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Recommendations

Recommendations of Controlling and Preventing Acute Health Risks of Fine Particulate Matter Pollution — China, 2021

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Editorial An expert consensus is the unanimous recognition of experts from multiple disciplines on specific research topics based on scientific evidence and interpretation. This expert consensus on recommendations of controlling and preventing acute health risks of fine particulate matter pollution completes the drafting process that was initiated by selecting several influential experts from different professional fields to form a writing group. After that, the membership of experts was expanded and opinions were obtained from various experts through email, focused discussions, and expert tribunals. Finally, the drafts were revised and feedback was provided until the expert members reach a consensus and formed the final consensus draft. This consensus provides scientific reference for improving and optimizing China's air pollution prevention and control policies, scientific guidance for public health protection, and research directions for carrying out related scientific research. In order to share the recommendation domestically and internationally, the Chinese version is jointly published in the *National Medical Journal of China*.

Summary

The task force has comprehensively reviewed efforts for air pollution prevention and control, the acute health effects of fine particles ($PM_{2.5}$), and the health benefits of air pollution prevention and control in China. It has been found that the overall prevention and control of ambient $PM_{2.5}$ pollution in China has made remarkable progress in recent years. However, it still remains at a relatively high level. Short-term exposure to ambient $PM_{2.5}$ significantly increases the mortality and morbidity risk of Chinese residents, resulting in changes to levels of relevant biological markers. Prolonged $PM_{2.5}$ heavily polluted weather greatly increases the risk of cardiovascular disease morbidity and mortality. Among chemical composition of $PM_{2.5}$, carbon-containing components, some inorganic salts, and heavy metals are linked with the health impacts. The health risks of $PM_{2.5}$ pollution are higher for children, the elderly, and patients with cardiovascular or respiratory diseases than for the general population because the former groups are vulnerable subpopulations. The implementation of air pollution prevention and control policies has significantly improved human health. The implementation of personal protective equipment can significantly reduce the health damage caused by short-term exposure to ambient $PM_{2.5}$ pollution. Based on scientific evidence of $PM_{2.5}$ pollution and acute health risks in China, the following three recommendations are proposed. 1) The policy recommendations for the prevention and control of ambient $PM_{2.5}$ pollution include the following: to continuously strengthen the widespread use and efficient development of clean energy; to further promote industrial upgrading; to focus on the control of transportation pollution; to keep improving the modernization system of air pollution control; to formulate and refine relevant standards for air quality gradually; and to estimate the effects and health benefits after the implementation of clean air actions, and relevant policies. 2) Prevention of ambient $PM_{2.5}$ pollution and protection of public health recommendations include the following: to strengthen the release of air pollution monitoring and relevant information; to strengthen awareness of air pollution hazards; to clarify the guidance and recommendations for protecting population health from air pollution; and to strengthen the health protection of population vulnerable to ambient air pollution. 3) Recommendations for research on health risks of air pollution include the following: to strengthen research on air pollutant monitoring technology and monitoring system based on the promotion of accurate exposure assessment; to systematically carry out full-spectrum identification and correlation studies of air pollutants and health effects; to conduct studies on key toxic components and early biomarker inventory of air pollution health effects; to discover the toxicity mechanisms of the key toxic components of air pollutants; to carry out research on population health risk assessment and early warning of combined exposure to air pollutants; and to execute comprehensive studies on the health and economic benefits of pollution and carbon reduction under the national strategies of carbon neutrality and beautiful China.

INTRODUCTION

The Global Burden of Disease Study 2019 data showed that ambient fine particulate matter ($PM_{2.5}$) is the fourth highest risk factor in the global burden of disease (*1*). In China, about 1,432,633 premature deaths were attributed to $PM_{2.5}$ during 2019 (*1*). It has an important impact on the occurrence, development, and prognosis of cardiovascular and respiratory diseases in the population. It has been a major environmental problem and an important health issue commonly faced by all countries in the world, especially developing countries (*2–4*). China currently experiences high levels of ambient air pollution. With rapid industrialization and urbanization, the prevention and control of air pollution is becoming more difficult. To this end, the State Council issued the "Air Pollution Prevention and Control Action Plan" in September 2013, implementing 10 measures for air pollution prevention and control and releasing and implementing the "Three-Year Action Plan to Win the Blue Sky Defense War" in June 2018. After years of continuous efforts, the overall ambient air quality of China has improved significantly. The average annual concentration of $PM_{2.5}$ has dropped from 72 μg/m^3 in 2013 to 33 μg/m^3 in 2020. Ambient inhalable particulate matter (PM_{10}), sulfur dioxide (SO_2), and carbon monoxide (CO) all showed remarkable downward trends, and the people's sense of the blue sky was significantly enhanced (*5–6*).

As an important measure to implement the "Air Pollution Prevention and Control Action Plan," the Ministry of Science and Technology released the national key research and development plan "Research on Air Pollution Causes and Control Technologies" special project in 2015, which aims to strengthen research and development on several aspects, including (1) the formation mechanism, source analysis, migration law, monitoring and early warning of air pollution; (2) the relationship between air pollution and human health; (3) air pollution control technologies such as desulfurization, denitrification, and high-efficiency dust removal; and (4) the transformation and application of technological achievements, providing scientific and technological support for pollution control. The implementation of this special project has strongly encouraged scholars to conduct extensive, in-depth, and systematic research on the scientific issue of "the relationship between air pollution and population health." The task force conducted a comprehensive review and in-depth discussion on the important innovative achievements in the field of acute health risks of ambient $PM_{2.5}$ pollution in recent years and formed this expert consensus in order to provide scientific evidence for the government and relevant professional institutions to develop relevant policies and/or strategic measures. It also aims to provide scientific information for clinicians, public health and environmental protection professionals to understand the acute health hazards of ambient $PM_{2.5}$ pollution, and to reduce air pollution exposure for the general public, including patients.

THE CURRENT SITUATION OF AMBIENT $PM_{2.5}$ POLLUTION IN CHINA

$PM_{2.5}$ refers to particulate matter with an aerodynamic equivalent diameter of less than or equal to 2.5 μm in ambient air. Its main sources include primary particulates and secondary particulate matter generated from the conversion of SO_2, nitrogen oxides (NO_x), ammonia, and volatile organic compounds emitted from fossil fuels (such as coal, gasoline, and diesel) and biomass combustion, metallurgy and chemical industries, vehicle exhaust, road dust, etc. The chemical composition of ambient $PM_{2.5}$ is very complex, usually consisting of carbon-containing components such as organic carbon and inorganic carbon, inorganic salt ions such as sulfate, nitrate and ammonium salt, and organic matters such as polycyclic aromatic hydrocarbons, metal elements, biological substances, and mineral dust.

Ambient $PM_{2.5}$ Pollution Control has Achieved Remarkable Results in China

The ambient air quality in China was not high a decade ago. In 2012, the first batch of 74 cities that implemented the new air quality standards had an average annual $PM_{2.5}$ concentration of 72 μg/m^3, which exceeded 106% of the secondary standard limit (annual average concentration of 35 μg/m^3) of the "Ambient Air Quality Standard" (GB 3095–2012) (*5*). With the release and implementation of the "Air Pollution Prevention and Control Action Plan," ambient $PM_{2.5}$ pollution has been effectively controlled. As of 2017, the annual average concentration of ambient $PM_{2.5}$ in 74 cities dropped to 47 μg/m^3, a decrease of 34.7% compared to 2013. The average number of days with air quality reaching the standard increased from 60.5% to 72.7%; the average concentration of ambient $PM_{2.5}$ in key regions such as Beijing-Tianjin-Hebei, the Yangtze River Delta, and the Pearl River Delta decreased by 39.6%, 34.3% and 27.7%, respectively (*7*). Due to the effective implementation of 6 important measures from 2013 to 2017, including upgrading the industrial sector, upgrading industrial boilers, eliminating outdated industrial production capacity, promoting the use of clean fuels in residents' lives, shutting down small polluting factories, and strengthening vehicle emission control, SO_2, NO_x, and primary $PM_{2.5}$ emissions in China decreased by 16.4 million, 8 million and 3.5 million tons, respectively (*8*). In 2020, the national ambient $PM_{2.5}$ pollution situation was further improved, and 87% of the 337 prefecture-level or higher cities met the air quality standard on average. The average annual concentration of $PM_{2.5}$ was 33 μg/m^3, lower than the secondary standard limit of "Ambient Air Quality Standards" (GB 3095–2012) (*6*).

Ambient $PM_{2.5}$ Pollution Is Still at a High Level in China

Currently, ambient $PM_{2.5}$ pollution levels in China are still relatively high, which is higher than the population-weighted annual $PM_{2.5}$ concentration in the United Kingdom, the United States, and other countries in the same time period (about 10 μg/m^3) (*9*), and far exceeding the air quality guidelines (5 μg/m^3) issued by the World Health Organization (WHO) in 2021. In 2020, 37.1% of the 337 cities (involved prefecture-level and municipality city) nationwide still have an average annual $PM_{2.5}$ concentration that does not meet the secondary standard limit of the "Ambient Air Quality Standards" (GB 3095–2012). At the same time, heavy pollution weather still occurs on a large scale across the country. In 2017, 2,311 days of heavy pollution occurred in those cities, and the number of days with heavy $PM_{2.5}$ pollution (daily average $PM_{2.5}$ concentrations higher than 150 μg/m^3) accounted for 74.2% of the days with heavy pollution and above (*7*). In 2020, the frequency of heavy pollution in the 337 cities was the same as in 2017, and the number of days with heavy $PM_{2.5}$ pollution accounted for 77.7% of the days with heavy pollution and above (*6*). From January to February 2020, the number of days with heavy $PM_{2.5}$ pollution in prefecture-level cities across the country was the lowest in the same period in record, which was reduced by 39.2% in the same period since 2015, and the number of hours with hourly $PM_{2.5}$ concentration exceeding 300 μg/m^3 has decreased by 47.8% compared to 2015. Among them, regional pollution was at a consistently high level in key polluted areas represented by Beijing-Tianjin-Hebei and the Fenwei Plain. In 2020, the average annual $PM_{2.5}$ concentration in Beijing-Tianjin-Hebei region was up to 51 μg/m^3, the average number of days exceeding the standard was 36.5%, and the number of days with $PM_{2.5}$ as the primary pollutant accounted for 48.0% of the total number of pollution days; the average annual concentration of $PM_{2.5}$ in the Fenwei Plain was up to 48 μg/m^3, the average number of days exceeding the standard was 29.4%, and the number of days with $PM_{2.5}$ as the primary pollutant accounted for 56.4% of the total number of days with pollution (*6*).

