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Extreme Heat Exposure and COPD Mortality: Insights from Sleep Time

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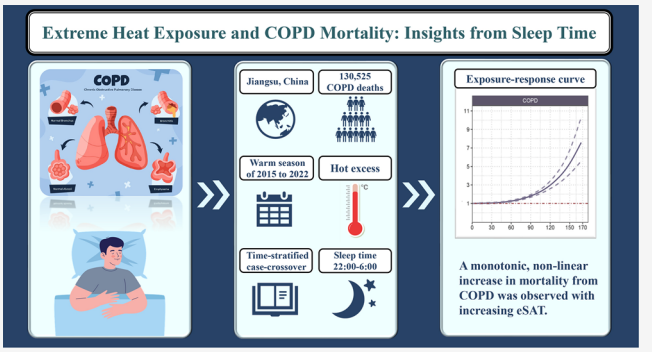
ABSTRACT: Extreme heat, a growing consequence of climate change, can disrupt sleep, potentially increasing the risk of life-threatening exacerbations in patients with chronic obstructive pulmonary disease (COPD). However, direct evidence linking sleep-time heat to COPD mortality is limited. We therefore conducted a time-stratified case-crossover study combining conditional logistic regression and a distributed lag nonlinear model to examine the association. Cumulative excess sleep-time apparent temperature (eSAT) was used to represent the intensity of extreme heat during sleep. Daily COPD mortality data from 2015 to 2022 were collected from Jiangsu Province, China. We also estimated the mortality burden attributable to eSAT. During the study period, a total of 130,252 COPD deaths were included in the analyses. A monotonic, nonlinear increase in mortality from COPD, acute exacerbation of COPD (AECOPD), and chronic bronchitis was observed with increasing eSAT. The effects were more prominent among females, older adults, widowed individuals, farmers, and individuals living in the city with lower ownership of air conditioners. Exposure to eSAT was responsible for 3.37%, 3.07%, and 4.59% of deaths from COPD, AECOPD, and chronic bronchitis, respectively. This study demonstrates the impact of extreme heat during sleep on COPD mortality and underscores the need for targeted interventions to protect respiratory health.



KEYWORDS: *excess apparent temperatures, sleep time, mortality, COPD, case-crossover study*

1. INTRODUCTION

Climate change is driving a decrease in diurnal temperature variation, resulting in a higher frequency of hot nights.[1] The detrimental effects of such nighttime heat on morbidity and mortality from all-cause and specific-cause diseases have been well-documented.[2] In addition to causing heat-related illnesses, such as heat exhaustion and heat stroke, night-time heat can disrupt sleep by affecting normal sleep physiology. This disruption poses a unique threat that may outweigh the health risks of daytime heat exposure.[3] Studies have shown that hotter nights are associated with disrupted sleep architecture, characterized by increased wakefulness and reductions in both rapid eye movement and slow-wave sleep.[4] This deterioration in sleep quality can ultimately impair human health.[5] Despite the growing body of evidence highlighting the health consequences of extreme heat exposure during sleep, research investigating its comprehensive understanding of health consequences remains limited.

Chronic obstructive pulmonary disease (COPD), the fourth leading cause of death globally in 2021, is a progressive and debilitating disease characterized by airflow limitation and persistent respiratory symptoms, including dyspnea, cough, sputum production, and wheezing.[6] Exposure to extreme heat during sleep may exacerbate these pathological features by increasing ventilatory demands and inducing bronchoconstriction, further impairing respiratory function and disrupting sleep.[7] The disrupted sleep itself has deleterious effects on breathing and gas exchange, including a reduction of inspiratory endurance and inhibition of accessory respiratory muscles, and is linked with poorer health outcomes in individuals with COPD, including diminished quality of life, increased disease severity, and higher risks of exacerbation and mortality.[8,9] While the aforementioned effects of sleep disruption may be mild in healthy individuals, these impairments can increase susceptibility to ambient heat during sleep in those with COPD.[10] Given the potential for synergistic effects of heat on respiratory function and sleep physiology, understanding the impact of sleep-time extreme heat on COPD mortality is crucial. However, epidemiological evidence of this association remains scarce.

To address the knowledge gap, we conducted a comprehensive time-stratified case-crossover study spanning 2015 to

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2022 to investigate the adverse effects of sleep-time extreme heat on patients with COPD, which may have profound implications for public health interventions and climate change adaptation strategies.

2. METHODS

2.1. Study Population. We analyzed mortality data from 13 prefecture-level cities in Jiangsu Province, China, spanning 2015 to 2022. Daily death records, encompassing demographic information (sex, age, race, marital status, education, occupation, residential address) and date of death, were obtained from the local Centers for Disease Control and Prevention. The study was approved by the Ethics Committee of the School of Public Health, Sun Yat-sen University, with a waiver of informed consent.

