

# **GeoHealth**

### **RESEARCH ARTICLE**

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#### **Key Points:**

- High temperatures are linked to a greater risk of Parkinson's disease (PD) mortality across the overall population, while low temperatures did not show significant effects
- The burden of PD mortality related to high temperatures was found to be substantial on a national scale
- The effects of temperature on PD mortality differ across various geographical and administrative regions

#### **Supporting Information:**

Supporting Information may be found in the online version of this article.

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# Effect of Short-Term Exposure to Ambient Temperatures on Parkinson's Diseases Mortality Among Elderly Aged 60 Years and Above in China, 2013–2020

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**Abstract** Parkinson's disease (PD) is a prevalent neurodegenerative disorder with significant negative health and economic implications for individuals, families and society. This study utilized an individual-level time-stratified case-crossover study design to investigate the relationship between ambient temperatures and PD mortality among the elderly in China. A combination of conditional logistic regression and distributed lag nonlinear model was employed to analyze the data, and the mortality burden attributed to ambient temperatures was quantified. The study included a total of 59,397 deceased PD patients aged 60 years and above who died between 2013 and 2020. Findings revealed that the effects of extremely low temperature  $(-1^{\circ}\text{C})$  could persist for up to 14 days, while the impacts of extremely high temperature (30°C) were acute and last for 4 days and showing a significant harvest effect. For the overall population, the high temperatures significantly increased the risk of death, where low temperature did not. A lag0-14 cumulative odds ratios (COR) of extremely low temperature compared to the reference temperature (15°C) was 1.024 (95% CI: 0.971, 1.080). The lag0-14 COR of extremely high temperature was 1.206 (95% CI: 1.116, 1.304). Additionally, high temperatures attributed greater AF of 4.013 (95% eCI: 1.990, 5.894) comparing to low temperatures did of 0.762 (95% eCI: -0.624, 2.017). Significant differences were found across regions. No statistically significant differences were found between the sex and age. This nationwide study provides evidence for tailored interventions in specific regions and populations to reduce temperature-related PD mortality among the elderly in China.

**Plain Language Summary** This research offers critical insights into how ambient temperatures influence Parkinson's disease (PD) mortality. The study analyzed data from 59,397 elderly individuals (aged 60 years old and above) who died from PD in China between 2013 and 2020. It quantified the relationships between daily mean temperatures and death risks, including how long these effects last and how demographic and regional factors play a role. The findings revealed that extremely high temperatures have immediate effects lasting about 4 days. Overall, high temperatures significantly increased the risk of death from PD, while low temperatures did not. These results provide essential scientific evidence for developing targeted strategies to reduce temperature-related PD mortality in specific regions and populations in China.

#### 1. Introduction

Parkinson's disease (PD) is the second most common neurodegenerative disease after Alzheimer's diseases (AD). It characterized by bradykinesia, resting tremor, rigidity, and postural instability, as well as other non-motor symptoms such as depression, insomnia, constipation (Huang et al., 2024; Tolosa et al., 2021). The prevalence of PD among the individuals over the age of 60 years in China was estimated to be 1.37%, with a total number of approximately 3.62 million cases (Qi et al., 2021). Age-standardized mortality rate (ASMR) of PD was 1.22 per 100,000 individuals in 2021. Furthermore, ASMR is projected to increase to 2.66 per 100,000 individuals by 2040 (Lv et al., 2024). This high prevalence and mortality rate of PD pose a substantial burden on individuals, families, and society, challenge our already overloaded healthcare system with significant health and economic implications, particularly in the context of a rapidly aging society (Yang et al., 2021).