ACUTE HEALTH RISKS OF AMBIENT $PM_{2.5}$ POLLUTION IN CHINA

The acute health risk of ambient $PM_{2.5}$ pollution usually means that short-term exposure to $PM_{2.5}$ (exposure duration usually at the level of hours to days) may cause acute damage to the body, trigger the onset of symptoms or diseases (mainly cardiovascular or respiratory disease), and lead to premature death and a series of adverse health effects.

Short-term Exposure to Ambient $PM_{2.5}$ Significantly Increases the Mortality Risk of Residents in China

$PM_{2.5}$ is the primary air pollutant in China. Short-term exposure to $PM_{2.5}$ will significantly increase the risk of non-accidental death of residents in China, especially the risks of death from cardiovascular and respiratory diseases (*10*–*12*). A time series study of 272 cities in China found that from 2013 to 2015, the annual average concentration of $PM_{2.5}$ across all cities was 56 μg/m^3. At this concentration level, the percentage increase in the risk of mortality due to non-accidental causes, cardiovascular diseases, and respiratory diseases per 10 μg/m^3 increase in $PM_{2.5}$ from lag0 to lag1 was 0.22%, 0.27%, and 0.29%, respectively (*10*). Compared to similar studies conducted in China and abroad, the relative risk of acute death of people exposed to short-term ambient $PM_{2.5}$ in China was lower than that in European and North American countries (*2–4*,*13*). A study investigating the association between ambient $PM_{2.5}$ and daily population death in 652 cities around the world found that per 10 μg/m^3 increase in $PM_{2.5}$ from lag0 to lag1, the risk of non-accidental death in the United States, Canada, Spain, and Greece increased by 1.58%, 1.70%, 1.96%, and 2.54%, respectively (*13*). The reason for the difference in effect estimates may be that the exposure-response relationship between $PM_{2.5}$ and death showed a nonlinear trend. The slope of the exposure-response relationship curve was larger at low concentration levels, thus the population death observed was more seriously affected by exposure to unit $PM_{2.5}$ concentration. With the increase of exposure level, the slope of the curve gradually decreases, and the curve becomes stable at higher exposure levels, indicating that the relative risk of acute death caused by $PM_{2.5}$ increases in a smaller magnitude (*13–14*). Currently, China is at a high exposure level of global $PM_{2.5}$ pollution concentration. For each unit level increase in $PM_{2.5}$ concentration, the relative risk of acute death in the Chinese population is relatively lower. In addition, the differences in effects may also be related to the chemical composition of $PM_{2.5}$ in different regions, climate characteristics, the health status of the study population, and the degree of socioeconomic development.

Short-term Exposure to Ambient $PM_{2.5}$ Significantly Increases the Incidence of Cardiovascular and Respiratory Diseases

Due to the small particle size and large specific surface area of ambient $PM_{2.5}$, it can enter the respiratory tract or be deposited in the alveoli, causing respiratory system damage and increasing the incidence of disease (*15–17*). Each 10 μg/m^3 increase in $PM_{2.5}$ (lag0 day) was associated with a 0.34% increase in the risk of hospitalization for respiratory diseases (including pneumonia, acute bronchitis, upper respiratory tract infection, chronic obstructive pulmonary disease, and bronchiectasis) in 252 cities in China (*15*); and each 10 μg/m^3 increase in moving average $PM_{2.5}$ (lag0–2 days) was associated with a 0.31% increase in the risk of hospitalization for pneumonia (*16*). Inhaled $PM_{2.5}$ enters the blood through macrophage phagocytosis and pulmonary capillaries and acts on the body's circulatory system, increasing the risk of cardiovascular diseases such as ischemic heart disease, stroke, and heart failure (*18–20*). A time series study of 184 cities in China from 2014 to 2017 found that a 10 μg/m^3 increase in the same-day $PM_{2.5}$ exposure was significantly associated with 0.26%, 0.31%, 0.27%, and 0.29% increases of hospital admissions for cardiovascular disease, ischemic heart disease, heart failure, and arrhythmia, respectively (*18*). A time series study of 248 cities in China from 2013 to 2017 found that a 10 μg/m^3 increase in $PM_{2.5}$ concentration was significantly associated with a 0.26% increase in same-day hospital admissions for ischemic stroke and transient ischemic attack (TIA) (*19*).

Prolonged Heavily $PM_{2.5}$ Polluted Weather Greatly Increases the Risk of Morbidity and Mortality

Heavy air pollution weather in China is usually characterized by persistent high concentrations of $PM_{2.5}$. Existing epidemiological evidence shows that prolonged heavily $PM_{2.5}$-polluted weather will greatly increase the risk of morbidity and mortality and cause more serious health problems (*21–23*). A study based on the continuous heavily polluted weather of ambient $PM_{2.5}$ occurred in Beijing from January 10 to 17, 2013, the average daily concentration of $PM_{2.5}$ was 231 μg/m^3, showed that compared with other periods in winter in 2013, emergency and outpatient risk of respiratory illness increased by 74% and 16%, respectively, during prolonged heavily polluted weather, indicating that continuous exposure to high concentrations of $PM_{2.5}$ has caused a substantial increase in the number of patients with respiratory diseases (*21*). Another time-stratified case-crossover study observed that persistent heavily or extremely heavily $PM_{2.5}$-polluted weather was associated with increased risk of cardiovascular disease hospitalization among Beijing residents. The odds ratios (ORs) associated with extremely heavy PM pollution events (PM concentration ≥150 μg/m^3 for 3 days or more) were 1.085, 1.112, 1.068, 1.071, and 1.060 for total cardiovascular disease, angina, myocardial infarction, ischemic stroke, and heart failure, respectively (*22*). The study also showed that the higher the concentration and the longer the duration of heavy pollution events, the greater the impact was on hospitalizations for various cardiovascular diseases (*22*). Among them, the risks of angina pectoris and ischemic stroke were more pronounced. However, existing research has not yet formed a unified standard for the definition of prolonged heavily $PM_{2.5}$ polluted weather (*21–23*), and the specific role of pollution concentration and duration in the health impacts of heavily polluted weather requires more researches.

The Chemical Composition of Ambient $PM_{2.5}$ is Related to the Degree of Health Hazards

Ambient $PM_{2.5}$ has a very complex chemical composition. Affected by factors such as local industrial pollution sources and energy structure, there are significant spatiotemporal differences in the chemical compositions of $PM_{2.5}$ across China. Current epidemiological studies believe that carbon-containing components (including organic carbon and elemental carbon or black carbon), some inorganic salts (mainly sulfates and nitrates), and metal elements [such as nickel (Ni), zinc, chromium, and lead] are closely related to health hazards caused by $PM_{2.5}$ (*24–28*). For example, a study on the acute effects of $PM_{2.5}$ chemical components on mortality in Xi'an found that organic carbon, elemental carbon, sulfate, and nitrate increased by an interquartile range (IQR) for 1-day lag, which were 19.3 μg/m^3, 8.8 μg/m^3, 27.8 μg/m^3, and 15.4 μg/m^3, respectively, will increase the risk of non-accidental, cardiovascular, and respiratory deaths in the population by more than 1%. An IQR increase of 0.01 μg/m^3 in 1-day lagged Ni was associated with 0.4%, 0.6%, and 0.9% increases in the risk of non-accidental death, cardiovascular, and respiratory mortality, respectively (*24*). A study on the acute effects of $PM_{2.5}$ chemical components on mortality in Beijing found that for a 0-day lag, an IQR (10.11 μg/m^3) increase in organic carbon was associated with 2.65% increase in respiratory mortality and an IQR (20.10 μg/m^3) increase in sulfate was associated with a 1.57% increase in cardiovascular disease mortality, and the acute death effect in the cold season was strengthened (*25*). The above chemical components mainly come from fossil fuel combustion (including coal combustion and vehicle emissions) and secondary particulate matters formed by ambient SO_2/NO_x. Their toxic effects are mainly produced by inducing oxidative stress and inflammatory responses. Greater $PM_{2.5}$-related acute health hazards could be observed when the content of these toxic chemical components was high (*24–28*).