2.2. Outcomes. According to the 10th Revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-10), we identified deaths from COPD (ICD-10: J41−J44) and further classified them into acute exacerbation of COPD (AECOPD; ICD-10: J44), chronic bronchitis (ICD-10: J41−J42), and emphysema (ICD-10: J43). This classification allows for a precise assessment of how environmental factors differentially affect these subtypes. AECOPD represents a sudden worsening of symptoms.[11] Chronic bronchitis is characterized primarily by airway inflammation and mucus hypersecretion, while emphysema involves the destruction of alveoli and impairment of gas exchange.[12,13]

2.3. Study Design. A time-stratified case-crossover design was employed to investigate the association between extreme heat exposure during sleep time and COPD mortality, which is commonly used in environmental epidemiology to explore the acute effect of ambient heat on health events.[14,15] The design uses each individual as their own control by comparing exposure on the case day against reference exposures on control days.[16] We selected the date of death as case days and the same days of the week within 1 month as control days. For instance, if a death occurred on January 1, 2015 (Thursday), January 1, 2015 is defined as the case day, and all the other Thursdays in January 2015 (i.e., January 8, 15, 22, 29) are defined as the control days. Due to the features of this design (self-control and specific time window), our study adequately controls for the influence of the day of the week, long-term trends, and seasonality on the exposure.[16]

2.4. Exposure Assessment. To focus on mortality risks related to extreme heat exposure, we restricted the analyses to the warmest months (i.e., May to September). We acquired gridded meteorological data sets (spatial resolution: 0.0625° × 0.0625°) of hourly air temperature (°C), hourly specific humidity (kg/kg), hourly surface pressure (mb), hourly wind speed (m/s), and daily relative humidity (%) from the China Meteorological Administration Land Data Assimilation System (CLDAS V2.0) of the National Meteorological Information Center.[17] Correlation coefficients between observed and modeled parameters were 0.97 (air temperature), 0.96 (surface pressure), 0.82 (wind speed), and 0.93 (relative humidity). We further converted these variables to apparent temperature using established formulas[18] to create exposure data sets. Unlike air temperature alone, apparent temperature takes into consideration multiple environmental factors that collectively influence human thermoregulation and physiological stress. This multidimensional approach aligns more closely with mechanisms of human heat balance, improving the accuracy of exposure assessment by better capturing microclimate variability.

To quantify the intensity of extreme heat exposure during sleep, we first defined general sleep time as the period between 22:00 and 6:00 (next day) according to previous sleep-related research.[19] We further employed cumulative excess sleep-time apparent temperature (eSAT) as proposed by previous studies to represent extreme heat exposure.[20] The indicator was calculated as the sum of excess apparent temperature during sleep time beyond a temperature threshold, the 95th percentile of daily minimum temperature (T_{min}) across Jiangsu Province, China during the whole study period, as

$$\text{eSAT} = \sum_{i}^{n=8} (T_{ij} - T_{\text{thr}}) \times I_{T_{\text{thr}}}(T_{ij})$$

where n_j, the number of sleep hours on day j; T_{ij}, the temperature during hour i on day j; T_{thr}, the temperature threshold; and $I_{T_{\text{thr}}}$, that is

$$I_{T_{\text{thr}}}(T_{ij}) = \begin{cases} 0 & \text{if } T_{ij} < T_{\text{thr}} \\ 1 & \text{if } T_{ij} \geq T_{thr} \end{cases}$$

In addition, we extracted several covariates including daily 24-h average fine particulate matter ($PM_{2.5}$) concentrations and maximum 8-h average ozone (O_3) concentrations from ChinaHighAirPollutants data sets (spatial resolution: 1 km × 1 km), as well as daily maximum temperature (T_{max}) from CLDAS.[21,22]

2.5. Statistical Analyses. To estimate the cumulative association between extreme heat exposure during sleep and COPD mortality, we used a conditional logistic regression model combined with a distributed lag nonlinear model. The eSAT cross-basis function was constructed by a natural cubic spline function with 2 internal knots at equally spaced percentiles of the concentrations, and a natural cubic spline function over a lag of 4 days with 1 internal knot on a log scale, according to the lowest Akaike Information Criterion value.[23−25] We controlled for the nonlinear and lagged effects of daytime temperature by adding a cross-basis function of T_{max} using identical arguments. The model also included a cross-basis function of O_3 with a lag of 1 day to control for the influence of air pollution during the warmest months. The main results are presented as cumulative exposure-response curves of eSAT and COPD mortality, and we also reported the estimated odds ratios (ORs) and their 95% confidence intervals (95% CIs) at a given eSAT in comparison to days without extreme heat exposure (eSAT = 0). A likelihood ratio test was used to examine the nonlinear association. Then, we estimated the population attributable fractions and numbers of attributable deaths based on the associations and the theoretical minimum risk exposure level (i.e., the minimum concentrations of eSAT), and their empirical CIs were computed through Monte Carlo simulation (simulation samples: 1000) to quantify the mortality burden of eSAT.[26,27] We excluded individuals without eSAT exposure on the day of death to avoid inflating the eSAT-related mortality burden as a result of including deaths that were unrelated to eSAT.