While the exact cause of PD remains unclear, genetic, environmental, and neuroinflammatory factors may play a role in its development (Bougea et al., 2023). Several studies have explored the contributions of environmental

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Songwang Wang, Qing Guo, Yu Wang, Peng Bi, Jing Wu Resources: Qing Guo Software: Rui Zhang, Ainan Jia, Huan Zheng, Chaonan Wang, Songwang Wang, Qing Guo Supervision: Yonghong Li, Siyuan Wu, Songwang Wang, Jing Wu Validation: Rui Zhang Writing – original draft: Rui Zhang Writing – review & editing: Ainan Jia, Yonghong Li, Siyuan Wu, Peng Bi, Jing Wu

factors to the onset of PD, including pesticides, heavy metals, viruses, and air pollution (Shermon et al., 2022). Climate change is the greatest health threat facing humanity in the 21st century. Global warming, a direct consequence of climate change, can exacerbate pre-existing diseases and increase temperature-related mortality and disability, especially in an era of aging (Romanello et al., 2023). This has sparked growing interest in investigating how meteorological variables affect individuals with PD. A research indicated that seasonal variations may influence the capacity of striatal dopamine synthesis, with increased synthesis capacity observed in the right putamen during fall and winter (Kaasinen et al., 2012). Seasonal variations significantly impact non-motor symptoms and temperature-sensitive motor symptoms of PD.2 Another research indicates that non-motor symptoms often worsen in winter, potentially linked to dysfunction in the body's master clock (van Wamelen et al., 2019). While coldness of the lower limbs typically occurs in winter, some patients experience severe this symptom during summer, affecting their mobility and daily activities (Kataoka & Ueno, 2016). A time-series analysis conducted in Madrid, Spain, found an increased PD mortality during heatwaves, suggesting that heatwaves may exacerbate the condition of affected individuals (Linares et al., 2016). Furthermore, the health risks associated with ambient temperature exposures are known to vary geographically. However, there is limited evidence in China regarding the quantitative association between ambient temperatures and PD mortality at either national or regional level.

This study aimed to quantify the relationship between ambient temperatures and PD mortality among the elderly at a national level in China. Additionally, we evaluated the mortality burden attributable to ambient temperatures. By analyzing a large-scale and long-term national data set, the findings could enhance the preparedness of regional health authorities and optimize the allocation of vital yet limited public health resources.

#### 2. Methods

# 2.1. Death Records and Meteorological Data

The de-identified individual death records for the elderly aged 60 years and above who died from PD in China between 1 January 2013 to 31 December 2020 were obtained from the China Cause of Deaths Reporting System (CDRS). CDRS is a critical public health tool designed to collect and analyze mortality data across the country. Established to provide comprehensive coverage of all deaths, the system employs standardized reporting protocols to ensure accuracy and consistency in data collection. As of 2013, this system comprises 605 communities from 322 cities, covering a population of 323.8 million, which represents 24.3% of the total population in China. All communities are subject to strict quality control procedures administered by the Chinese Center for Disease Control and Prevention at the county/district, prefecture, province, and national levels to ensure the accuracy and completeness of death data (Chen et al., 2017). The data set included cause of death, date of death, sex, age, and residential address. The cause of death was classified using the International Statistical Classification of Diseases and Related Health Problems (ICD-10), where codes G20 (Parkinson's disease) - G21 (Secondary parkinsonism) were used to define deaths caused by PD.

The meteorological data were obtained from the Resource and Environmental Science Data Platform, collected from 2,417 national-level surface meteorological observation stations across China, spanning the period from 1 December 2012 to 31 December 2020. The data set encompassed five variables: longitude, latitude, daily mean temperature, daily mean relative humidity, and daily mean pressure. We initially applied the inverse distance weighting (IDW) method to interpolate the discrete station data into continuous raster data with a spatial resolution of 15 km by 15 km. Subsequently, at the individual level, we established the exposure to meteorological variables for each decedent on their day of death, as well as corresponding control days and lag days, based on their residential addresses (longitude and latitude).

#### 2.2. Study Design

An individual-level time-stratified case-crossover design was employed to examine the acute effects of short-term ambient temperatures increase on PD mortality. First, the assessment of acute temperature-related health impacts based on individual temperature exposures. Unlike classical time series studies that rely on data from central monitoring stations, this approach explicitly considered small-scale spatial contrasts in temperature exposure by evaluating exposures and mortality at the individual level, thereby achieving greater precision in estimation (Zhang, Sun, Jia, Wu, et al., 2024). Second, in the time-stratified approach, ambient temperature exposure on and before the day of death was compared with exposure during control days. Control days were matched to the same

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day of the week within the month that the death occurred to avoid overlap bias. Thus, a maximum of four control days per death was possible. The time-stratified approach accounts for the confounding effects of long-term time trends, seasonality and day-of-week (DOW) by design (Bateson & Schwartz, 1999; Zhu et al., 2023). Third, the case-crossover study design uses each decedent as their own control by comparing exposure during the case period to exposure during control periods, thereby eliminating the potential influence of individual-level differences. The design effectively accounts for potentially confounding effects of time-invariant characteristics, such as age, sex, lifestyle, and comorbidities (Jiang et al., 2022; Liu et al., 2023).