Short-term Exposure to Ambient $PM_{2.5}$ Can Cause Changes in the Level of Biological Effect Markers Reflecting Early Health Damage in the Population

Epidemiological studies of the Chinese population have shown that ambient $PM_{2.5}$ mainly produces damage by causing oxidative stress and inflammatory responses in the body, as well as autonomic dysfunction. After $PM_{2.5}$ is inhaled through the respiratory tract, changes in biomarkers of lung inflammation could be observed in a short period of time, followed by systemic inflammatory response and oxidative stress, resulting in changes in the levels of biomarkers related to cardiovascular effects such as coagulation, vasoconstriction, and vascular endothelial function (*27–33*). Short-term exposure to $PM_{2.5}$ could also activate the human "hypothalamus-pituitary-adrenal axis," affecting cardiovascular health through the neuro-endocrine pathway (*31*). In a fixed panel study of healthy and prediabetic people (50–65 years old), increased $PM_{2.5}$ exposure was associated with an increment in exhaled nitric oxide (FeNO) (*34*). In a randomized double-blind controlled intervention trial of healthy college students, the reduction of $PM_{2.5}$ exposure significantly reduced the level of exhaled FeNO (*35*). The possible mechanism of cardiovascular system damage caused by short-term exposure to ambient $PM_{2.5}$ is relatively complex. In addition to triggering a systemic inflammatory response and oxidative stress, it can also cause autonomic dysfunction and changes in coagulation function, destroy vascular endothelial structure, and damage endothelial function (*35–38*). A randomized double-blind controlled intervention trial found that high $PM_{2.5}$ exposure can cause an increase in inflammatory markers such as soluble CD40 ligand (sCD40L), interleukin-1β (IL-1β), and C-reactive protein (CRP), as well as blood pressure in healthy college students (*31*). With the decrease of $PM_{2.5}$ exposure, soluble sCD40L, IL-1β, and blood pressure of healthy college students were significantly reduced (*35*). Another randomized double-blind cross-over controlled trial conducted during a typical haze event found that a 10 μg/m^3 increase in time-weighted individual $PM_{2.5}$ exposure concentration was significantly associated with an increment of 1.31%–5.33% in cytokine concentrations of IFN-α2, GM-CSF, IL-1RA, sCD40L, IL-4, MIP-1α, MCP-1, Eotaxin, and FGF-2, respectively, in circulatory system (*39*). A study on air pollution and cardiovascular dysfunction in healthy adults in Beijing found that short-term $PM_{2.5}$ exposure was associated with increased levels of atherosclerotic plaque damage or thrombosis-related markers such as fibrinogen, CRP, and IL-1β (*33*). Due to the wide range of health effects of $PM_{2.5}$ exposure, in addition to the cardiovascular and respiratory systems, it may also act on the genitourinary system, causing a decrease in glomerular filtration rate (*40*) and the total number and concentration of sperm (*41*).

Children, the Elderly, and Patients with Cardiovascular and Respiratory Diseases are Groups Vulnerable to Ambient $PM_{2.5}$ Pollution

Several studies have confirmed that children, the elderly, and patients with cardiovascular and respiratory diseases are vulnerable groups for ambient $PM_{2.5}$ pollution (*10–11*,*42–43*). The respiratory system of children was more susceptible to the harm of ambient $PM_{2.5}$ than that of adults, and short-term exposure to $PM_{2.5}$ could result in an increase of FeNO exhaled by children (*30*,*43–46*) and increased airway resistance, causing asthma attacks (*44*). The reduction of $PM_{2.5}$ exposure would greatly reduce the level of exhaled FeNO (*30*). Short-term exposure to $PM_{2.5}$ can also cause an increase in heart rate and norepinephrine in preschool children, resulting in damage to the sympathetic-adrenal medulla (*44*). Both time series studies conducted in 272 cities and 130 districts and counties in China found that short-term exposure to $PM_{2.5}$ significantly increased the risk of non-accidental deaths and cardiovascular disease deaths in the elderly over 75 years old, and its increased risk of death exceeded the acute effect of $PM_{2.5}$ on death in the general population (*10–11*). In addition, patients with cardiovascular and respiratory diseases are particularly sensitive to $PM_{2.5}$ exposure, and short-term exposure will cause oxidative stress damage to their cardiovascular and respiratory systems, causing dysfunction and reduction, and subsequently increasing their incidence rates. In patients with chronic obstructive pulmonary diseases, a 10 μg/m^3 increase in daily average $PM_{2.5}$ concentrations was associated with a 26 mL decrease in forced vital capacity (FVC), a 26 mL decrease in forced expiratory volume in 1 second (FEV_1), and a 0.96% decrease in FEV_1% (*46*). $PM_{2.5}$ exposure for 0–6 hours significantly increased the levels of serum fibrinogen, CRP, tumor necrosis factor-α (TNF-α), and other biomarkers in patients with chronic obstructive pulmonary disease (*32*). The results of a cohort study of 4 cities (Beijing, Shanghai, Wuhan, and Xi'an) in high-risk groups of cardiovascular disease showed that an increase of 1- to 9-hour moving average $PM_{2.5}$ concentration was associated with 0.22 to 0.39 mmHg increase in systolic pressure, while the effect of $PM_{2.5}$ was attenuated in patients with controlled blood pressure (*47*).

HEALTH BENEFITS OF $PM_{2.5}$ POLLUTION PREVENTION AND CONTROL IN CHINA

The Implementation of Air Pollution Prevention and Control Policies has Significantly Improved the Public Health

During the implementation of the "Air Pollution Prevention and Control Action Plan," air pollution represented by $PM_{2.5}$ was effectively controlled, and the health benefits of the population were significant (*48–52*). A study on the health benefits of emission reduction scenarios based on short-term exposure-response relationships estimated that if the average daily concentration of ambient $PM_{2.5}$ reached the current ambient air quality secondary standard (75 μg/m^3), a total of 69,000 years of life lost could be avoided and increase life expectancy by 0.06 years among residents of 72 cities in China. Reaching the WHO-recommended transitional target 2 (25 μg/m^3) could avoid a total of 168,000 years of life lost each year and increase life expectancy by 0.14 years (*48*). A study simulating the annual ambient $PM_{2.5}$ concentration via chemical transport model and estimating the health benefits under emission reduction policy scenarios during 2013–2017, considering the chronic exposure-response relationship, demonstrated that the deaths due to the $PM_{2.5}$ were reduced from 1.389 million in 2013 to 1.102 million in 2017 in China, of which, 88.7% of contributions were from emission reductions (*49*). A long-term health benefits study focusing on emissions reduction policies in 74 cities across the country estimated that the $PM_{2.5}$ pollution was reduced by 33.3%, the death number of people due to the $PM_{2.5}$ pollution was reduced by 47,000, and the years of life lost were avoided by 710,000 years. The number of the deaths attributable to $PM_{2.5}$ pollution decreased by 26,000 premature deaths, and the years of life lost attributable to $PM_{2.5}$ were avoided by 390,000 years in Beijing-Tianjin-Hebei, the Yangtze River Delta, and the Pearl River Delta regions (*50*). Other studies have pointed out that measures such as civilian clean energy replacement will reduce indoor and outdoor $PM_{2.5}$ pollution levels simultaneously and further improve human health (*51*). For example, the integrated population-weighted exposure to $PM_{2.5}$ (IPWE) in China decreased by 47% from 2005 to 2015; 90% of the reduction was attributed to the reduction in the use of household solid-fuel, and the resulting health benefits were the avoidance of around 0.40 million premature deaths annually. If we replaced the remaining household solid fuels with clean fuels, an additional 0.51 million premature deaths would be avoided (*51*). It is worth noting that the potential benefits of emissions reduction with end-of-pipe control will be exhausted by 2030. In order to reduce the air pollution level in China to the value recommended by the WHO and effectively protect public health from pollution effects, a deep transformation of low-carbon energy under the goal of the carbon neutrality is crucial (*52*).

The short-term implementation of air pollution control policies has greatly improved air quality and brought certain population health benefits. During the 2008 Beijing Olympic Games, a series of measures to control industrial emissions and traffic pollution were implemented, and the concentration of ambient particulate matter was significantly reduced. Consequently, the economic costs associated with human health decreased by 38% and 16% before and after the Beijing Olympic Games, respectively (*53*). During the meeting of Asia-Pacific Economic Cooperation (APEC) held in November 2014 (12 days) and the military parade to commemorate the 70th anniversary of the victory of the Chinese People's War of Resistance against Japanese Aggression in September 2015 (15 days), the short-term air pollution control policies have also been carried out in Beijing. During the 2 events, the ambient $PM_{2.5}$ concentration was decreased by more than 40% compared with that before the event in Beijing. According to estimates, 39–63 and 41–65 deaths were avoided due to the decrease in $PM_{2.5}$ concentration during the APEC meeting and the military parade, respectively (*54*).

Implementation of Individual Protective Interventions Can Significantly Reduce Health Damage from Short-Term Exposure to Ambient $PM_{2.5}$

With the deepening of awareness of the health hazards of the $PM_{2.5}$ pollution, the utilization rate and popularization range of personal protective measures such as air purification devices and wearing masks have increased and expanded significantly. A number of current intervention studies have shown that the proper wearing of masks or using air purifiers can reduce individual $PM_{2.5}$ exposure effectively, thereby reducing their health hazards to varying degrees (*30–31,37,55–57*). A randomized double-blind controlled intervention trial using N95 masks as an intervention measure showed that the use of masks for protection in heavily polluted weather could reduce the levels of serum inflammatory markers and $PM_{2.5}$-related airway inflammatory responses in healthy young people (*55*). Another randomized crossover study of healthy young adults observed that the wearing particulate-filtering respirators in a short-term might reduce cardiovascular risks through enhancing the function of autonomic nervous and decreasing blood pressure (*56*).

A randomized double-blind crossover study which took healthy college students as the research object found that the $PM_{2.5}$ average concentration in the environment with air purifiers was much lower than that in the environment without air purifiers, and higher $PM_{2.5}$ environmental exposure might induce metabolic alterations associated with the hypothalamus-pituitary-adrenal and sympathetic-adrenal-medullary axes activations, indicating that air purification measures could effectively reduce the health damage caused by $PM_{2.5}$. A randomized double-blind crossover experiment on school-aged children also observed that air purifiers had a good removal effect on indoor particles of different sizes and could protect the respiratory health of children by increasing energy production and anti-inflammatory and antioxidant capacities (*30,57*).

