insect repellent on the skin, to clothing, and to outer bedding of anyone who engages in outdoor activities in an area that is an endemic focus for plague; 3) abstaining from handling or skinning wild or domestic animals that died of unknown reasons and using gloves when handling animals killed by trapping or hunting; 4) taking prophylactic antibiotics if risk of exposure is high; and 5) keeping pet dogs and cats in natural plague foci free from fleas and not allowing them to wander freely (*1*).

In response to the events reported above, key preventive measures have been implemented in Inner

Mongolia. These include: 1) enhanced surveillance for plague in rodents and rodent predators in enzootic areas; 2) use of insecticides and rodenticides to eliminate wild rodent fleas and reservoirs; 3) strengthening of professional training and alerting doctors to the forms of plague; 4) strengthening of professional training for local CDC and clinical laboratory staff; 5) monitoring rodent die-offs and educating the public to report sightings of dead animals and reductions in animal colony size; and 6) considering plague in the differential diagnosis of ill domestic animals, including dogs and cats, in the natural plague foci areas.

Discussion

Plague is an acute, often fulminating, infectious disease caused by *Y. pestis*. There are three main forms of plague, with the specific form depending upon route of infection: bubonic plague, septicemic plague, and pneumonic plague (*1*). Most human plague cases are of the bubonic form, which results from bites by infected fleas. However, plague can also be transmitted to humans by handling infected animals or by inhaling infectious aerosols from persons with pneumonic plague and from diseased or dead animals. The family of patients A and B lived in an independent house in a grassland, and investigators determined that the index patient most likely became infected while working the soil on his farm, an area where *M. unguiculatus* serves as a primary plague host. Five hundred meters from the house of Patients A and B, a live *M. unguiculatus* was trapped and found to be culture-positive for *Y. pestis*. A large rodent die-off was also observed in the area, raising the possibility that the decayed bodies in the dirt or in rat holes could have produced infectious aerosols. The wife (Patient B) most likely was infected from contact with her husband.

Plague is primarily a rodent-hosted, transmitting disease. Animal to animal transmission is mediated by the bites of fleas that were became infected by biting infected animals. Humans can be infected by the bites of bacterium-bearing fleas or by direct contact with wild or domestic animals that died from plague or are diseased with plague (marmots, foxes, lynxes and badgers, dogs (*2*), Tibetan sheep (*3*), and cats). Person-to-person transmission occurs only with pneumonic plague. Plague is categorized as a Class A infectious disease, the most serious category under China's Law on the Prevention and Treatment of Infectious Diseases (*4*).

Plague in Inner Mongolia

Human plague has been well controlled since 1959 in Inner Mongolia. During 1960-2018, only nine human plague cases with two deaths occurred in Inner Mongolia (*5*). The most recent human plague cases were reported from this focus in 2004, and as with Patient C, were due to skinning a dead hare (*6*).

There are four plague foci in Inner Mongolia (*7*). These are an *M. unguiculatus* plague focus in the Inner Mongolian Plateau, a *Microtus brandti* plague focus in the Xilin Gol Grassland, a *Spermophilus Dauricus* plague focus in the Song-Liao Plain and a *Marmota sibirica* plague focus in the Hulun Buir Plateau (a silent plague focus). The *M. unguiculatus* plague focus in Inner Mongolia can be divided into two parts - the Ordos plateaus and the desert steppe of the Ulanqab plateaus. The *S. dauricus* focus includes the Song-Liao plain hills and the dry steppe of Qahar area (*5*).

Combining previous plague epizootic data (*5*) and recent surveillance data, the Inner Mongolia animal plague epidemic can be divided into four phases, as illustrated in Table 1. The Inner Mongolia plateau focus of *M. unguiculatus* was first identified in 1954. The total area of this focus is 134,803 km^2 and encompasses 22 counties (Qi) in the middle and western parts of Inner Mongolia (*5*). In the last 5 years, the Inner Mongolia natural foci of animal plague has been active. In 2019, virulent animal plague epidemics occurred in this focus, which has a high density of rats.

Since the founding of the People's Republic of China, this is the first instance in which pneumonic plague was imported into a major city in China. Although clearly a transported case, awareness and appropriate measures should always be implemented. These three cases can provide important lessons for public health practitioners.

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TABLE 1. Animal plague epidemics in Inner Mongolia in the last 70 years.

Phase	Years	Main host in epizootic	Plague sub-focus †
First epizootic	1954-1955	*S. dauricus*	Qahar area (1985-1989)
Second epizootic *	1969-1972	*M. unguiculatus*	Ordos plateau, Ulanqab plateaus (1968-1969)
		S. dauricus	Qahar area (1970)
Third epizootic	1973-1998	*M. unguiculatus*	Ordos plateau (1973-1976,1987-1990,1996)
			Ulanqab plateaus (1974,1979,1991)Baoto City (1982,1985)
		S. dauricus	Song-Liao Plain (1985-1989)
			Qahar area (1973-1974, 1988-1994)
Fourth epizootic	2001-2019	*M. unguiculatus*	Ordos plateau (2015, 2016)
			Spread throughout all *M. unguiculatus* plague focus (2019)

*Virulent animal plague epidemics occurred in the second phase. The epidemics swept all three foci of Inner Mongolia. †*Microtus brandti* plague focus of the Xilin Gol Grassland was not included because the *Y. pestis* isolated in this focus was considered to have low pathogenicity to humans.

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