#### 2.3. Statistical Analysis

In this study, we utilized a conditional logistic regression model combined with the distributed lag non-linear model (DLNM), a state-of-the-art model in environmental epidemiology, to quantify the relationship between ambient temperatures and PD mortality at the individual level. The DLNM was used to construct the cross-basis function of temperatures, which captured the non-linear and lag effects of temperatures on the mortality (Gasparrini, 2011; Gasparrini et al., 2010). Model selection was based on the Akaike Information Criterion (AIC) to ensure optimal parameter fit. To maintain consistency and comparability across regions and outcomes, we set the maximum lag period to 14 days, allowing us to capture the cumulative effects of temperature exposure over this period. We used natural cubic splines to generate equally spaced knots for the daily temperature basis, specifying a degree of freedom of 4 and a quadratic spline. These knots are designed to capture potential nonlinear exposure-response relationships. Additionally, the lag-response relationships were modeled using 3 internal knots set on a logarithmic scale. Relative humidity and pressure were adjusted by using natural cubic splines with 3 degrees of freedom (Zhu et al., 2023). The model also controlled holidays as confounding factors. The model is fitted as follows:

```
Logit(P(\text{Case} = 1 \text{ in stratum } i \mid T\text{mean}, RH\text{mean}, P\text{mean}, \text{holidays}))
= \alpha_{\text{stratum } i} + cb(T\text{mean}, \text{lag} = 14) + ns(RH\text{mean}, df = 3) + ns(P\text{mean}, df = 3) + \text{holidays}
```

Where a stratum consists of 1 case (case = 1) and its 3 or 4 controls (case = 0),  $P(\text{Case} = 1 \text{ in stratum } i \mid T\text{mean, } RH\text{mean, } P\text{mean, holidays})$  is the conditional probability of being a case in the ith stratum given the value of daily mean temperature and other covariates.  $\alpha_{\text{stratum } i}$  represents the constant or interception of stratum i. cb(Tmean, lag = 14) represents the cross-basis function used to model the lag effects of daily mean temperature over a period of up to 14 days. The term stratum is defined as the combination of the same year, month, and DOW. ns(RHmean, df = 3) represents a natural spline function with 3 degrees of freedom, used to model the daily mean relative humidity. ns(Pmean, df = 3) represents a natural spline function with 3 degrees of freedom, used to model the daily mean pressure. Holidays is categorical variable.

The temperature of  $-1^{\circ}$ C (approximately the 5th percentile of observed temperatures) was considered representative of extremely low temperatures, while the temperature of 30°C (approximately the 95th percentile) was considered representative of extremely high temperatures. The lag-response relationships for both extremely low and high temperatures were then studied separately, alongside analyses of the cumulative odds ratios (CORs). Cumulative temperature-mortality associations were evaluated across the whole lag period for each subgroup of stratification, including sex, age, geographical regions, and administrative regions. These associations were centered around the minimum mortality temperature (MMT), which served as the reference temperature (RT), following the common approach of studies applying DLNM (Gasparrini & Leone, 2014). The MMT is defined as the temperature associated with the least mortality risk, corresponding to an odds ratio (OR) of 1. The MMT was constrained to values between the 5th and 95th percentile of the ambient temperature distribution in this study.

