Indoor temperature and respiratory disease-related emergency department visits: a study of cumulative effects among older adults in Taiwan

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Abstract

Background
Studies have demonstrated that exposure to extreme outdoor temperatures increases respiratory diseases related mortality and morbidity, especially in older adults. However, older adults spend over 80% of their time indoors, and the cumulative effects of exposure to indoor temperature on the risk of respiratory diseases have not been investigated. The objective of this study was to study the cumulative effect of indoor temperature exposure on emergency department visit due to respiratory diseases among older adults.

Methods
Participant data were collected from the Longitudinal Health Insurance Database from 2000 to 2014 in Taiwan. The cumulative degree hour was used to reflect the cumulative effect of indoor temperature exposure. A distributed lag nonlinear model was used to analyze the association between cumulative degree hour and emergency department visit due to respiratory diseases.

Results
Our findings revealed a significant risk of emergency department visits due to respiratory diseases at 27, 28, 29, 30, and 31 °C when cooling cumulative degree hours exceeded 60, 30, 19, 1, and 1, respectively, during the hot season (May to October) and at 19, 20, 21, 22, and 23 °C when heating cumulative degree hours exceeded 1, 1, 1, 39, and 49, respectively, during the cold season (November to April).

Conclusions
We conclude that the cumulative effects of indoor temperature exposure should be considered to reduce respiratory disease risk under climate change.

Background
Extreme temperature has a critical effect on human health [1], numerous studies have investigated the risk of extreme temperature exposure on respiratory diseases [2–7]. People spend over 80% of their time indoors [8, 9], and several factors affect indoor temperature change, such as building materials, air conditioning usage, and human activities [10]. Therefore, indoor temperature may be a more decisive factor in the risk of respiratory diseases than outdoor temperature is.

According to our knowledge, only one study investigated the association between indoor temperature
exposure and the risk of respiratory diseases [11]. They determined that indoor temperature can affect the level of PM$_{2.5}$ and NO$_2$ during the hot season, which contribute to respiratory diseases. However, this study did not directly investigate the effect of indoor temperature exposure on occupants’ health and consider the cumulative effects of high or low temperature. Sexton and Hattis reported that exposure time, frequency, and level were crucial parameters when researching the effects of environmental factors on human health [12]. In a study by Frank, the Cumulative Heat Strain Index (CHSI) was used to investigate the cumulative effect of heat on human health, they indicated that the CHSI outperformed conventional indicators, such as the physiological strain index [13]. Moreover, studies have used heating (HDGd) and cooling (CDGd) degree hours to assess the association between cumulative degree hours and energy consumption indoors [14, 15]. Therefore, considering the cumulative effects of high or low indoor temperature exposure on human health is necessary.

Numerous studies have identified a higher risk of disease and a lower ability to respond to temperature change among older people than among younger people [16–18]. Moreover, United Nations report indicated that the global population of people over 60 years old was 962 million in 2017 and will reach about 2 times in 2050 [19]. Taiwan’s rate of population aging is ranked number one in the world. According to the Statistical report from Taiwan’s Ministry of the Interior [20], the population aged over 65 years was 7% in 1993 and will reach 20% in 2026. We cannot ignore the impact of indoor temperature exposure on older adults. Besides, men and women have different ability in thermoregulation [21], and one study demonstrated gender-related differences in sweat loss [22]. A study indicated that older adults spend significantly more time indoors compared with adolescents (age: 12–19) and adults (age: 20–59) [23]. However, no study investigated the cumulative effects of indoor temperature exposure on health among differences with respect to gender.

The objective of this study was to investigate the cumulative effects of indoor temperature exposure on emergency department visits for respiratory diseases among older adults and further examine the differences between age groups and genders.
Methods
Cumulative degree hour calculation
Cumulative degree hours (CDHs) can be used to reflect the cumulative effects of indoor temperature exposure on participants. The indoor temperature data were important parameter in calculating the CDHs. The indoor temperature was calculated from a prediction model of indoor temperatures. The detailed processes and materials of indoor temperature prediction estimation are reported in our previous study [24]. In brief, we collected hourly levels of indoor and outdoor weather data, land surface temperature, the normalized difference vegetation index (NDVI), building characteristics, occupants’ behavior, and electricity consumption from 30 study houses in Taiwan from 2012 to 2015, then a mixed effect model was used to build a prediction model of hourly indoor temperature. Because weather conditions differ by month, we estimated the prediction model of indoor temperature for each month.