We categorized our study population into different subgroups by sex (male, female), age (<80 years, ≥80 years), marital status (married, widowed), occupation (farmer, nonfarmer), and ownership of air conditioners (low, high) to identify susceptible populations, assessing the difference within the stratum using a

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two-sample z-test.[28] Moreover, we conducted several sensitivity analyses with regard to (1) extension with a maximum lag of 7 or 10 days; (2) with or without the adjustment of air pollutants, including $PM_{2.5}$ and O_3; (3) the alternative of temperature thresholds (90th and 99th percentiles of T_{min}); (4) the peak months (July and August) of eSAT. Data analyses were conducted in R (version 4.4.1).[29] Two-sided $p < 0.05$ was regarded as statistically significant.

3. RESULTS

Table 1 provides detailed characteristics for the population during the corresponding period. During the warmest months (May to September) of 2015−2022, a total of 130,252 COPD deaths (case days) were identified across the 13 study cities in Jiangsu Province, China, with 446,428 corresponding control days. The mean age of the study population was 82.3 years, and the majority were male (58.9%). The spatial distribution of the deaths over the period is presented in Figure 1A. Figure 1B summarizes the temporal distribution of the daily mean eSAT during the whole study period. Mean eSAT exposure was 10.0 °C (ranging from 0 to 156.9 °C) on case days and 8.6 °C (ranging from 0 to 164.1 °C) on control days, showing a consistent peak in July and August throughout the study period.

Table 1. Baseline Characteristics of the Study Population from 2015 to 2022 in Jiangsu Province, China[a]

Characteristic	Values
COPD mortality, *n* (ICD-10 codes: J41−J44)	130,252
Case day, *n*	130,252
Control day, *n*	446,428
Sex, *n* (%)	
Male	76,722 (58.9)
Female	53,530 (41.1)
Age at death, years	
Mean (SD)	82.3 (8.7)
Median (IQR)	83.5 (10.6)
<80	43,162 (33.1)
≥80	87,090 (66.9)
Race, *n* (%)	
Han	129,582 (99.5)
Other	180 (0.1)
Unknown	490 (0.4)
Marital status, *n* (%)	
Unmarried	3645 (2.8)
Married	71,871 (55.2)
Divorced	682 (0.5)
Widowed	53,283 (40.9)
Unknown	771 (0.6)
Education, *n* (%)	
Junior high school or below	125,440 (96.3)
High school or above	4322 (3.3)
Unknown	490 (0.4)
Occupation, *n* (%)	
Farmer	110,394 (84.7)
Nonfarmer	19,368 (14.9)
Unknown	490 (0.4)
Ownership of air conditioner per household, *n* (%)	
Low	54317 (41.7)
High	75935 (58.3)
Subgroup, *n* (%)	
AECOPD (J44)	28,730 (22.1)
Chronic bronchitis (J41−J42)	93,265 (71.6)
Emphysema (J43)	8083 (6.2)

[a]Notes: AECOPD, acute exacerbation of COPD; COPD, chronic obstructive pulmonary disease; ICD-10, 10th Revision of the International Statistical Classification of Diseases and Related Health Problems; IQR, interquartile range; SD, standard deviation.

The exposure-response curves for COPD mortality associated with eSAT are presented in Figure 2. A monotonic, nonlinear increasing association was observed for overall COPD mortality, AECOPD, and chronic bronchitis (P for likelihood ratio test <0.001). This association was initially flat, followed by a rapid increase at higher eSAT levels. Table 2 presents the cumulative ORs and 95% CIs for eSAT at the 99th percentile. The estimated ORs (95% CIs) for mortality due to COPD, AECOPD, chronic bronchitis, and emphysema related to eSAT were 2.05 (1.88, 2.24), 2.07 (1.87, 2.30), 2.24 (1.85, 2.70), and 1.25 (0.88, 1.79), respectively. We also described the lag patterns of COPD mortality associated with eSAT (Figure S1). Immediate effects were observed on the day of death, with the association decreasing steadily over 4 days for COPD and AECOPD and 3 days for chronic bronchitis and emphysema. Table 2 and Figure S2 further stratify these associations by sex, age, marital status, and occupation. Elevated estimates for COPD mortality associated with eSAT were observed among females, individuals aged 80 years or older, widowed individuals, farmers, and individuals living in the city with lower ownership of air conditioners (P for two-sample z test <0.05).