When assessing the contribution of an environmental hazard to health outcomes, a commonly used metric in environmental epidemiology and public health is the Attributable fraction (AF). Defined as the proportion of health effects directly attributable to a specific environmental exposure (e.g., ambient temperatures), the AF quantifies the relative risk of adverse health outcomes in populations exposed to the hazard compared to those who are unexposed. In this study the AFs of AD and other dementia mortality due to full, low, and high temperatures were calculated, respectively. A general definition of the AF $_x$  for a given exposure x can be expressed as:

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$$AF_x = 1 - \exp(-\beta_x)$$

Where  $\beta_x$  refers to the association with a specific exposure intensity x, compared to the reference temperature. Uncertainty in the estimated AFs was quantified using empirical confidence intervals (eCIs), which were derived from Monte Carlo simulations conducted over 1,000 repetitions (Gasparrini, 2011; He et al., 2023).

Based on the main model described above, we conducted several subgroup analyses to explore potential modification based on sex (male and female), age (60–74 years and ≥75 years), geographical regions (northern China and southern China), and administrative regions (North China, North-east China, East China, South-central China, South-west China, and North-west China). The geographical regions analysis focused on understanding the influence of natural factors like climate and environment, while the administrative regions analysis aimed to gain insights into differences in the characteristics of socio-economic, climatological, and infrastructural aspects, as well as policy environments, providing finer granularity of understanding. Effect modification was examined

by the difference and 95% CI of effect estimates by strata, calculated as  $(\hat{Q}_1 - \hat{Q}_2) \pm 1.96\sqrt{\widehat{SE}_1^2 + \widehat{SE}_2^2}$ , where  $\hat{Q}_1$  and  $\hat{Q}_2$  are the estimates for the two categories, and  $\widehat{SE}_1$  and  $\widehat{SE}_2$  are standard error (Zhang, Sun, Jia, Wang, et al., 2024).

#### 2.4. Sensitivity Analyses

The robustness of the model was assessed through three sensitivity analyses: first, by changing the degrees of freedom (df) for relative humidity while keeping the others unchanged; second, by changing the df for temperature while maintaining the others; third, by not adjusting pressure while keeping the other variables constant.

We used R software, version 4.1.2 (R Project for Statistical Computing, Vienna, Austria, http://www.r-project. org) to perform all analyses, with the "dlnm" package to conduct DLNM, the "survival" package to fit conditional logistic regression, and the "attrdl" function to calculate the AFs. For all statistical tests, two-sided and a *p*-value <0.05 were considered statistically significant.

#### 2.5. Patient and Public Involvement

Individual patient consent was not required for our analysis of de-identified data collected from CDRS.

This study was approved by the ethics committee of National Institute of Environmental Health, Chinese Center for Disease Control and Prevention with the approval number 201606.

#### 3. Results

#### 3.1. Descriptive Statistics

A total number of 59,397 decedents caused by PD aged 60 years and above between 2013 and 2020 were included in the study. Table 1 summarizes the demographic characteristics of PD deaths across different subgroups over the study period. A higher percentage of males (55.47%) died from PD compared to females (44.53%). The majority of PD deaths (64.45%) occurred in aged 75 years and above group. The stratification of geographical regions shows that northern China has 16,491 deaths (27.76%), whereas southern China consists of 42,906 deaths (72.24%), underscoring a significantly higher representation in the southern region. The stratification of administrative regions indicates that East China has the highest number of deaths with 29,337 (49.39%), while North-west China has the lowest with 1,694 deaths (2.85%), revealing a significant disparity in mortality across these regions.

Figure S1 in Supporting Information S2 shows the decomposition analysis of the additive time series of daily death cases of PD in China among individuals aged 60 and above from January 2013 to December 2020. This analysis includes the observed cases, long-term and seasonal trends, as well as random variation. The long-term trend indicates that the death cases exhibited a gradual increase from 2013 to 2020. The seasonal curve demonstrates significant seasonality, revealing a bimodal pattern characterized by peaks in PD deaths during the summer and winter months, with the winter peak being higher than the summer's.