MAIN RECOMMENDATIONS ON PREVENTION AND CONTROL OF AMBIENT $PM_{2.5}$ POLLUTION IN CHINA

Recommendations on Policy Development for Prevention and Control of Ambient $PM_{2.5}$ Pollution

At present, the situation of air pollution in China is still severe, the ambient $PM_{2.5}$ concentration is still relatively high, and the ozone (O_3) pollution has not been effectively controlled and even has an upward trend in some areas. Exposure to various air pollutants together threatens the health of local residents. Air pollution is a clear hazard to human health, and when measures are taken to reduce air pollution, it can bring significant health benefits. This complies with the primary prevention requirements of the three categories of the prevention strategy. Therefore, the task force recommends that the policies for preventing and controlling air pollution should be formulated by reducing source emissions and strengthening regional control to further reduce the level of air pollution and promote the continuous improvement of the health of residents by focusing on the national strategic goals of beautiful China and healthy China in combination of the mission requirements of carbon peaking and carbon neutrality.

First, the widespread use and efficient development of clean energy should be continuously strengthened. It is necessary to strengthen source control through energy structure reform, reduce the proportion of fossil energy consumption, and build a new energy system with hydropower, nuclear power, solar power, and wind power as the main components. Energy coupling technology should be vigorously developed to increase energy efficiency, and at the same time, the application of clean energy for civilian use should be promoted. As a result, a green and efficient energy system should be ultimately formed, which will control source emissions of air pollution and improve the health benefits brought by energy structure improvement.

Second, the promotion of industrial upgrading should be continued. Measures should be taken to strictly limit high energy consumption and high emission enterprises and accelerate the development of low energy consumption and low emission enterprises. The research and promotion of cleaner production technology should be increased to provide assistance for industrial upgrading. Rational industrial structure composition should be planned to enhance regional pollution control benefits.

Third, pollution in the transportation sector should be effectively controlled. According to the development characteristics of large cities, the number of vehicles should be controlled and the proportion of energy-saving and environmentally-friendly vehicles should be expanded via planning. It is necessary to gradually improve the fuel quality and emission standards of vehicles, vigorously develop urban green transportation, and increase the proportion of clean transportation. The health benefits of urban populations would be increased by comprehensively improving the level of cleanliness in the transportation field through multiple measures and reducing the proportion and level of pollution from transportation sources.

Fourth, the modernization of the air pollution control system should be continuously enhanced. Regular capacity building such as laws and regulations, policy mechanisms, monitoring, and supervision should be further deepened from a scientific perspective. Combined with carbon peaking and carbon neutral policy situations to optimize the construction framework of the system, carbon emission control and related contents should be included in the current air pollution control chain. The coordinated management should be strengthened to realize the dual reduction goal of carbon emission and air pollution. In the meantime, it is necessary to guide and encourage the public to adopt a green and low-carbon lifestyle and increase the participation of the whole society in pollution reduction and carbon reduction policies.

Fifth, the formulation and revision of relevant air quality standards need to be carried out gradually. Compared with the air quality guidelines issued by the WHO, combined with the latest research evidence on the health impacts of air pollution, and according to the actual situation in China, the current standards for air quality should be revised. Air pollution prevention and control should be ensured by gradually tightening the standard limits of air pollutants and increasing the protection of human health from a legal perspective.

Sixth, effects after the implementation of clean air actions and policies should be estimated, including the health benefits assessment after the implementation of relevant policies. The policies formulated and implemented by various localities for the prevention and control of air pollution should be evaluated regularly. The prevention and control policy can be optimized by screening the level of pollution concentration reduction and the degree of health benefits. Local governments are encouraged to prioritize measures that maximize population health benefits when formulating air pollution control programs.

Recommendations on Public Health Protection Linked with the Prevention and Control of Ambient $PM_{2.5}$ Pollution

Combined with the existing evidence of the impact of air pollution on human health, the research advances of human health protection, and the new air quality guideline value issued by the WHO, multiple measures should be taken to improve the public's awareness of the health hazards of $PM_{2.5}$ pollution, strengthen scientific protection capabilities, improve the overall health literacy of the public, and reduce health damage caused by $PM_{2.5}$ exposure.

First, the release of air pollution monitoring and relevant information should be strengthened and the formulation of protection policies should be promoted to ensure that the public is informed. Accurately and promptly release pollution and health-related information to ensure that the public could grasp information on changes in pollution and can take timely health protection measures and change outdoor activities. Based on the continuously strengthened air pollution monitoring network, more valid data can be obtained. By comprehensively analyzing these environmental data and health impact data, it is possible to formulate effective pollution control and health protection policies in China.

Second, the propagation of air pollution health hazards should be enhanced to help the public to understand the health hazards of air pollution and the benefits of prevention and control, and improve their relevant knowledge base. Knowledge of air pollution health hazards should be widely publicized through health education via new media dissemination, communities, healthcare institutions, primary medical staff and other channels and forms. In addition, scientific measures of health protection against air pollution should be demonstrated to promote the public to understand relevant information and strengthen risk awareness. Improve the public's awareness of the health hazards of air pollution, and improve their knowledge reserve for taking timely and effective health protection behaviors.

Third, air pollution health protection guidance and recommendations should be clarified and the operability should be improved to ensure the effectiveness of public health protection. According to the air quality forecast or warning information released by relevant agencies and combined with the results of some pollution prevention studies, different air pollution health protection guidance and suggestions could be given. These suggestions include formulating reasonable outdoor travel arrangements, correctly wearing masks that filter $PM_{2.5}$ when going out, opening windows for indoor ventilation in a timely and appropriate manner according to air quality conditions, and using purification equipment to reduce indoor $PM_{2.5}$ concentrations when the air pollution is heavy. Through the above practical guidance and suggestions, the protection skills of the public against air pollution can be effectively improved.

Fourth, it is necessary to strengthen the health protection of sensitive groups who are vulnerable to air pollution and reduce the exposure risk of the $PM_{2.5}$ for sensitive groups. For vulnerable groups such as children, the elderly, and patients with cardiovascular and respiratory diseases, the guidance and recommendations for individual protection should be targeted. The risk prevention awareness and self-protection ability of vulnerable groups should be improved through continuous health education and information dissemination in specific locations (such as hospitals, communities, kindergartens, nursing homes, and schools). This will enable these vulnerable groups to take correct protective measures based on air quality forecasts and their own characteristics to reduce health hazards caused by air pollution.

Recommendations on Research for Assessing Population Health Risks of Air Pollution

At this stage, studies focusing on acute health risks of the $PM_{2.5}$ pollution in China have basically clarified the impact of short-term exposure to $PM_{2.5}$ on local residents' health. Since the air pollution level in China is much higher than the air quality guidelines recommended by the WHO, and the health consequences of air pollution are a long-term and complex process, it is of great social and economic benefits to continue to carry out in-depth scientific research in this field. Based on the current research hotspots and technical difficulties, the task force recommends that the related research on air pollution and population health should be strengthened from the following six aspects during "the Fourteenth Five-Year Plan" period.

First, strengthen the research on air pollutant monitoring technology and monitoring system based on the promotion of accurate exposure assessment. Combined with new technologies and methods, high-density, high-precision, and real-time air pollution monitoring stations should be established; research on population and individual exposure assessment and monitoring methods should be strengthened, and the research and development of exposure model simulation and source apportionment technologies should be promoted. Based on the current monitoring system, the refined exposure data should be gradually included, and the types of air pollutants that can be monitored could be expanded. This enables monitoring systems to include both large-scale regional data and nationally mandated pollutant data, as well as small-scale individual exposure data and key pollutant data. The monitoring system can provide data support for subsequent identification and traceability of key toxic components of different types of air pollutants, as well as carrying out research on air pollution-related health effects.

Second, a full-spectrum identification and correlation study of air pollutants and health effects should be systematically carried out. Through targeted and non-targeted high-throughput screening technologies, the analysis of the $PM_{2.5}$ pollution spectrum should be carried out in-depth, and the identification of gaseous pollutants including volatile organic compounds (VOCs) should be gradually carried out. The acute and chronic health effects of air pollution in China on different human systems and the joint effects of the $PM_{2.5}$ and the O_3 should be further explored. It should be concentrated on sorting out the full health effect spectrum of $PM_{2.5}$ and gaseous pollutants and carrying out correlation research to support further identification of typical health hazards and degrees of specific substances in the pollution spectrum.

Third, studies on key toxic components and early biomarker inventory of air pollution health effects should be carried out. Based on the obtained full spectrum of the association between air pollution and health, systematic evaluation and toxicological verification studies of key components and effect biomarkers should be carried out via population epidemiological survey methods. Health impact assessment indicators should be established to dynamically monitor the health effects of the $PM_{2.5}$ and its components. And carried out stepwise and cross validation for potential key components and biomarkers through research methods at different levels of evidence. Key components and early health effect biomarkers with high sensitivity and specificity that have been consistently validated in the cell, animal, and human studies could be included in the inventory. It can provide a scientific basis for the early detection and early intervention of the health effects of air pollution in China.

Fourth, the toxicity mechanism of key toxic components of air pollutants should be explored. Based on multi-omics technologies such as genome, epigenome, transcriptome, metabolome, proteome, and gut microbiome, research on the molecular mechanism of the impact of air pollution on human health should be systematically carried out. It can also explain the relationship between key toxic components of air pollutants and related diseases, key toxic pathways, and molecular mechanisms, in order to provide a possible toxicological mechanism basis for explaining the causal relationship between air pollution and health effects in China.

Fifth, research on health risk assessment and early warning of combined exposure to air pollutants should be carried out. In view of the characteristics of complex ambient pollution in China, combined with high-precision exposure assessment, the health risk characteristics of regional air pollution should be accurately quantified to reveal regional risk levels for different types of air pollutants. It is necessary to actively carry out research on air pollution health risk early warning, further promote health risk intervention research after the early warning is released, provide the public with risk warning according to local conditions, improve public health service capabilities, and reduce health risks caused by air pollution. Research on disease prevention and control closely related to air pollution should be strengthened to accurately assess and estimate the health benefits of the population under air pollution reduction measures, and to promote the formulation of air pollution and health prevention and control strategies focusing on "health risk control."