As shown in Figure 3, the attributable fractions of mortality associated with eSAT were 3.37% (95% CI: 2.37%, 4.37%) for COPD, 3.07% (1.77%, 4.27%) for AECOPD, and 4.59% (2.45%, 6.42%) for chronic bronchitis. The estimated number of attributable deaths due to eSAT (Table S1) was 4,385 (95% CI: 3,084, 5,693) for COPD, 2,860 (1,651, 3,981) for AECOPD, and 1,320 (703, 1,845) for chronic bronchitis. Figure S3 and Table S1 illustrate the mortality burden of COPD attributable to eSAT across different population strata. Elevated attributable fractions were observed among females (3.84%, 5,003 deaths), individuals aged 80 years or older (3.89%, 5,073 deaths), widowed individuals (5.08%, 6,622 deaths), farmers (3.58%, 4,666 deaths), and individuals living in the city with lower ownership of air conditioners (4.78%, 6224 deaths). Analysis restricted to individuals with exposure on the day of death further supports the substantial short-term effects of sleep-time extreme heat on COPD mortality (Table S2).

In sensitivity analyses, the exposure-response curve and cumulative estimates for COPD mortality associated with eSAT remained consistent after the lag period was extended to 7 or 10 days (Table S3 and Figures S3 and S4) and after adjusting for air pollutants (Table 3 and Figures S5 and S6). Similarly, using the 90th percentile of T_{min} as the threshold for eSAT did not significantly alter the findings (Table S4 and Figure S7). While an inverse V-shaped relation was observed when using the 99th percentile of T_{min} as the threshold, the lag structure and overall estimates remained comparable (Table S4 and Figure S8). We also conducted additional analysis focusing on the peak months of eSAT and found slightly higher estimates for COPD mortality, indicating that the majority of the effects were concentrated during these peak months and highlighting the importance of targeted intervention (Figure S9).

4. DISCUSSION

This study provides evidence of a significant association between extreme heat exposure during sleep time and increased

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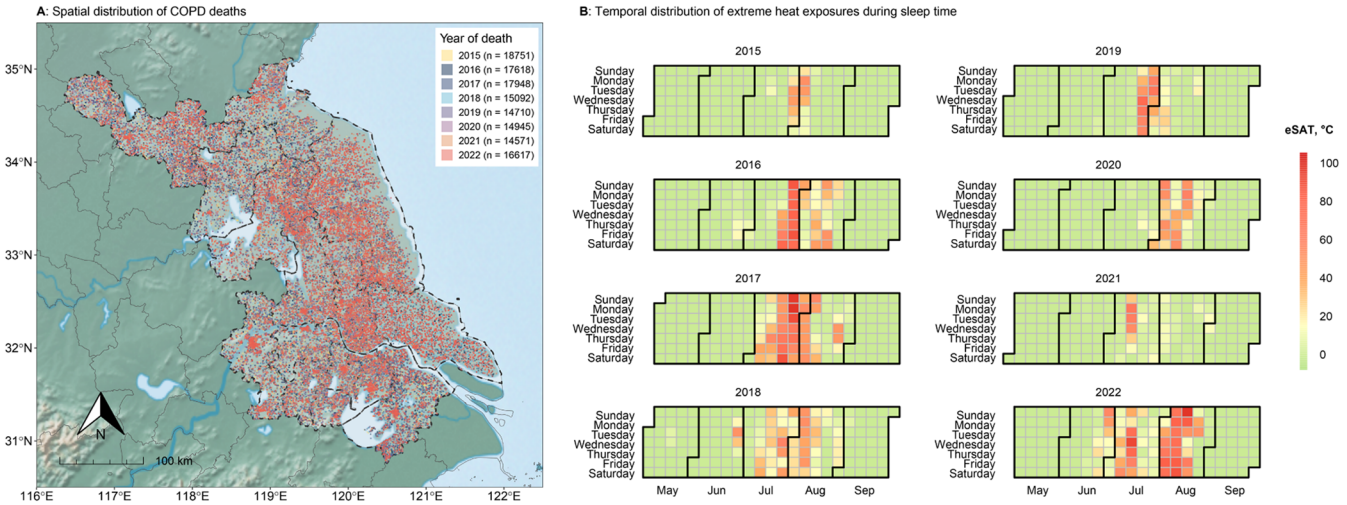

Figure 1. Spatial distribution of the included COPD deaths (A) and temporal distribution of extreme heat exposure during sleep (B) from 2015 to 2022 in Jiangsu Province, China. COPD, chronic obstructive pulmonary disease; eSAT, excess sleep-time apparent temperature.