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**Table 1**Number of Deaths From Parkinson's Disease by Stratifications, 2013–2020, China

Citiita				
Groups	Number of deaths	Proportion (%)		
Total number of deaths	59,397	_		
Sex				
Male	32,949	55.47		
Female	26,448	44.53		
Age				
60–74	21,118	35.55		
≥75	38,279	64.45		
Geographical regions				
northern China	16,491	27.76		
southern China	42,906	72.24		
Administrative regions				
North China	5,017	8.45		
North-east China	4,497	7.57		
East China	29,337	49.39		
South-central China	11,307	19.04		
South-west China	7,545	12.7		
North-west China	1,694	2.85		
		•		

The mean and standard deviation of daily mean temperature, daily mean relative humidity and daily mean pressure during the study period were recorded as  $16.05^{\circ}\text{C}$   $\pm$   $10.05^{\circ}\text{C}$ , 72.23%  $\pm$  15.90%, and  $994.92 \text{ hPa} \pm 39.144 \text{ hPa}$ , respectively (Table S1).

# 3.2. Associations Between Temperatures and PD Deaths Among the Elderly in China

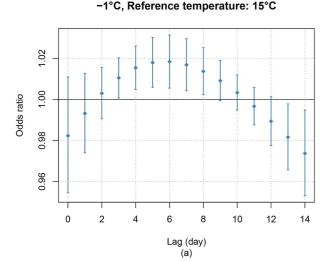
Figure 1 presents the lag-response relationship between extremely low (approximately the 5th percentile, around  $-1^{\circ}$ C) and extremely high temperatures (approximately the 95th percentile, around 30°C) and the risk of PD mortality, with a reference temperature of 15°C. Figure 1a shows the significant odds ratios of PD death associated with extremely low temperature were observed from lag3, reached the maximum at lag6, remained significant until lag8. Figure 1b illustrates that extremely high temperature had an acute and immediate effect, with the highest mortality risk occurring on the day of exposure, followed by a gradual decrease. Then the risk remained below normal levels for an extended period (lag6-lag13) after exposure. This lagresponse relationship pattern of extremely high temperature and mortality risk demonstrated as the harvest effect.

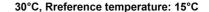
Figure 2 presents the overall exposure-response curves between ambient temperatures and PD mortality, with a reference temperature of 15°C. Figure 2a shows that high temperatures increased the mortality risk, while low temperatures did not. Figure 2b illustrates that the acute short-term (lag0-4) effects of high temperatures on the PD mortality risk, which was much higher than the longer-term (lag0-14) effects. Additionally, exposure-response

curves for different administrative regions are provided in Figure S2 in Supporting Information S2, high-lighting regional variations in the exposure-response relationship.

According to Figure 3, for the overall population, the lag0-14 COR of extremely low temperature compared to the reference temperature (15°C) was 1.024 (95% CI: 0.971, 1.080). The lag0-14 COR of extremely high temperature was 1.206 (95% CI: 1.116, 1.304). Notably, the lag0-4 COR of 30°C was 1.371 (95% CI: 1.282, 1.466), suggesting a stronger acute effects of extremely high temperature for the shorter period.

For the demographic stratified analysis, extremely low temperature did not significantly increase the mortality risk. In contrast, extremely high temperature for both lag 0–14 and lag 0–4 significantly increased the mortality





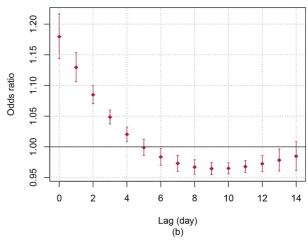


Figure 1. Exposure-lag curves of extremely low and high temperatures on Parkinson's disease mortality, 2013–2020, China.

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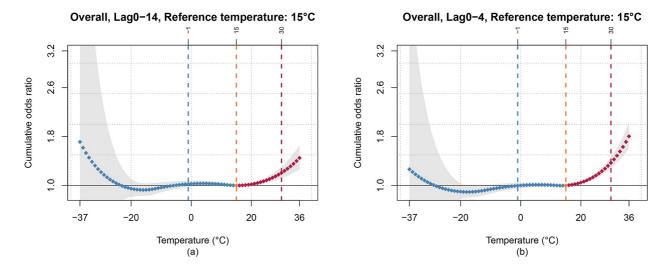


Figure 2. Cumulative exposure-response curves for associations between ambient temperatures and Parkinson's disease mortality, 2013–2020, China.

risk in people of different sexes and age groups, but there were no significant differences between sex or age group (Figure 3).