Sixth, research on the health and economic benefits of pollution reduction and carbon reduction under the carbon neutrality and beautiful China strategies should be carried out. Economy, energy, and emissions scenarios for China to achieve carbon neutrality and beautiful China strategies should be established. At the same time, by coupling the global change assessment model, global climate model, and regional meteorological-chemical model, the regional air pollution and climate change trends in China under different scenarios could be predicted. The acute health impacts of air pollution from various emergencies, including the COVID-19 pandemic and policy responses, should be assessed. Combined with the latest epidemiological evidence, the health benefits from improved air quality and climate change mitigation could be quantified, and the comprehensive economic costs of pollution and carbon reduction and health co-benefits could be estimated.

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Preplanned Studies

Effects of Cold Spells on Mortality — Ningbo City, Zhejiang Province, China, 2014–2018

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Summary

What is already known about this topic?

In recent years, climate change may lead to an increase in cold spells in the middle latitudes, and there is a positive correlation between cold spells and population mortality.

What is added by this report?

The acute response period and the vulnerable population were identified under the optimal definition of cold spells, and the mortality burden caused by cold spells were estimated.

What are the implications for public health practice?

This research would provide evidence on the acute mortality effects of cold spells in southern China. Therefore, vulnerable populations, especially the elderly, should take timely measures to reduce the health damage caused by cold spells, especially in the first week after cold waves.

The frequency of extremely cold events has gradually decreased due to globing warming around the world, but there are cold spells caused by the continuous transfer of the Arctic polar vortex in the mid-latitude regions (*1*–*2*). As most cities in China are located in mid-latitude areas, the frequency of cold waves is expected to increase, especially in southern China. A study showed that the cold spells in 2008 swept through south-central China, resulting in a sharp mortality increase with estimated losses exceeding US $22.3 billion (*3*). Additionally, the varying tolerance and adaptability of populations in different regions led to inconsistencies on the definition of cold spells and its health effects in different regions (*4*). This study applied time-stratified case-crossover analysis to explore the associations between cold spells and mortality during different lag periods and among different population groups during cold months of 2014–2018 in Ningbo City, China. The mortality burden attributed to cold spells was also estimated. It was found that an acute effective response period appeared within about a week. Circulatory and respiratory system diseases were sensitive diseases and the elderly over 65 years old were more vulnerable. About 21.6% deaths could be attributed to cold spells.

The daily death data, meteorological data (e.g., temperature), and air pollution data (eg. $PM_{2.5}$, O_3) during 2014–2018 came from Ningbo CDC, China Meteorological Administration, and Ningbo Environmental Protection Bureau. The research period was defined as the November–March of each year from 2014 to 2018 to exclude the impact of heatwave events. We defined cold spells as days when the daily mean temperature was at or below the P_{10} (5.5 ℃) or P_5 (3.9 ℃) percentile for at least 2, 3, or 4 consecutive days of the study period (1=cold spell days, 2=non-cold spell days). We compared the results of different definitions and selected the optimal one for stratified analysis to identify potential vulnerable populations and sensitive diseases.

The associations between cold spells and mortality were investigated in a two-stage analysis. First, the associations between cold spells and mortality were estimated by using a time-stratified case-crossover design combined with a distributed lag non-linear model (DLNM) (*5*), controlling for relative humidity and air pollutants. In order to identify the temporal characteristics of cold spells, we assessed the associations during different lag periods. Stratified analysis by sex, age, and cause of mortality were also conducted to identify sensitive diseases and vulnerable populations. Second, the attributable fractions (AFs) were estimated according to the associations between cold spells and mortality to evaluate the attributable mortality burden of cold spells (*6*). In addition, the stability of the model was validated by conducting sensitivity analysis (Supplementary Table S1, available in http://weekly.chinacdc.cn/). All analyses were implemented by using R statistical software (version 4.0.2, The R Foundation for Statistical Computing, Vienna, Austria).

During the study period, the total number of deaths was 83,532. The average daily mean temperature was 9.1 ℃ and the daily mean deaths of all causes were 120±19 per day (Table 1). This study shows the summary information of cold spells under different definitions (Supplementary Table S2, available in http://weekly.chinacdc.cn/). Under the same temperature threshold, the shorter the duration, the more cold spells and days would occur.

Figure 1 depicted the lag responses of associations between cold spells under 6 different definitions and the mortality. All cold spells had a non-linear effect on the risk of total death. The death risk showed a trend of decreasing first and then increasing, and it was the largest on the day of exposure (lag0).

According to the lag effects, the cumulative relative risks (CRR) of total mortality associated to cold spells under different definitions were obtained for different lag periods (lag0, lag0–7, lag0–14, and lag0–21) (Supplementary Table S3, available in http://weekly.chinacdc.cn/). Based on the value of CRR, we selected "cold spell A" (temperature threshold $\leq P_5$, duration ≥2d) as the best cold spell definition to conduct the stratified analysis by sex, age, and cause of death. Under the "cold spell A", the value of CRR increased with the increasing of lag periods. While a sharp increment of CRR value on lag0–7 was detected (Table 2), which indicated that there was an acute effect period about 7 days after the cold spell appeared.

The CRR for males and females were 1.322 [95% confidence interval (CI): 1.171, 1.493] and 1.220 (95% CI: 1.068, 1.394), respectively, within 21 days after cold spell happened compared with non-cold spell periods. The people above 65 years old increased the most when cold spell appeared, the CRR was 1.325 (95% CI: 1.186, 1.481). No statistically significant association was found for the people of 0–14 years, and the CRR was 1.772 (95% CI: 0.613, 5.120).

The CRR of death from respiratory diseases and circulatory diseases were 1.444 (95% CI: 1.173, 1.777) and 1.465 (95% CI: 1.261, 1.702) on lag0–21,

TABLE 1. Summary statistics of meteorology, air pollution, and mortality of cold season in 2014 to 2018 in Ningbo City, China.

Variable	N	`X (SD)	M (P_{25}, P_{75})
Meteorology			
Daily mean temperature (℃)	/	9.1 (4.8)	8.6 (5.6, 12.4)
Relative humidity (%)	/	79.4 (12.5)	81 (71.3, 89)
Average pressure (hPa)	/	1,023.9 (5.5)	1,024 (1,020, 1,027.8)
Air pollution			
$PM_{2.5}$ (μg/m³)	/	52.4 (29.9)	46 (31, 66)
O_3 (μg/m³)	/	73.1 (29.9)	73 (53, 92)
PM_{10} (μg/m³)	/	80.2 (42.1)	71 (49, 101)
CO (mg/m³)	/	1.0 (0.3)	0.9 (0.8, 1.1)
Death data			
All causes of death	83,532	120 (19)	119 (107, 132)
Sex			
Female	37,006	53 (11)	53 (46, 60)
Male	46,526	67 (12)	66 (59, 74)
Age (years old)			
15–65	16,291	23 (5)	23 (20, 27)
>65	66,771	96 (18)	94 (84, 106)
Cause of mortality			
Respiratory diseases	13,101	19 (6)	18 (14, 23)
Circulatory system diseases	26,550	38 (9)	38 (32, 44)
Genitourinary system diseases	933	1 (1)	1 (0, 2)
Endocrine system diseases	2,724	4 (2)	4 (2, 5)

Note: "/" means not applicable.
Abbreviations: N=total deaths; `X=mean; SD=standard deviation; M=median; P_{25}=the 25th percentile; P_{75}=the 75th percentile.

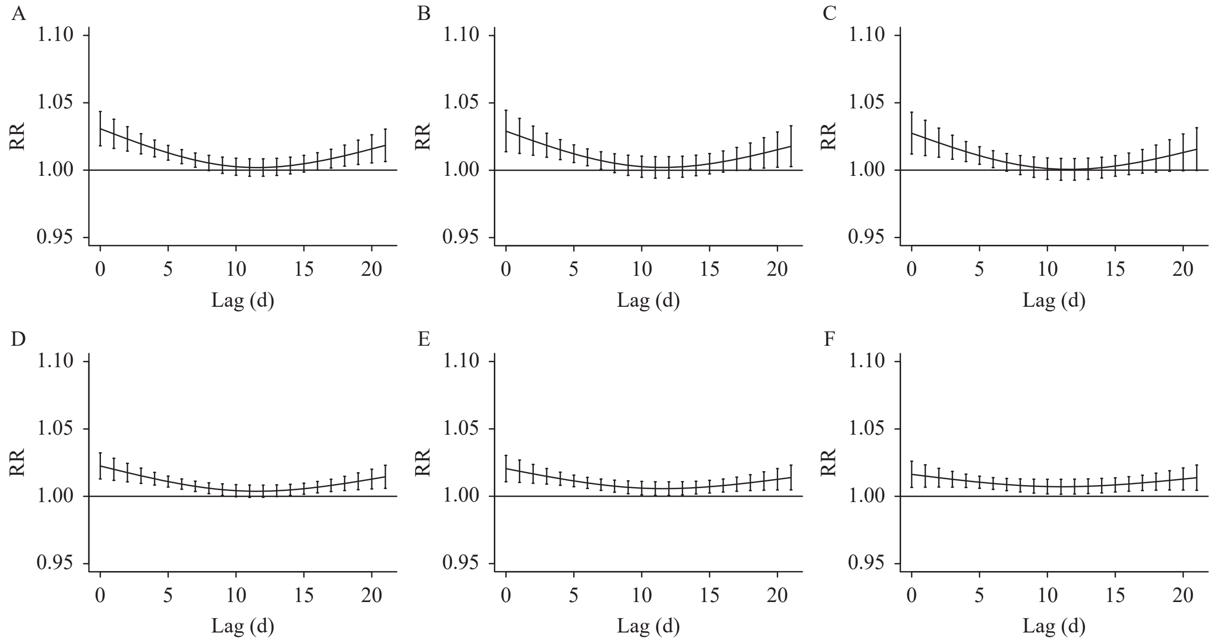

FIGURE 1. Lag-response associations between cold spells and total death under 6 different definitions in cold seasons of Ningbo, China, 2014–2018.
Note: "A–F" refers to 6 different definitions of cold spells, which were defined as days when the daily mean temperature was at or below the P_{10} (5.5℃) or P_5 (3.9℃) percentile for at least 2, 3, or 4 consecutive days during the study period. (A) P_5, ≥2 consecutive days; (B) P_5, ≥3 consecutive days; (C) P_5, ≥4 consecutive days; (D) P_{10}, ≥2 consecutive days; (E) P_{10}, ≥3 consecutive days; (F) P_{10}, ≥4 consecutive days.
Abbreviations: P_5=the 5th percentile; P_{10}=the 10th percentile; RR=relative risk.