In this study, we collected the weather, land surface temperature, NDVI, electricity consumption, and building characteristics from Taiwan’s Central Weather Bureau, National Aeronautics and Space Administration (NASA, US), NASA, Taiwan power company, and statistical report of Ministry of the Interior in Taiwan, respectively, to calculate the hourly indoor temperature from 2000 to 2014 based on the prediction models [24]. After calculating the indoor temperature, the data was used to calculate the CDHs. CDHs can be calculated using equations 1 and 2 for cooling and heating degree hours in hot (May to October) and cold (November to April) seasons [24], respectively:

\[
\text{Cooling degree hours} = \sum_{i=1}^{N} (T_i - T_b)
\]  
\[
\text{Heating degree hours} = \sum_{i=1}^{N} (T_b - T_i)
\]

where \(T_i\) is the indoor temperature, \(T_b\) is the threshold, and \(N\) is the hours in a day. According to our previous study [25], the risk of emergency department visits due to respiratory diseases was significant at indoor temperatures of 27–31 °C during the hot season (May to October) and 19–23 °C during the cold season (November to April). Therefore, the thresholds were 27 °C and 23 °C of indoor temperature of both hot and cold seasons, respectively.

Study Participants
The emergency department visit data for respiratory diseases were collected from the Longitudinal Health Insurance Database (LHID) of the National Health Insurance program. According to the statistical report from the Taiwan National Health Insurance [26], 99.6% of Taiwan’s population was enrolled in this insurance program in 2014. Therefore, the emergency department visit data from the National Health Insurance program accurately reflected the actual situation in Taiwan. The LHID data were collected from January 1, 2001, to December 31, 2014. The LHID contains data for 2,000,118 participants from 317 townships on the island of Taiwan. After excluding the population younger than 65 years, a total of 231,282 participants were included in this study. These subjects were further divided into three age groups: 65–74 years old, 75–84 years old, and > 85 years old. The diagnoses of emergency department visits were based on the International Classification of Diseases, Ninth Revision, Clinical Modification (codes 460–519).

Data Analysis For Cdhs And Emergency Department Visit
A distributed lag nonlinear model (DLNM) was used to analyze the association between CDHs and emergency department visits for respiratory diseases until cumulative degree hours were associated with emergency department visit risk for respiratory diseases. In our previous study [25], temperatures of 27–31 °C indoors during the hot season (May to October) and 19–23 °C during the cold season (November to April) were associated with significant risks of respiratory diseases. Therefore, we calculated the CDHs at 27–31 °C during the hot season and at 19–23 °C during the cold season and further analyzed the association between emergency department visits due to respiratory diseases and CDHs.

Studies have indicated that air pollution is one of the principal factors that influences temperature-related diseases [27, 28]; therefore, we collected air pollutant concentration data (NOx, PM2.5, and O3) from Taiwan’s Environmental Protection Administration from 2000 to 2014 to control the association between CDHs and emergency department visits for respiratory diseases. The average concentrations of PM2.5, O3, and NOx from 2000 to 2014 are displayed in the supplemental document (Table S1). Previous study indicated that pneumonia and influenza (PI) affected the diagnosis for respiratory diseases [28, 29], so this study also collected the number of pneumonia and influenza
from LHID (code 480–487) to control the association between CDHs and emergency department visits due to respiratory diseases. The number of emergency department visit were different in different study day, we adjusted the day of the week (DOW); moreover, the number of emergency department visits could increase due to the outpatient was closed during holiday [30], we also adjusted the holiday.