For geographical region subgroups, extremely low temperature significantly increases the mortality risk in southern China, but not in northern China. Extremely high temperature of lag0-14 significantly increases the mortality risk in both southern and northern China, with no difference between them, while the mortality risk of lag0-4 in southern China is significantly higher than it in northern China (Figure 3).

Examining administrative regions, extremely low temperature only increased the mortality risk in East China. Extremely high temperature of lag0-14 increased the mortality risk in North China, North-east China, and East China, and it increased the lag0-4 mortality risk across all administrative regions (Figure 3).

## 3.3. The AF of PD Deaths Attributed to Temperatures

Figure 4 demonstrates high temperatures have greater AF comparing to low temperatures. However, southern China and East China exhibited a greater AF of PD mortality attributed to low temperatures compared to AF by high temperatures.

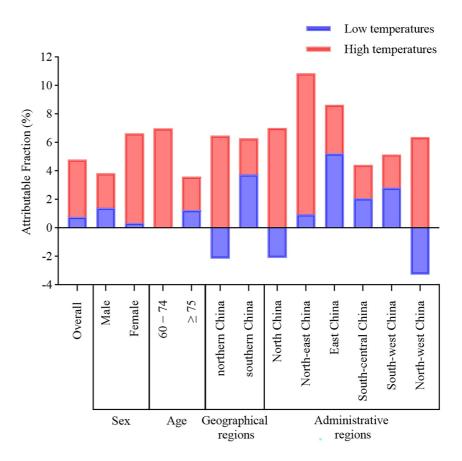
Groups	COR of -1°C (lag0-14)		COR of 30°C (lag0-14)	COR of 30°C (lag0-14)		COR of 30°C (lag0-4)	
Overall	1.024 (0.971, 1.080)	+	1.206 (1.116, 1.304)	i i de l	1.371 (1.282, 1.466)	¦ ⊯н	15
Sex							
Male	1.043 (0.962, 1.131)	<b>.</b>	1.132 (1.026, 1.250)	<b>i♦</b> 1	1.286 (1.181, 1.400)	i <b>∳</b> i	17
Female	1.007 (0.934, 1.085)	i <del>ķ</del> i	1.313 (1.165, 1.480)	<b>+</b> ++	1.480 (1.335, 1.640)	+++	14
Age group (years)		1					
60 - 74	0.991 (0.907, 1.083)	ı <del>ķ</del> ı	1.356 (1.193, 1.541)	<b>⊢</b>	1.500 (1.343, 1.674)	<b>→</b>	15
≥ 75	1.042 (0.975, 1.114)	•	1.129 (1.023, 1.247)	141	1.305 (1.198, 1.420)	I <b>∳</b> I	15
Geographical region	s						
northern China	0.958 (0.847, 1.083)	н <del>і</del>	1.456 (1.225, 1.729)	<b>→</b>	1.693 (1.468, 1.952)		15
southern China	1.166 (1.007, 1.349)	<b>→</b>	1.158 (1.086, 1.236)	i <b>∳</b> i	1.251 (1.184, 1.322)	101	22
Administrative region	ns	į		į		į	
North China	0.957 (0.740, 1.239)	<b>⊢</b>	1.462 (1.037, 2.060)	<del></del>	1.923 (1.464, 2.525)	·	15
North-east China	1.037 (0.843, 1.277)	<b>⊢</b>	2.286 (1.471, 3.550)	·		<b>├</b>	12
East China	1.164 (1.013, 1.338)	· <del>j</del> ⊷⊣	1.234 (1.125, 1.353)	H♦H	1.356 (1.256, 1.464)	1∳1	21
South-central China	1.028 (0.826, 1.278)	<b>⊢</b>	1.109 (0.966, 1.272)	<b>∔</b>	1.212 (1.085, 1.355)	i+++	22
South-west China	0.907 (0.436, 1.889)	<b>←</b>	1.188 (0.966, 1.461)	<del>-</del>	1.305 (1.087, 1.568)	<b>├</b>	18
North-west China	0.949 (0.625, 1.443)	<b>⊢</b>	1.627 (0.936, 2.831)	+	→ 1.720 (1.080, 2.740)	·	15
		0.5 1 1.5 2 2.	5 3 3.5	0.5 1 1.5 2 2.5	3 3.5	0.5 1 1.5 2 2.5 3 3.	5
		COR		COR		COR	

 $\label{eq:abbreviation: COR = cumulative odds ratio; RT = reference temperature.}$ 

Figure 3. Cumulative relative risks of low and high temperatures on Parkinson's disease mortality, 2013–2020, China.