TABLE 2. The cumulative relative risks and attributable fractions of mortality caused by cold spell for different populations.

Variables	CRR (95% CI)				AF, %(95% CI)
	Lag0	Lag0–7	Lag0–14	Lag0–21	Lag0−21
Total death	1.031 (1.018, 1.044)*	1.156 (1.095, 1.221)*	1.181 (1.099, 1.268)*	1.276 (1.153, 1.411)*	21.6 (13.3, 29.1)*
Sex					
Male	1.035 (1.020, 1.051)*	1.174 (1.100, 1.254)*	1.198 (1.099, 1.305)*	1.322 (1.171, 1.493)*	24.4 (14.6, 33.0)*
Female	1.025 (1.009, 1.042)*	1.133 (1.054, 1.219)*	1.160 (1.056, 1.274)*	1.220 (1.068, 1.394)*	18.0 (6.4, 28.3)*
Age (years old)					
14–65	1.030 (1.006, 1.055)*	1.110 (1.000, 1.232)*	1.050 (0.916, 1.204)	1.072 (0.884, 1.299)	6.7 (−13.1, 23.0)
>65	1.031 (1.017, 1.045)*	1.168 (1.100, 1.241)*	1.213 (1.122, 1.312)*	1.325 (1.186, 1.481)*	24.5 (15.7, 32.5)*
Causes					
Respiratory system	1.027 (1.001, 1.053)*	1.168 (1.044, 1.307)*	1.266 (1.094, 1.464)*	1.444 (1.173, 1.777)*	30.7 (14.7, 43.7)*
Circulatory system	1.037 (1.018, 1.056)*	1.203 (1.108, 1.305)*	1.270 (1.142, 1.412)*	1.465 (1.261, 1.702)*	31.7 (20.7, 41.2)*
Genitourinary system	1.058 (0.970, 1.153)	1.326 (0.906, 1.941)	1.284 (0.777, 2.120)	1.021 (0.495, 2.109)	1.4 (−50.6, 35.4)
Endocrine system	0.993 (0.942, 1.047)	0.976 (0.773, 1.232)	0.996 (0.738, 1.344)	1.014 (0.664, 1.549)	2.1 (−10.2, 52.6)

* P<0.05.
Abbreviations: CRR=cumulative relative risk; CI=confidence interval; AF= attributable fraction.

respectively. No statistically significant associations were found between cold spell and mortality of genitourinary and endocrine system diseases.

It was shown in Table 2 that 21.6% (95% CI: 13.3%, 29.1%) of deaths could be attributed to cold spells during cold season in Ningbo. The attributable fraction (AF) for males and females was 24.4% (95% CI: 14.6%, 33.0%) and 18.0% (95% CI: 6.4%, 28.3%), respectively. Among different age groups, the population over 65 years old had the highest death burden ascribed to cold spell, with the AF of 24.5% (95% CI: 15.7%, 32.5%). The AF value of respiratory system diseases and circulatory system diseases was 30.7% (95% CI: 14.7%, 43.7%) and 31.7% (95% CI: 20.7%, 41.2%), respectively.

DISCUSSION

Our study assessed the relationship between cold spells and mortality in Ningbo. One week after cold spells appeared, there was an acute high-effect period. And 21.6% of total mortality could be attributed to cold spells during cold season. In the first week after the cold spells, decision-makers in relevant department should consider adaptive measures in time to decrease the death risk and disease burden.

In this study, it was shown that CRR of population deaths was greater under the definition of cold wave with lower temperature threshold and shorter duration compared with higher temperature threshold. This is consistent with the research of Liang et al., that is, the optimal cold wave was defined as temperature threshold $\leq P_5$ and duration ≥2 days (*4*). However, Liu et al. found that the optimal cold wave was defined as the days with temperature threshold $\leq P_{10}$ and duration ≥4 days for COPD hospitalized population in Beijing (*7*). This suggested that different definitions may apply to different regions, climates, and health outcomes. In general, more effective cold spell definitions and early warning systems should be explored in the future to adapt to changes in the regional economy, climate, disease, and population mobility.

Within 7 days of lag, there was an acute high-effect period of the cold spell on the death risk. However, the current studies lack more evidence for the acute effect of the cold spell, especially in the southern regions in China. These findings may provide evidence for the optimal time for the prevention and control of sensitive diseases after cold waves. Additionally, the results discovered that the elderly aged above 65 years were the most vulnerable population, and circulatory and respiratory system diseases were sensitive diseases to cold spells, which were mirror with other studies (*8–10*).

For example, a study in Wuhan found that cold wave weather could increase the death risk of residents, and patients with cardiovascular disease and the elderly were the sensitive groups. But they found higher CRR values on sensitive groups (1.960 and 1.670) than our research, with the CRR of 1.465 and 1.325 for cardiovascular disease and the population of over 65 years (*8*). Moreover, the results of this study showed that the risk of death in the age group of 14–65 years also increased significantly within a short lag period (lag0–7). It is speculated that young people, especially outdoor workers, spend more time outdoors and have more opportunities to be exposed to cold waves.

This research also evaluated the mortality burden attributed to cold spells and found that 21.6% of mortality could be ascribed to cold spells during cold season in Ningbo. It was of great significance for the health risk early warning, the formulation of health preventive measures against cold waves, and the evaluation of potential benefits of public health intervention.

The study was subject to at least two limitations. First, the research area only involved one city, and the generalizability of results was limited. Second, the sample size of the group of <14 years and the group of genitourinary system diseases was too small, which may cause certain deviations in the results. However, the study will provide important evidence for evaluating the impact of cold wave on population health in southern regions in China. At the same time, health departments and medical institutions should strengthen cooperation and take active actions to do their best in providing monitoring, forecasting, and early warning services. It is suggested that vulnerable groups, especially the elderly and patients with circulatory and respiratory diseases, should take timely measures to keep warm to reduce the health damage caused by extremely cold weather events.

Conflicts of interest: No conflicts of interest.

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SUPPLEMENTARY MATERIAL

SUPPLEMENTARY TABLE S1. Sensitivity analysis under different variables.

Variable	*df*	CRR (95% CI)			
		Lag0	Lag0–7	Lag0–14	Lag0–21
Average pressure	4	1.031 (1.018, 1.043)*	1.155 (1.093, 1.220)*	1.178 (1.097, 1.265)*	1.272 (1.150, 1.406)*
	5	1.031 (1.018, 1.044)*	1.157 (1.095, 1.222)*	1.180 (1.099, 1.267)*	1.275 (1.153, 1.411)*
Relative humidity	3	1.031 (1.019, 1.044)*	1.158 (1.097, 1.223)*	1.181 (1.100, 1.269)*	1.278 (1.156, 1.413)*
	5	1.031 (1.019, 1.044)*	1.158 (1.097, 1.223)*	1.181 (1.100, 1.269)*	1.278 (1.156, 1.414)*
PM_{10}	4	1.030 (1.018, 1.043)*	1.154 (1.093, 1.218)*	1.178 (1.096, 1.265)*	1.272 (1.150, 1.407)*
CO	5	1.033 (1.020, 1.046)*	1.167 (1.105, 1.233)*	1.187 (1.105, 1.275)*	1.265 (1.143, 1.401)*
PM_{10}+CO	4	1.032 (1.019, 1.044)*	1.162 (1.101, 1.227)*	1.183 (1.101, 1.271)*	1.258 (1.137, 1.393)*
Temperature	3	1.029 (1.013, 1.045)*	1.149 (1.072, 1.230)*	1.178 (1.086, 1.277)*	1.282 (1.147, 1.432)*
	4	1.029 (1.013, 1.045)*	1.149 (1.073, 1.231)*	1.178 (1.085, 1.278)*	1.282 (1.146, 1.433)*
	5	1.029 (1.013, 1.045)*	1.148 (1.072, 1.230)*	1.178 (1.086, 1.278)*	1.282 (1.147, 1.434)*

* P<0.05.
Abbreviations: *df*=degree of freedom; PM_{10}=inhalable particulate matter; CRR=cumulative relative risk.

SUPPLEMENTARY TABLE S2. Overview information of cold spells under different definitions during cold season in 2014 to 2018 in Ningbo city of China.

Definitions	Temperature threshold (℃)	Duration (days)	Cold spell episodes	Cold spell days	Non-cold spell days
A	≤P_5 (3.9)	≥2	19	82	613
B	≤P_5 (3.9)	≥3	10	51	644
C	≤P_5 (3.9)	≥4	6	42	653
D	≤P_{10} (5.5)	≥2	24	163	532
E	≤P_{10} (5.5)	≥3	19	131	564
F	≤P_{10} (5.5)	≥4	14	112	583

Note: "A–F" refers to 6 different definitions of cold spells, which were defined as days when the daily mean temperature was at or below the P_{10} (5.5℃) or P_5 (3.9℃) percentile for at least 2, 3, or 4 consecutive days during the study period.
Abbreviations: P_5=the 5th percentile; P_{10}=the 10th percentile.