The equation of DLNM is as follow:

\[
\log(E(Y)) = \beta_0 + \sum_{i=0}^{7} NS(CDH_i, DF, 5; \text{lag}, 7) + \sum_{i=0}^{1} Lin(PM_{2.5i}) + \sum_{i=0}^{1} Lin(O_{3i}) \\
+ \sum_{i=0}^{1} Lin(NO_{ix}) + NS\left(\frac{Time}{\text{year}}, \frac{7}{\text{day}}\right) + DOW + \text{Holiday} + PI
\]

(3)

where \(Y\) is the emergency department visits for cardiovascular diseases, \(NS\) is the nature cubic spline, \(CDH\) is the cumulative degree hour, \(DF\) is the degree of freedom (DF is 5), \(\text{lag}\) is the lag day (7 days), \(\text{time}\) is the node, \(DOW\) is the day of the week, \(PI\) is the pneumonia and influenza. For example, a DLNM was applied to analyze the relationship between the CDHs (independent variable) and daily emergency visits (dependent variable) when indoor temperature exceeding 27°C, the significance level would show the relative risk (RR) and the CDHs when indoor temperature exceeding 27°C.

We used SAS 9.4 software (v9.4, SAS Institute Inc., Cary, NC, USA) to analyze all data. Statistical significance was set at \(p < 0.05\).

Results
Emergency department visits for cardiovascular diseases
The CDHs of indoor temperatures are presented in Table S2. The summary of emergency department visits due to respiratory diseases in each study group is presented in Table 1. The rates of emergency department visit due to respiratory diseases were 107,364 and 123,918 during hot and cold seasons, respectively. The population was 43,048, 46,760, and 17,556 in the age groups of 65 to 74 years, 75 to 84 years, and > 85 years, respectively, during the hot season, and 50,891, 53,302, and 19,725, respectively, during the cold season. Moreover, 63,796 emergency department admittees were men and 43,568 were women during the hot season, and 72,535 admittees were men and 51,383 were
women during the cold season.

Table 1
Summary of cardiovascular disease–related emergency department visits from 2000 to 2014 in hot and cold seasons based on different subgroups.

|                  | Hot season | Cold season |
|------------------|------------|-------------|
| Older adults (≥ 65 years old) | 107,364 | 123,918 |
| Age              |            |             |
| 65 to 74 years   | 43,048     | 50,891      |
| 75 to 84 years   | 46,760     | 53,302      |
| > 85 years       | 17,556     | 19,725      |
| Gender           |            |             |
| Man              | 63,796     | 72,535      |
| Woman            | 43,568     | 51,383      |

Association Between Indoor Temperature And Cardiovascular Diseases

Table 2 presents the CDHs at different indoor temperatures. During the hot season, there was a significant risk of emergency department visits due to respiratory diseases at 27, 28, 29, 30, and 31 °C when the CDHs exceeded 60, 30, 19, 1, and 1 (p < 0.05), respectively. During the cold season, there was a significant risk of emergency department visits due to respiratory diseases when the CDHs exceeded 1, 1, 1, 39, and 49 at 19, 20, 21, 22, and 23 °C (p < 0.05), respectively.

Table 2
Cooling and heating cumulative degree hours for cardiovascular disease–related emergency department visits for older adults from 2000 to 2014 in hot and cold seasons, respectively.

| Setpoint temperature (indoor) | CDH | Relative risk (95% CI) |
|-------------------------------|-----|------------------------|
| Hot season                    |     |                        |
| 27 °C                         | 60  | 1.107 (1.005, 1.218)   |
| 28 °C                         | 30  | 1.080 (1.004, 1.162)   |
| 29 °C                         | 19  | 1.060 (1.003, 1.121)   |
| 30 °C                         | 1   | 1.008 (1.005, 1.013)   |
| 31 °C                         | 1   | 1.041 (1.012, 1.070)   |
| Cold season                   |     |                        |
| 23 °C                         | 49  | 1.070 (1.0005, 1.143)  |
| 22 °C                         | 39  | 1.056 (1.000, 1.114)   |
| 21 °C                         | 1   | 1.004 (1.001, 1.006)   |
| 20 °C                         | 1   | 1.006 (1.002, 1.010)   |
| 19 °C                         | 1   | 1.003 (0.996, 1.009)   |

CDH: Cumulative degree hours; CI: Confidence interval.