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**Figure 4.** Attributable fractions of Parkinson's disease mortality due to low and high temperatures by stratifications, 2013–2020, China.

Table \$2 summaries AFs of PD mortality due to ambient temperatures. For the overall population, 4.769% (95% eCI: 3.113%, 6.297%) of PD deaths attributed to full temperatures. Additionally, 0.762% (95% eCI: -0.624%, 2.017%) and 4.013% (95% eCI: 1.990%, 5.894%) of PD deaths were attributable to low and high temperatures, respectively.

AFs for females and the group aged 60–74 years due to high temperatures were relatively higher, whereas the AFs attributable to low temperatures were the opposite. However, there were no significant differences between sex or age groups (Table S2).

The AF due to low temperatures was 3.737% (95% eCI: 0.234%, 7.010%) in southern China, while it was not significant in northern China (Table S2).

For administrative regions, East China had the greatest AF of 5.227% (95% eCI: 0.781%, 8.926%) due to low temperatures, while North-east China had the greatest AF of 9.911% (95% eCI: 4.276%, 14.956%) due to high temperatures (Table S2).

## 3.4. Sensitivity Analysis

The sensitivity analysis results (Table S3) showed that the CORs remained almost unchanged, which indicated that the models were stable.

#### 4. Discussion

The study utilized a national individual mortality data set to investigate the relationships between ambient temperatures and PD mortality among the elderly aged 60 years and above in China. The findings revealed that for the overall population, the high temperatures were associated with an increased risk of PD mortality, while no

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significant effects of low temperatures were observed. Nationally, the disease burden of PD mortality attributable to high temperatures was significant, whereas the impact of low temperatures was not. Moreover, the impact of temperatures on PD mortality varied by geographical and administrative regions, while sex and age did not appear to moderate this relationship. The findings of this study underscore the crucial need to consider the impact of ambient temperatures in the control and prevention strategies for PD among the elderly, in light of climate change and rising temperatures.

The study found that exposure to high temperatures significantly increases the risk of PD mortality, which is consistent with previous research findings (Su et al., 2021). Several cellular physiological mechanisms may explain how high temperatures affect organisms. These include oxidative stress, alterations in cardiovascular and cerebrovascular hemodynamics, excitotoxicity, microglial activation, and cellular apoptosis, as well as the resulting physiological changes such as dehydration and electrolyte imbalance (Kaasinen et al., 2012; Linares et al., 2016; Zammit et al., 2021). Furthermore, exposure to high temperatures has been shown to worsen symptoms of PD, leading to increased fatigue, irritability, and cognitive decline (Bongioanni et al., 2021). Indeed, research have showed abnormal temperature regulation exists in patients with PD (Huang et al., 2024). Autonomic failure in Parkinson's disease can be exacerbated by high temperatures, potentially leading to orthostatic hypotension and increasing the risk of trauma from syncope and falls (Pathak et al., 2005). Our results could provide valuable epidemiological evidence on the response of PD to heat exposure, which is essential for guiding public health interventions.

The study found a harvest effect of high temperatures, where the heat exposure leads to an initial spike in mortality of the most vulnerable individuals, followed by a period of subnormal mortality rates as the pool of susceptible people is reduced (Anderson & Bell, 2009; Shrestha et al., 2024). This phenomenon may be attributed to the increased lethality of hot weather for vulnerable populations, whose physiological ability to adapt to extreme temperatures is compromised (Huang et al., 2024). This suggests that implementing immediate precautions can significantly reduce the risk of death during hot weather. Regular collaboration with frontline healthcare providers is central to ensure that patients receive timely advice and treatment plans to mitigate the risks associated with high temperatures. Proactive strategies should be in place before the onset of hot weather to provide emergency assistance and facilitate access to healthcare resources, ensuring that those affected by heat can receive prompt treatment and support.