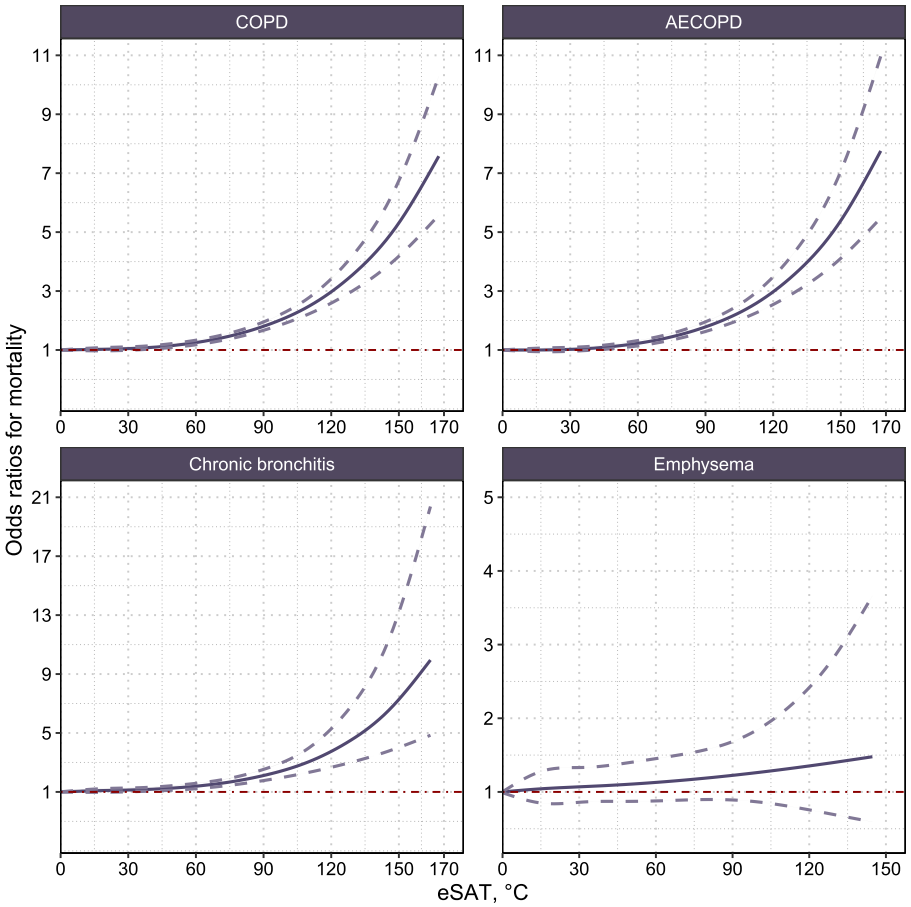

Figure 2. Exposure-response curves of COPD mortality associated with eSAT. The associations were presented as cumulative ORs over lags of 0−4 days with adjustment for O_3 and T_{max} using the distributed lag nonlinear models. All *P* values for nonlinear examination were <0.05. Solid lines represent the ORs of COPD mortality, and dashed lines represent their 95% CIs. AECOPD, acute exacerbation of COPD; CI, confidence interval; COPD, chronic obstructive pulmonary disease; eSAT, excess sleep-time apparent temperature; O_3, ozone; OR, odds ratio; T_{max}, daily maximum temperature.

COPD mortality in Jiangsu Province, China. Notably, the detrimental effects of eSAT were more pronounced among females, older adults, widowed individuals, farmers, and individuals living in the city with lower ownership of air conditioners. These findings highlight the potential for reducing premature COPD deaths by mitigating extreme heat exposure during sleep, emphasizing the importance of considering sleep-time temperature in heat-related health risk assessments and interventions.

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Table 2. Cumulative ORs (95% CIs) of COPD Mortality Associated with eSAT at the 99th Percentile from 2015 to 2022 in Jiangsu Province, China[a]