This study further analyzed the differences between gender and age groups regarding the cumulative effects of indoor temperature exposure, as displayed in Tables 3 and 4, respectively. Among men, a significant risk of emergency department visits due to respiratory diseases during the hot season occurred when the CDHs exceeded 64, 33, 6, 1, and 1 at 27, 28, 29, 30, and 31 °C (p < 0.05), respectively; a significant risk occurred during the cold season when the CDHs exceeded 1, 1, 1, 9, and 47 at 19, 20, 21, 22, and 23 °C (p < 0.05), respectively. Among women, a significant risk of emergency department visits due to respiratory diseases during the hot season occurred when the CDHs exceeded 54, 26, 16, 1, and 1 at 27, 28, 29, 30, and 31 °C (p < 0.05), respectively; a significant
risk occurred during the cold season when the CDHs exceeded 1, 1, 1, 38, and 64 at 19, 20, 21, 22, and 23 °C (p < 0.05), respectively.

**Table 3**

Cooling and heating cumulative degree hours for cardiovascular disease–related emergency department visits for older adults from 2000 to 2014 (sex stratified) in hot and cold seasons, respectively.

| Setpoint temperature (indoor) | Man | Woman |
|-------------------------------|-----|-------|
| Hot season                    |     |       |
| 27 °C                         | 64  | 54    |
| Relative risk (95%CI)         | 1.134 (1.006, 1.278) | 1.111 (1.005, 1.229) |
| 28 °C                         | 33  | 26    |
| Relative risk (95%CI)         | 1.096 (1.001, 1.201) | 1.083 (1.0001, 1.173) |
| 29 °C                         | 6   | 16    |
| Relative risk (95%CI)         | 1.042 (1.0001, 1.086) | 1.087 (1.001, 1.182) |
| 30 °C                         | 1   | 1     |
| Relative risk (95%CI)         | 1.023 (1.012, 1.034) | 1.021 (1.007, 1.034) |
| 31 °C                         | 1   | 1     |
| Relative risk (95%CI)         | 1.106 (1.059, 1.155) | 1.095 (1.043, 1.149) |
| Cold season                   |     |       |
| 23 °C                         | 47  | 64    |
| Relative risk (95%CI)         | 1.083 (1.003, 1.171) | 1.102 (1.0005, 1.215) |
| 22 °C                         | 9   | 38    |
| Relative risk (95%CI)         | 1.027 (1.00004, 1.054) | 1.086 (1.001, 1.179) |
| 21 °C                         | 1   | 1     |
| Relative risk (95%CI)         | 1.007 (1.003, 1.010) | 1.005 (1.001, 1.009) |
| 20 °C                         | 1   | 1     |
| Relative risk (95%CI)         | 1.005 (1.0001, 1.009) | 1.008 (1.003, 1.014) |
| 19 °C                         | 1   | 1     |
| Relative risk (95%CI)         | 1.010 (1.003, 1.018) | 1.010 (1.002, 1.019) |

CDH: Cumulative degree hours; CI: Confidence interval
Table 4
Cooling and heating cumulative degree hours for cardiovascular disease-related emergency department visits for older adults from 2000 to 2014 (age stratified) in hot and cold seasons, respectively.