Previous studies found that the impact of low temperatures on all-cause mortality was greater than that of high temperatures (Chen et al., 2018; Gasparrini et al., 2015). In contrast, our study revealed that, for the overall population, the heat-related PD mortality burden was significant, with no notable impact from cold temperatures. This finding aligns with a previous study (Yin et al., 2023). Although the exact mechanisms behind these differences remain unclear, it highlights the distinctive vulnerability of PD patients to thermal stress. This finding is particularly important in the context of climate change. As the frequency and intensity of hot weather increases, the heightened health burden on the PD population could become even more severe. It is crucial for public health authorities to develop adaptation policies and intervention methods to be well-prepared with this increased risk. These include increasing public awareness, establishing cooling centers, and reasonably allocating medical resources to vulnerable populations. Notably, a recent study from Japan reported that low temperatures may increase the risk of mortality in patients with PD, whereas the effects of high temperatures were not significantly observed, except among elderly patients aged 85 years and above (Lin et al., 2023). This difference may be related to regional variations and population adaptability, emphasizing the importance of research conclusions applicability in different regions.

According to the regional stratified analyses, low temperatures have a more severe health impact on Parkinson's patients in southern China and East China. Consistent with a study that has been conducted in these regions demonstrated some symptoms have been deteriorated in the winter (Wang et al., 2023). In southern and eastern China, residents may be accustomed to warmer climates, making them more vulnerable to health issues in low-temperature environments. Additionally, lacking effective heating systems results in lower indoor temperatures during winter and further impacts health in these areas. Finally, population structure disparities also play a significant role (Chen et al., 2013; He et al., 2023). Hence, in these regions, public health policy should not only focus on the mortality burden caused by high temperatures but also place significant emphasis on low temperatures. In contrast, in northern China, North China, and North-east China, the PD mortality burden attributable to high temperatures is significantly higher than those in other regions. These findings emphasize that for these

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areas, establishing a high temperature early warning system is essential to effectively forecast risks. Additionally, it is important to provide more cooling facilities during the summer for vulnerable groups within the communities.

There are several limitations. First, variations in the quality and completeness of death records across different regions may significantly skew the accuracy of findings, as inconsistent data collection methods, classification practices, and reporting standards may lead to misclassification and underreporting, affecting the generalizability of the results. Second, potential confounding variables, such as air pollution, socioeconomic status, and healthcare access, were not accounted for in the analysis. Future research should aim to address these confounders for a more comprehensive understanding of the relationship. Third, our model captures acute effects but does not adequately consider the long-term impacts of non-optimal temperatures on health. These long-term effects may include the exacerbation of chronic diseases, adaptive changes, and the sustained influence of environmental factors on population health. The absence of assessment of these long-term impacts may lead to an overestimation of the mortality risks associated with temperatures. Specifically, temperature stress may significantly affect mortality in the short term, but its cumulative effects and interactions with other health issues may become apparent over a longer time frame. Therefore, future research should incorporate considerations of long-term temperature impacts to provide a more comprehensive and accurate public health assessment.

#### 5. Conclusions

This nationwide study has significantly enhanced our understanding of the impact of temperature on PD mortality among the elderly in China and has important implications for guiding public health interventions. The study highlights the significant mortality burden posed by high temperatures on older people with PD, and this burden varies among different populations and regions. Armed with this knowledge, policymakers and healthcare authorities can implement strategies to effectively minimize the impact of ambient temperatures on individuals with PD, potentially leading to a significant reduction in PD mortality and an improvement in the overall well-being and quality of life for this vulnerable population.

#### **Conflict of Interest**

The authors declare no conflicts of interest relevant to this study.

# **Data Availability Statement**

The mortality data can only be applied from National Population and Health Science Data Sharing Platform: https://www.phsciencedata.cn/Share/ky\_sjml.jsp?id=6b5fc8c0-cffb-4a57-af26-a72070c65954.

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