SUPPLEMENTARY TABLE S3. Cumulative lag effect of cold spells and population death under 6 different definitions.

Definitions	CRR (95% CI)			
	Lag0	Lag0–7	Lag0–14	Lag0–21
A	1.031 (1.018, 1.044)*	1.156 (1.095, 1.221)*	1.181 (1.099, 1.268)*	1.276 (1.153, 1.411)*
B	1.029 (1.014, 1.045)*	1.148 (1.075, 1.225)*	1.173 (1.074, 1.281)*	1.265 (1.110, 1.442)*
C	1.027 (1.012, 1.043)*	1.134 (1.062, 1.210)*	1.147 (1.050, 1.252)*	1.220 (1.068, 1.393)*
D	1.022 (1.013, 1.032)*	1.122 (1.076, 1.169)*	1.158 (1.098, 1.220)*	1.239 (1.151, 1.334)*
E	1.020 (1.011, 1.030)*	1.119 (1.072, 1.168)*	1.169 (1.104, 1.238)*	1.255 (1.156, 1.363)*
F	1.016 (1.007, 1.026)*	1.102 (1.056, 1.151)*	1.161 (1.093, 1.234)*	1.254 (1.147, 1.370)*

Note: "A–F" refers to 6 different definitions of cold spells, which were defined as days when the daily mean temperature was at or below the P_{10} (5.5℃) or P_5 (3.9℃) percentile for at least 2, 3, or 4 consecutive days during the study period. and "*" was P<0.05.
Abbreviations: P_5=the 5th percentile; P_{10}=the 10th percentile; CRR=cumulative relative risk.

Methods and Applications

Preliminary Study of Pulsed Ultraviolet Technology for Low-Temperature Disinfection

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ABSTRACT

Introduction: To explore the feasibility of pulsed ultraviolet (UV) light technology for low-temperature disinfection, a series of experiments were conducted.

Methods: Pulsed UV technology's effectiveness in disinfecting Gram-positive *Staphylococcus aureus* and Gram-negative *Escherichia coli* on different carriers were studied under varying temperatures.

Results: Under different temperatures and constant radiation illumination (i.e., distance), the disinfection effect was correlated with irradiation time; among the three carriers, the disinfection effect of cloth sheets was the best, followed by stainless steel sheets, and corrugated paper sheet. The disinfection effect on Gram-negative bacteria *Escherichia coli* was better than that on Gram-positive bacteria *Staphylococcus aureus* overall.

Discussion: Temperature has a limited effect on pulsed UV disinfection. Irradiation times and carrier types are influencing factors.

INTRODUCTION

Disinfection is an effective measure to cut off the transmission of infectious diseases which is important in the prevention and control of infectious diseases. Temperature is one of the most important factors affecting the effectiveness of disinfection, and all commonly used disinfection techniques, whether chemical or physical, have a range of applicable temperatures. There are sometimes problems with disinfection in cold environments, especially as transmission of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) from contaminated cold-chain shipments to humans has been listed as one of the possible transmission routes for the epidemic (*1–2*). Not only is it difficult to apply most physical disinfection methods at this time, but the commonly used chemical disinfectants freeze and are ineffective.

Therefore, in order to cope with the cold chain and the low temperature environment in alpine regions, there is an urgent need for research into low temperature disinfection technology. Some initial progress has been made in the field of cryogenic disinfection. In terms of chemical disinfection, several studies have shown that some disinfectants suitable for ambient temperatures can maintain their disinfection performance at low temperatures when certain conditions are met, such as the addition of antifreeze agents and increased doses of disinfectant, or thermal fogging with custom optimized thermal foggers (*3–6*). In terms of physical disinfection, research is directed towards ultraviolet (UV) light, γ-rays, X-rays, electron beams, microwaves, and high-voltage pulsed electric fields (*7–10*). But there are no clear and feasible disinfection methods or evaluation criteria yet.

This study used pulsed UV technology. The experiment was designed and the disinfection effect was determined in accordance with Technical Standard For Disinfection (2002 version) to investigate the disinfection effect of pulsed UV technology on two microbial indicator bacteria at different temperatures and on different carriers. The study was carried out to verify whether there was an effect of temperature on the disinfection effect of pulsed UV technology. The cloth sheet in the carriers is a conventional carrier for disinfection experiments. The stainless steel sheet was selected to take into account the possible need for disinfection in cold chain environments such as van walls and shelves. And the corrugated paper sheet was selected considering the outer packaging of common goods. Because the resistibility of coronavirus to ultraviolet light is weaker than that of bacterial propagules, a gram-positive bacterium Staphylococcus aureus and a gram-negative bacterium Escherichia coli were selected as indicator microorganisms.

METHODS

The two bacterial species selected in this study were

Staphylococcus aureus (ATCC 6538) and *Escherichia coli* (8099). Staphylococcus aureus (ATCC 6538) was from American Type Culture Collection (ATCC), *Escherichia coli* (8099) was from China General Microbiological Culture Collection Center (CGMCC).

The three selected carriers were cloth sheet (10 mm × 10 mm in size), stainless steel sheet (12 mm in diameter and 0.5 mm in thickness) and corrugated paper sheet (10 mm × 10 mm in size). All carriers were sterilized by pressure steam before use. Among them, the production method of the corrugated paper sheet was to peel off the outer layer of the common corrugated cardboard box in daily life, and cut into square pieces of 10 mm × 10 mm. In this study, tryptone soy agar (TSA) was used as the medium, tryptone soy broth (TSB) was used as the organic interferent, and 0.03 mol/L phosphate-buffered saline (PBS) containing 0.1% tween 80 was used as a diluent.

The instruments required for this experiment include a heating and cooling circulator (the temperature is set to −20.0 °C, 0.0 °C, 20.0 °C, and the temperature difference is ±0.05 °C), a pulsed UV xenon lamp (model GZU7280, with a pulse flicker frequency of 20 Hz and an instantaneous irradiation intensity of 332.87 mW/cm^2 at a distance of 1 meter), a hand-held infrared thermometer (the measurement range is −38 ℃ to 520 ℃, and the temperature difference is ±2 ℃). Other required equipment were 37 ℃ constant temperature incubator, electric mixer, graduated straws (1.0 mL, 5.0 mL), disposable sterile petri dishes, autoclaved spare glass petri dishes, and pipette (10 μL) and matching plastic pipette tips, etc.

Bacteria freshly cultured from 18 h to 24 h were diluted with TSB to the desired concentration. 10 μL of fresh bacterial propagule suspension was applied on the vector separately, and 16–19 pieces of each bacteria carrier were prepared, of which 12–15 pieces were used for the test, 2 pieces were used as positive control, and 2 pieces were set aside. The amount of recovered bacteria for positive control should be 1×10^6–5×10^6 CFU/tablet.

The stainless steel tablets were placed in a constant temperature incubator at 37 ℃ for 20 minutes to dry and ready for use. The corrugated paper tablets were set at room temperature (25 ℃) for 15 minutes to dry and reserve, and the cloth tablets for 5 minutes to dry and reserve.

The heating and cooling circulator was adjusted to −20.0 ℃ and the temperature was stabilized for the test. For each test, one piece of each of the three bacteria carrier was placed flat in a disposable sterile Petri dish with a glass Petri dish over it and put into the water bath of the heating and cooling circulator (Figure 1). The actual temperature of the carriers was measured and recorded with a hand-held infrared thermometer 5 minutes later. A pulsed UV lamp was placed above the water bath and fix the lamp height 10 centimeters away from the bacteria piece. The waiting time was set to 5 seconds, and the experiment was conducted in 4 groups respectively, with each group disinfecting for 15 seconds, 30 seconds, 1 minute, and 2 minutes. After disinfection, the bacteria piece was inoculated in an aseptic manner with appropriate dilution as the test group sample. The heating and cooling circulator was set to 0.0 ℃ and 20.0 ℃, and the experimental method to −20.0 ℃. Two pieces of each contaminated vector without disinfection by pulsed UV light were taken as positive control. The medium from the same test batch was used as the negative control.

The test group samples, positive control and negative control were incubated in a constant temperature incubator at 37 °C for 48 hours to observe the results. The test was repeated three times. The results were observed and the killing log value were calculated. On the basis of this, *Escherichia coli* was tested again with three sets of disinfection times of 5, 10, and 20 seconds. This experiment is a quantitative carrier kill test, killing log value ≥3.00 can be judged as disinfection qualified, otherwise judged as disinfection failed.

Statistical Product Service Solutions (26.0, International Business Machines Corporation, Armonk, America) was applied to statistically analyse the data, comparing the differences in the disinfection effect of each influencing factor including temperature, irradiation time, carrier type, and test strain.

RESULTS

The test was repeated with a total sample size of 297. The disinfection effect of the pulsed UV technology on two microbial indicator bacteria on different carriers at different temperatures, expressed as the average killing log value (Tables 1–2). When the set temperature was 20.0 ℃, the average carrier temperature was 20.4 ℃, ranging from 20.1 ℃ to 20.7 ℃; when the set temperature was 0.0 ℃, the average carrier temperature was 1.3 ℃, ranging from −0.8 ℃ to 2.0 ℃; when the set temperature was −20.0 ℃, the average carrier temperature was

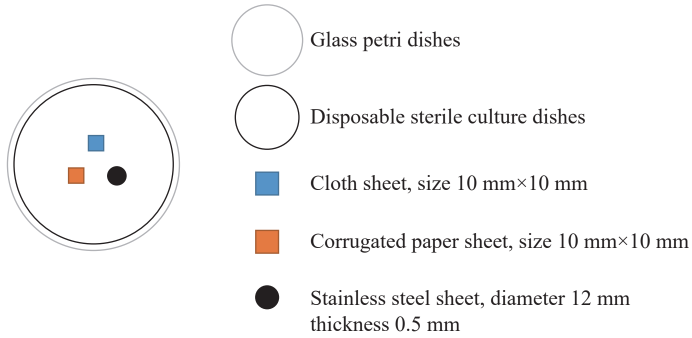

FIGURE 1. Schematic diagram of the placement of the contaminated vector in the water bath of the heating and cooling circulator during the test.