| Setpoint temperature (indoor) | 65 to 74 years old | 75 to 84 years old | > 85 years old |
|-------------------------------|--------------------|--------------------|----------------|
|                               | CDH*               | Relative risk (95%CI) | CDH*           | Relative risk (95%CI) | CDH*           | Relative risk (95%CI) |
| Hot season                    |                    |                    |                |                    |                |                    |
| 27 °C                         | 69                 | 1.167 (1.0006, 1.360) | 53             | 1.105 (1.003, 1.218) | 60             | 1.207 (1.005, 1.451) |
| 28 °C                         | 35                 | 1.121 (1.001, 1.255) | 26             | 1.083 (1.001, 1.171) | 36             | 1.176 (1.010, 1.369) |
| 29 °C                         | 19                 | 1.068 (1.003, 1.136) | 13             | 1.083 (1.005, 1.167) | 12             | 1.122 (1.011, 1.247) |
| 30 °C                         | 1                  | 1.019 (1.008, 1.031) | 1              | 1.020 (1.007, 1.034) | 1              | 1.037 (1.017, 1.057) |
| 31 °C                         | 1                  | 1.094 (1.049, 1.090) | 1              | 1.121 (1.069, 1.176) | 1              | 1.161 (1.094, 1.233) |
| Cold season                   |                    |                    |                |                    |                |                    |
| 23 °C                         | 52                 | 1.084 (1.002, 1.172) | 46             | 1.091 (1.002, 1.189) | 56             | 1.130 (1.001, 1.277) |
| 22 °C                         | 40                 | 1.090 (1.0003, 1.188) | 1              | 1.004 (1.001, 1.008) | 30             | 1.108 (1.001, 1.227) |
| 21 °C                         | 1                  | 1.005 (1.001, 1.009) | 1              | 1.007 (1.003, 1.011) | 1              | 1.011 (1.005, 1.016) |
| 20 °C                         | 1                  | 1.005 (1.001, 1.011) | 1              | 1.008 (1.0103, 1.013) | 1              | 1.013 (1.006, 1.020) |
| 19 °C                         | 1                  | 1.002 (0.993, 1.010) | 1              | 1.008 (0.999, 1.016) | 1              | 1.019 (1.009, 1.029) |

CDH: Cumulative degree hours; CI: Confidence interval.

During the hot season (Table 4), participants aged 65 to 74 years had a significant risk of emergency department visits due to respiratory diseases at 27, 28, 29, 30, and 31 °C when CDHs exceeded 69, 35, 19, 1, and 1 (p < 0.05), respectively; participants aged 75 to 84 years had a significant risk at more than 53, 26, 13, 1, and 1 CDHs, respectively; and participants older than 85 years had a significant risk at more than 60, 36, 12, 1, and 1 CDHs, respectively. During the cold season, participants aged 65 to 74 years had a significant risk of emergency department visits due to respiratory diseases at 19, 20, 21, 22, and 23 °C when CDHs were more than 1, 1, 1, 40, and 52 (p < 0.05), respectively; participants aged 75 to 84 years had a significant risk at more than 1, 1, 1, 1, and 46 CDHs, respectively; and participants older than 85 years had a significant risk at more than 1, 1, 1, 30, and 56 CDHs.

Discussion
This study investigated the cumulative effects of indoor temperature exposure on emergency
department visits due to respiratory diseases. Our findings demonstrated that a significant risk of emergency department visits occurred when the indoor temperature exceeded 27°C during the hot season and the CDHs decreased with increases in temperature; the risk was significant when the indoor temperature was lower than 23°C during the cold season, and the CDHs decreased with decreasing temperature. Moreover, our data also revealed that the CDHs differed by gender and age groups. These results suggest that cumulative effects should be considered when making an adaptation policy for reducing the health effects of extreme temperature exposure, especially for older adults.

Our findings indicated that indoor temperature exposure was associated with the risk of emergency department visits due to respiratory diseases. Studies have indicated that high temperature exposure increases the levels of inflammatory indicators, which induces respiratory symptoms among patients with respiratory diseases [31]. High temperature exposure also causes blood to become more concentrated, which increases the risk of mortality for respiratory diseases [32]. Cold exposure induces tracheal contraction [33] or increased inflammatory indicator concentrations in plasma, such as interleukin-6 or norepinephrine, which induce the development of respiratory diseases [34]. Thus, high or low temperature exposure is one of the risk factors for respiratory diseases.