Subgroup	COPD	AECOPD	Chronic bronchitis	Emphysema
Total	2.05 (1.88, 2.24)	2.07 (1.87, 2.30)	2.24 (1.85, 2.70)	1.25 (0.88, 1.79)
Sex				
Male	1.70 (1.52, 1.90)	1.75 (1.53, 2.00)	1.85 (1.45, 2.36)	0.97 (0.62, 1.50)
Female	2.37 (2.08, 2.70)	2.32 (1.99, 2.71)	2.57 (1.96, 3.36)	1.71 (0.98, 3.00)
P value[b]	<0.001	0.01	0.08	0.09
Age				
<80 years	1.59 (1.37, 1.85)	1.54 (1.29, 1.83)	1.75 (1.26, 2.44)	1.78 (1.02, 3.11)
≥80 years	2.22 (2.00, 2.46)	2.28 (2.02, 2.58)	2.33 (1.88, 2.89)	0.97 (0.62, 1.51)
P value[b]	<0.001	<0.001	0.16	0.10
Marital status				
Married	1.63 (1.45, 1.83)	1.65 (1.44, 1.89)	1.78 (1.39, 2.29)	1.18 (0.75, 1.86)
Widowed	2.52 (2.21, 2.87)	2.51 (2.15, 2.94)	2.70 (2.06, 3.54)	1.36 (0.78, 2.38)
P value	<0.001	<0.001	0.04	0.68
Occupation				
Farmer	2.07 (1.89, 2.26)	2.09 (1.88, 2.32)	2.25 (1.85, 2.73)	1.22 (0.84, 1.78)
Nonfarmer	1.41 (1.10, 1.80)	1.37 (1.01, 1.84)	1.48 (0.88, 2.48)	1.42 (0.55, 3.61)
P value[b]	0.004	0.01	0.14	0.74
Ownership of air conditioner				
Low	2.49 (2.08, 2.98)	2.43 (1.96, 3.01)	2.59 (1.78, 3.79)	2.58 (1.25, 5.31)
High	1.61 (1.43, 1.81)	1.61 (1.43, 1.81)	1.65 (1.44, 1.89)	0.95 (0.62, 1.45)
P value[b]	<0.001	0.003	0.16	0.02

[a]AECOPD, acute exacerbation of COPD; CI, confidence interval; COPD, chronic obstructive pulmonary disease; eSAT, excess sleep-time apparent temperature; OR, odds ratio; T_{max}, daily maximum temperature. Estimates were generated using conditional logistic regression models and distributed lag nonlinear models over lags of 0−4 days with adjustment for O_3 and T_{max}. [b]Difference within stratum were compared by two-sample *z* test.

Table 3. Cumulative ORs (95% CIs) of COPD Mortality Associated with esat at the 99th Percentile with Additional Adjustment for Air Pollution[a]

Adjustment	COPD	AECOPD	Chronic bronchitis	Emphysema
Without	2.08 (1.91, 2.28)	2.10 (1.89, 2.33)	2.30 (1.91, 2.77)	1.29 (0.90, 1.83)
+ O_3	2.05 (1.88, 2.24)	2.07 (1.87, 2.30)	2.24 (1.85, 2.70)	1.25 (0.88, 1.79)
+ $PM_{2.5}$	2.07 (1.90, 2.26)	2.09 (1.88, 2.32)	2.27 (1.88, 2.74)	1.30 (0.91, 1.85)

[a]Estimates were generated using conditional logistic regression models and distributed lag nonlinear models over lags of 0−4 days. AECOPD, acute exacerbation of COPD; CI, confidence interval; COPD, chronic obstructive pulmonary disease; eSAT, excess sleep-time apparent temperature; OR, odds ratio; O_3, ozone; $PM_{2.5}$, fine particulate matter.

Global warming and the consequent increase in extreme temperatures pose significant health risks, particularly for individuals with COPD.[30] While emerging studies conducted in Southern Europe and East Asia have established a link between nighttime extreme heat and respiratory mortality, these investigations primarily focused on the entire night without specifically isolating the impact of heat exposure during sleep.[23,31] This distinction is critical because sleep itself induces unique physiological changes in the respiratory system, including reduced ventilatory drive, blunted CO_2 responsiveness, and elevated cholinergic tone.[32,33] These changes render the respiratory system inherently more vulnerable to environmental stressors during sleep compared with waking hours. To the best of our knowledge, this represents the first study to directly investigate the relationship between extreme heat exposure specifically during sleep time and COPD mortality. Our findings provide novel evidence of the adverse effects of sleep-time heat and COPD mortality, highlighting the essential need for optimal thermal conditions during sleep to protect respiratory health.

Sleep is fundamental to maintaining cognitive function, work performance, and overall physical and mental health.[34] Studies have demonstrated a strong link between poor sleep quality and increased COPD exacerbation risk, with individuals experiencing both a higher frequency of exacerbations and a shorter time to exacerbation.[35] Furthermore, short sleep duration has been