TABLE 1. Killing effect of pulsed UV light on *Staphylococcus aureus* under different temperature conditions.

Test strain	Bacterial vector	Setting temperature (℃)	Pulsed UV irradiation disinfection average elimination killing log value			
			15 s	30 s	1 min	2 min
Staphylococcus aureus	Paper sheets	20.0	1.42	2.81	6.40	>6.32
		0.0	1.30	2.36	6.40	>6.32
		−20.0	1.27	1.86	5.80	5.29
	Stainless steel sheet	20.0	2.60	5.08	>6.32	>6.32
		0.0	2.41	3.27	>6.32	>6.32
		−20.0	1.51	3.38	>6.32	>6.32
	Cloth sheet	20.0	>6.32	>6.32	>6.32	>6.32
		0.0	>6.32	>6.32	>6.32	>6.32
		−20.0	5.50	>6.32	>6.32	>6.32

Notes: Negative control sterile growth. Positive control number: 1.00×10^6–4.20×10^6 CFU/sheet. The mean logarithmic value of the positive control was 6.32. >6.32 indicates sterile growth in the test group.
Abbreviations: UV=ultraviolet; CFU=colony forming units.

TABLE 2. Killing effect of pulsed UV light on *Escherichia coli* under different temperature conditions.

Test strain	Bacterial vector	Setting temperature (℃)	Pulsed UV irradiation disinfection average elimination killing log value						
			5 s	10 s	15 s	20 s	30 s	1 min	2 min
Escherichia coli	Paper sheets	20.0	1.61	2.86	3.63	4.42	5.84	>6.31	>6.31
		0.0	2.04	2.38	3.14	3.23	4.02	>6.31	>6.31
		−20.0	1.82	2.01	2.45	3.37	3.77	>6.31	>6.31
	Stainless steel sheet	20.0	2.65	4.41	4.37	>6.31	>6.31	>6.31	>6.31
		0.0	1.98	3.60	3.62	>6.31	>6.31	>6.31	>6.31
		−20.0	1.70	2.98	3.92	>6.31	4.35	>6.31	>6.31
	Cloth sheet	20.0	2.75	4.28	>6.31	>6.31	>6.31	>6.31	>6.31
		0.0	1.55	4.37	6.69	>6.31	>6.31	>6.31	>6.31
		−20.0	1.37	4.88	6.21	>6.31	>6.31	>6.31	>6.31

Notes: Negative control sterile growth. Positive control number: 1.00×10^6–3.83×10^6 CFU/sheet. The mean logarithmic value of the positive control was 6.31. >6.31 indicates sterile growth in the test group.
Abbreviations: UV=ultraviolet; CFU=colony forming units.

−16.7 ℃, ranging from −18.7 ℃ to −15.0 ℃.

To enhance the comparability of the analysis, the same irradiation time as the *Staphylococcus aureus* was selected in the experimental results of *Escherichia coli*. That is, four sets of data with irradiation times of 15 seconds, 30 seconds, 1 minute, and 2 minutes. The four influencing factors of temperature, irradiation time, carrier type and test species were used as groups, respectively, and the mean killing log values were calculated for each group. The differences in the disinfection effect of each influencing factor were compared using a non-parametric test for independent samples. The value of *P* less than 0.05 indicates that the difference is statistically significant (Table 3).

The effect of temperature on the disinfection effect of pulsed UV light is limited. A non-parametric test of disinfection effectiveness for independent samples with temperature as a group at $P>0.05$, which was not significant, concluded that the difference in disinfection effectiveness at each temperature was not statistically significant. No significant effect of temperature on the disinfection effect of pulsed UV was found (Table 3).

The irradiation time is the influencing factor of pulse UV disinfection effect. A non-parametric test of disinfection effect for independent samples with irradiation time as a group found a significant *P*-value, $P<0.05$. Further comparisons between groups, the *P*-values were less than 0.05 between all other groups except between the 1-minute and the 2-minute groups. This means that the differences in disinfection effectiveness between the groups were considered statistically significant within the irradiation time of 15 seconds to 1 minute. The longer the irradiation time, the better the disinfection effectiveness was.

The carrier type is an influential factor in the effectiveness of pulsed UV disinfection. A non-parametric test of disinfection effectiveness was performed on independent samples using carriers as groups and found $P<0.05$. Further comparisons between groups, the *P*-values were less than 0.05 between any two groups, which means that the differences in disinfection effect of each carrier were considered statistically significant.

The test strain is an influential factor in the effectiveness of pulsed UV disinfection. A non-parametric test of disinfection effect for independent samples with test strains as groups found $P<0.05$, which concluded that the difference in disinfection effectiveness between the two test strains was statistically significant.

DISCUSSION

There are a number of environmental and safety issues that may arise from the use of low temperature disinfectants. These include the safety risks associated with the high concentrations required for disinfection, the pollution of the environment caused by excessive use of disinfectants, the corrosion of metals and the potential for bacteria to acquire antimicrobial resistance, the short-term and long-term effects of disinfection by-products on human health, and the safety of storage and transport of disinfectants and raw materials. It is necessary to explore physical cryogenic disinfection techniques.

Conventional UV germicidal lamps are generally low-pressure mercury vapor discharge lamps, microwave induction lamps or UV light-emitting diode (UV-LED) (*11–12*), which is far less irradiating than pulsed UV. *Ultraviolet germicidal lamp* (GB/T 19258-2012) states that, for the nominal power of 36W double-ended lamps and single-ended lamps, measured at a distance of 1 m, the initial UV radiation

TABLE 3. Comparison of the effect of different influencing factors on the effectiveness of pulsed UV disinfection.

Influencing Factors	Median (Q1, Q3)	Statistics	*P*
Setting temperature			
20.0 ℃	6.31 (5.27, 6.32)	1.792	0.408
0.0 ℃	6.31 (3.72, 6.32)		
20.0 ℃	6.26 (3.81, 6.31)		
Irradiation time			
15 s	3.63 (2.41, 6.21)	28.667	0.000
30 s	5.46 (3.38, 6.31)		
1 min	6.31 (6.31, 6.32)		
2 min	6.31 (6.31, 6.32)		
Bacterial vector			
Paper sheets	5.55 (2.54, 6.31)	23.292	0.000
Stainless steel sheet	6.31 (3.70, 6.32)		
Cloth sheet	6.32 (6.31, 6.32)		
Test strain			
Staphylococcus aureus	6.32 (2.93, 6.32)	5.465	0.000
Escherichia coli	6.31 (4.74, 6.31)		

Abbreviation: UV=ultraviolet.

illumination should be no less than 125.55 μW/cm^2 and 139.5 μW/cm^2 (*13*). And UV germicidal lamps are susceptible to environmental conditions and have poor applicability in complex environments. Continuous UV-LED is also susceptible to ambient temperatures and drive currents leading to higher solder temperatures, which ultimately affects disinfection efficiency (*14*).

Compared to this, pulsed UV technology has great advantages. Pulsed UV technology is a pulsed engineering technique using instantaneous discharge and special inert gas lamps to excite xenon gas in a pulsed form, emitting ultraviolet to near-infrared light. Its spectrum is very similar to that of sunlight, but thousands to tens of thousands of times more intense (*15*). It kills bacteria through the interplay of photochemical, photothermal and continuous pulse effects. Not only is the irradiation intensity high, the irradiation time short and no ozone or other harmful by-products have been detected, making it safer *(16)*. Therefore, the pulsed UV technique was chosen for experimental exploration in this study. The GZU7280 UV xenon lamp used in this study has a pulsed flicker frequency of 20Hz. The instantaneous radiation illumination at an experimental distance of 10 cm was calculated by laboratory measurements and formula simulations to be approximately 11,845–13,000 mW/cm^2.

This study intended to explore the initial application of pulsed UV technology in the field of low-temperature disinfection, and the influencing factors studied are mainly carrier temperature, test strains, carrier type and irradiation time. It was experimentally confirmed that the carrier temperature has a limited effect on the disinfection effect of pulsed UV. It was found that corrugated paper sheets were slightly less effective in disinfection than cloth and stainless steel sheets, suggesting that the type of carrier may have a greater effect on the disinfection effect at low temperatures. The disinfection effect of pulsed UV was also related to the irradiation time, the longer the irradiation time, the more desirable the disinfection effect. The disinfection effect of the Gram-negative bacterium *Escherichia coli* was found to be better than that of the Gram-positive bacterium *Staphylococcus aureus* overall.

This experiment verified that temperature has limited effects on the disinfection effect of pulsed UV, and irradiation time and carrier type are the influencing factors of pulsed UV disinfection effect. It suggests the feasibility of the application of pulsed UV technology in the field of low-temperature disinfection, and the preliminary application may be possible after an in-depth study.

However, there were some limitations in this study. In this experiment, only the contaminated carriers were controlled in low-temperature conditions, and the complete disinfection equipment was not put into the same environment. It was not clear whether there was an effect of ambient temperature on the irradiation intensity of the pulsed UV-Xenon lamp. Therefore, subsequent studies should be conducted in a simulated low-temperature environment to further verify the applicable temperature range of pulsed UV. The carrier type has a large effect on the disinfection effect of pulsed UV. Later tests should pay attention to the use of other common commodity outer packaging to make carriers, refine the experimental conditions, and verify the disinfection effect of pulsed UV.

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