Although numerous studies have demonstrated that indoor and outdoor temperature exposure is associated with the risk of respiratory diseases [2–6, 11, 35], we further considered the cumulative effects of indoor temperature exposure on respiratory disease occurrence. As displayed in Table 2, the risk of emergency department visits was significant when the indoor temperature exceeded 27°C during the hot season, and the minimum CDHs decreased as the temperature increased; during the cold season, the risk was significant when the indoor temperature was lower than 23°C, and the minimum CDHs decreased with the temperature decrease. The study results could support efforts to policymakers to estimate an elastic temperature adaptation policy for reducing the risk of adverse health effects under extreme temperature exposure. For instance, during the cold season, a significant risk of emergency department visits due to respiratory diseases appeared when the CDHs were more than 49 at 23 °C and more than 1 at 21 °C (Table 2), which reflects that more emergency
rescues were necessary at an indoor temperature of 21 °C than at 23 °C.

We further investigated the cumulative effects based on gender and age groups, as summarized in Tables 3 and 4, respectively. Our data demonstrated that less CDHs induce an emergency department visit in women than in men at 27 and 28°C during the hot season. We speculate that because pulse oximetry and pulse rate are typically lower in women than in men [36], this reduces women's ability to overcome the effects of temperature change. Moreover, studies have indicated that women have a higher risk of respiratory diseases [37-39], such as spontaneous pneumothorax, pulmonary hypertension, and pregnancy-associated asthma exacerbation, than men. In Taiwan, cooking is an important source of particulate pollution among women [40] and studies indicated that cooking caused a reduction in forced expiratory volume in one second (FEV₁) among women [41], which indicates that women have a weaker ability to respond to the influence of high or low temperatures. However, the CDH were lower in men than in women during the cold season. Studies have indicated that women have less effective in thermoregulation with respect to cold compared with men [42], those results were not consistent with our data. We speculate that women often keep warm to overcome the temperature change during the cold season, which decreases the influence of low temperature exposure on health. That may explain the fewer CDHs in men than in women during the cold season.

Table 4 indicates that the group of participants aged 75 to 84 years exhibited illness with fewer CDHs compared with the other age groups. We speculate that the group aged over 85 years had a higher proportion of comorbidities [43] and respiratory diseases were not logged in the LHID database. Moreover, because the group aged over 85 years may have more comorbidities, the effects of the influencing factors on the thermoregulation mechanism may be more complex [44]. This may explain why the fewest CDHs occurred in the group of participants aged over 85 years.

There were some limitations to this study. First of all, a prediction model of indoor temperature was used to estimate indoor temperature, and thus, our data may not reflect the real exposure situation with respect to skin exposure. However, a study indicated that indoor temperature was associated with skin temperature [45]; thus, we conclude that using the indoor temperature from the prediction
model can still reflect the cumulative effect of exposure to indoor temperatures on the outcome. Second, certain data are not available in the LHID, such as alcohol consumption or smoking, for controlling the relationship between CDHs and emergency department visits due to respiratory diseases. Alcohol consumption and smoking are more common among men than women in Taiwan [46, 47]. In this study, we analyzed the association between indoor temperature exposure and emergency department visits due to respiratory diseases for different genders to control the confounder. Third, human activities in indoors was highly associated with the variation of indoor temperature. However, the human activities was not included in the predictive model. We speculated that the lack of detailed records of respective frequencies and time point of event. In the future, applying feasible technology to collect frequency and time of human activities in indoors is imperative. Fifth, the indoor temperature from the prediction model may not reflect the real exposure situation indoors in Taiwan. Yet, the average building age, building characteristics (included number of floors, building category, and building material), and population density in buildings in which the 30 selected households resided were similar to the characteristics of buildings in Taiwan [20]. Therefore, the data from the study households can present the indoor temperature distributions of the majority of households in Taiwan.

Conclusion
This paper applied CDHs to investigate the cumulative effect of indoor temperature exposure on emergency department visits due to respiratory diseases among older adults during both hot and cold seasons and analyzed the differences between gender and age groups. Our data revealed that during the hot season, the CDHs decreased as the indoor temperature increased, and during the cold season, the CDHs decreased as the indoor temperature decreased. Moreover, the CDHs were different in different gender and age groups in both the hot and cold seasons. These results indicate that policymakers should further consider the cumulative effects of indoor temperature exposure on hot- or cold-related respiratory diseases.