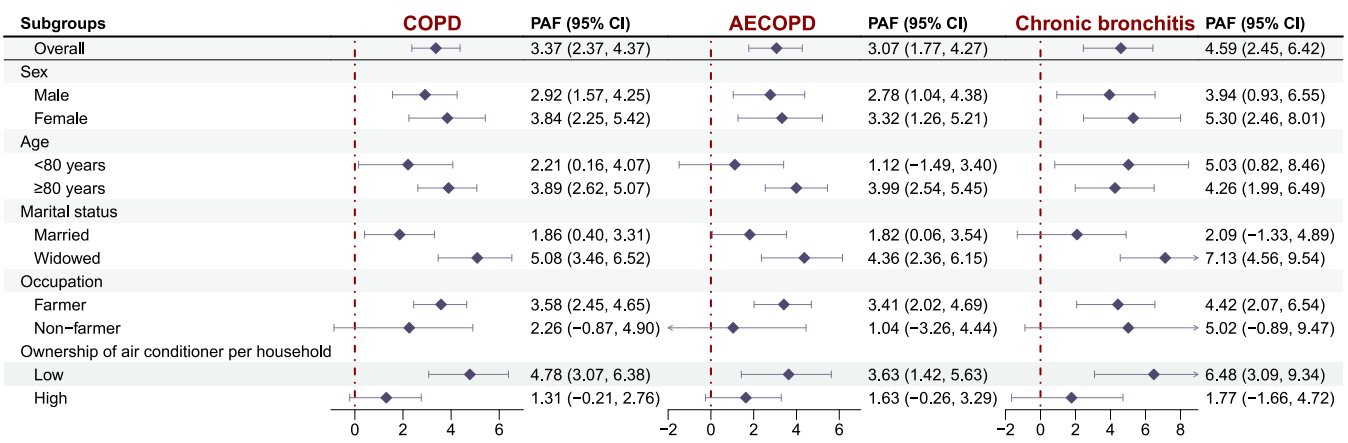

Figure 3. PAF (95% CIs) of COPD mortality associated with eSAT from 2015 to 2022 in Jiangsu Province, China. AECOPD, acute exacerbation of COPD; CI, confidence interval; COPD, chronic obstructive pulmonary disease; eSAT, excess sleep-time apparent temperature; PAF, population attributable fractions.

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shown to negatively impact the quality of life in COPD patients, while sleep disturbances are associated with poorer overall health status.[36] These associations extend beyond COPD, as sleep disturbances have also been linked to an increased mortality risk from chronic lower respiratory diseases in general.[37] Ambient temperature is a key regulator of sleep. Elevated temperatures disrupt sleep architecture through thermoregulatory mechanisms, leading to increased wakefulness and reductions in both slow-wave sleep and rapid eye movement sleep.[38] This susceptibility to heat-induced sleep disruption is particularly pronounced in older adults, who experience age-related physiological changes that compromise thermoregulation and alter sleep patterns.[39] Even young individuals exhibit incomplete adaptation to prolonged heat exposure, as evidenced by persistent sleep fragmentation observed after five consecutive days.[40] Our findings suggest that sleep-time extreme heat contributes to increased COPD mortality, potentially by exacerbating the detrimental effects of impaired sleep on respiratory health. This highlights the importance of ensuring a cooler sleep environment for individuals with COPD, which could mitigate these negative effects, alleviate strain on their respiratory systems, and ultimately reduce mortality risk.

In the study, we observed a null association between eSAT and emphysema mortality. The plausible mechanism remains unclear. One possible explanation is that structural lung damage (e.g., alveolar destruction) of emphysema may render patients less responsive to acute thermal stressors compared to those with airway-predominant disease (e.g., chronic bronchitis), where inflammation and mucus are more dynamically modulated.[25,41] Emphysema patients often have more advanced disease with severe airflow limitation and may use long-term oxygen therapy or noninvasive ventilation, potentially mitigating temperature-related risks.[42−44] The severity of emphysema may correlate more strongly with air pollutants than with temperature. A cross-sectional study in Taiwan also supported the finding that elevated temperature was associated with a decrease in the percent of low attenuation area (measurement for the severity of emphysema), but $PM_{2.5}$ mainly mediated the effects.[45] In addition, relatively small emphysema subgroups ($n = 8083$) may reduce the power to detect modest associations. More research is needed to confirm the association between extreme heat and emphysema mortality.

Moreover, the associations between sleep-time extreme heat and COPD mortality were particularly pronounced in specific subgroups. Apart from other categories, of greater interest is the evident disparity in different marital statuses, where widowed individuals had an elevated mortality risk of COPD. This aligns with studies from France and Brazil reporting heightened heat susceptibility among the widowed.[46,47] Nowadays, marital status has become synonymous with a stable family structure or social isolation. Marriage could benefit the health of a spouse by encouraging healthy lifestyles, reducing risk-taking behaviors, as well as enhancing social networks and caregiving within marital relationships.[48,49] Conversely, widowed individuals suffer higher mortality compared to married people, and this widowhood effect could be longstanding.[50] Spousal loss might lead to reduced self-care for diseases, neglect of own needs, an increase of risk behaviors, and ultimately impairment of human health.[51] Overall, the findings underscore the importance of tailored interventions for vulnerable population to mitigate health disparities.

In recent years, China has vigorously implemented climate adaptation strategies across its population to mitigate global warming. For the health sector, maximum and mean temperatures representing general daytime exposure are the primary focus of heat stress adaptation. However, it remains less recognized that ambient heat during sleep also unconsciously diminishes human health unconsciously. Our results demonstrate the adverse effects of sleep-time extreme heat on COPD mortality, supporting the hypothesis that extreme heat during sleep time might exert an independent effect of mortality beyond general time exposure. The findings of this study underscore the critical need to address extreme heat during sleep in public health communication and implement appropriate protective measures against the effects of sleep-time heat on respiratory health.

This study has crucial implications for policy. First, our study provides evidence on the adverse effects of sleep-time extreme heat on COPD mortality. The assessment of sleep-time temperature is more likely to be neglected in the consideration of heat-related health impacts. Our results could help policymakers develop more comprehensive strategies. Second, we found that higher ownership of air conditioners per household was associated with a lower mortality risk of COPD caused by extreme heat during sleep. Our findings suggest the importance and use of air conditioning. Without sacrificing comfort, the use of an electric fan as an alternative to air conditioning might also help contribute to heat loss.[52] Third, our results also highlight the necessity for efficient interventions. Green and blue spaces in urban planning are environmentally friendly and cost-effective ways to reduce the night-time surface temperature.[53] Ventilation corridors connecting buildings, water, and afforestation to reduce heat have been created in China.[54] Fourth, when developing a heat-related warning system, sleep-time heat should be considered, particularly for vulnerable populations.

There are several strengths in our study. First, we applied the eSAT as an exposure variable to estimate the association. Previous studies tended to use specific temperatures to define the occurrence of extreme heat events. The eSAT was more sensitive, as it could quantify the intensity of extreme heat and well reflected the accumulative effect of heat stress.[20] Second, high-spatiotemporal-resolution data sets were used in our study for individual-level exposure assessment of meteorological conditions. Our method was superior to those used in same-topic studies. Third, we applied apparent temperature to calculate the heat indices, which took several meteorological variables into account and had been widely used in estimating the effects of ambient temperature on human health.[55,56] Finally, the time-stratified case-crossover design helps control for time-invariant variables and time-variant covariates that alter very slowly.

Several limitations still need to be admitted. First, although we performed the exposure assessment based on a precise data set, the method does not take individual activity and indoor exposure into account. Although this may lead to exposure misclassification, the misclassification was considered non-differential.[57] Second, although we artificially set a universal sleep period by referring to available sleep-related research, individual variations of the period might still bias the results. Third, although we have applied the time-stratified case-crossover design to adequately control for the influence of time-independent variables (e.g., sex, smoking history, occupational history, genetics), day of the week, and seasonality and included daily maximum temperature and air pollutants in the model to control for the influence of daytime heat and air pollution, there were still unmeasured confounders in the

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assessment of the association between extreme heat during sleep and COPD mortality that might still bias our results. Finally, this study was restricted to a specific area in China, and the generalization of our findings to other populations should still be wary.

In brief, this case-crossover study provides novel evidence of a significant association between sleep-time extreme heat and COPD mortality. Females, individuals aged 80 years or older, widowed individuals, farmers, and individuals living in the city with lower ownership of air conditioners were more vulnerable to sleep-time extreme heat. Reducing exposure to extreme heat during sleep could help prevent premature deaths from COPD. Our findings emphasize the need for tailored strategies on sleep-time temperature to protect respiratory health.

■ ASSOCIATED CONTENT

Data Availability Statement

The meteorological condition data (CLDAS version 2.0) are available at the National Meteorological Information Center in China (http://data.cma.cn). The air pollution data (China-HighAirPollutants data set) are available at https://weijing-rs.github.io/product.html. The surveillance data on mortality from COPD used in this study are not publicly available.

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.est.5c02153.

Number of COPD deaths attributable to eSAT during sleep time (Table S1); disease burden of subjects with extreme heat exposure on the day of death (Table S2); estimates of different lag patterns (Table S3); estimates with additional adjustment for air pollution (Table S4); estimates using different temperature thresholds (Table S5); lag structure (Figure S1); exposure-response curves of different strata (Figure S2); exposure-response curves over lags of 0−7 days (Figure S3); exposure-response curves over lags of 0−10 days (Figure S4); exposure-response curves with single adjustment for T_{max} (Figure S5); exposure-response curves with multiadjustment for $PM_{2.5}$ and T_{max} (Figure S6); exposure-response curves using the threshold of daily minimum temperatures at the 90th percentile (Figure S7); exposure-response curves using the threshold of daily minimum temperatures at the 99th percentile (Figure S8); exposure-response curves restricting to the peak months of eSAT (Figure S9) (PDF)

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Notes

The authors declare no competing financial interest.

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