Declarations
Ethical Approval and Consent to participate
The study was approved by the Human Research Ethics Committee of National Cheng-Kung University.
Notification of Exemption
HREC (Exempt) No. 106-001

Application No. 105-336

Project Title: Indoor health risks and adaptive design in the built environment under impact of climate change - Effects of estimated temperature in indoors on health of susceptible population

Principal Investigator: Huey-Jen Su
Affiliation: National Cheng Kung University

Date of HREC exempt determination: 1/9/2017

Dear Professor Huey-Jen Su,

This project meets the criteria for exemption from further Human Research Ethics Committee at National Cheng Kung University (NCKU HREC) review per the regulations found at NCKU human research protection policies.

Exemption is not approval. The project materials may include the statement that “the project has certified for exemption from Human Research Ethics Committee at National Cheng Kung University.”

Although an exemption determination eliminates the need for further NCKU HREC review and approval, you still have an obligation to understand and abide by generally accepted human research protection principles, regulations and policies of responsible conduct of research which can be found in guidance from professional societies and scientific organizations. In addition, you may not make changes to this research activity without first discussing them with NCKU HREC to determinate that such changes are within the parameters for exemption.

If you have any questions, please contact the NCKU HREC office at +886-6-2757575-51020. NCKU HREC appreciates your commitment towards the ethical conduct of human research.

Yours sincerely,

Mei-Chih Huang, Ph.D.

[Signature]
Consent For Publication
The manuscript was reviewed and approved by all authors.

Competing interests
The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

- The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

- The authors agreed to submit the manuscript to the journal for publication.

None.

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Authors’ contributions
Chein-Cheng Jung: Drafting the manuscript, data analysis, and conduct study design.
Ying-Fang Hsia: Drafting the manuscript, data analysis, and make tables.
Nai-Yun Hsu: Investigation.
Yu-Chun Wang: Data analysis and reviewing.
Huey-Jen Su: Conception and reviewing.

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References
1. Intergovernmental Panel on Climate Change. Summary for policymakers. In: Climate Change 2014: Impacts, Adaptation, and Vulnerability. Part A: Global and Sectoral Aspects. Contribution of Working Group II to the Fifth Assessment Report of the IPCC. In. Cambridge. UK: Cambridge University Press: Intergovernmental Panel on Climate Change; 2014.

2. Anderson GB, Dominici F, Wang Y, McCormack MC, Bell ML, Peng RD. Heat-related emergency hospitalizations for respiratory diseases in the Medicare population. Am J Respir Crit Care Med. 2013;187(10):1098–103.

3. Lim Y-H, Hong Y-C, Kim H. Effects of diurnal temperature range on cardiovascular and respiratory hospital admissions in Korea. Science of The Total Environment. 2012;417:55–60.

4. Tam WW, Wong TW, Chair S, Wong AH. Diurnal temperature range and daily cardiovascular mortalities among the elderly in Hong Kong. Arch Environ Occup Health. 2009;64(3):202–6.
5. Turner LR, Barnett AG, Connell D, Tonga S. Ambient temperature and cardiorespiratory morbidity: a systematic review and meta-analysis. Epidemiology 2012:594–606.

6. Yang L-T, Chang Y-M, Hsieh T-H, Hou W-H, Li C-Y. Associations of ambient temperature with mortality rates of cardiovascular and respiratory diseases in Taiwan: a subtropical country. Acta Cardiologica Sinica. 2018;34(2):166.

7. Zhao Q, Zhao Y, Li S, Zhang Y, Wang Q, Zhang H, Qiao H, Li W, Huxley R, Williams G. Impact of ambient temperature on clinical visits for cardio-respiratory diseases in rural villages in northwest China. Sci Total Environ. 2018;612:379–85.

8. Klepeis NE, Nelson WC, Ott WR, Robinson JP, Tsang AM, Switzer P, Behar JV, Hern SC, Engelmann WH. The National Human Activity Pattern Survey (NHAPS): a resource for assessing exposure to environmental pollutants. Journal of Exposure Science Environmental Epidemiology. 2001;11(3):231.

9. Leech JA, Nelson WC, T BURNETT R, Aaron S, Raizenne ME. It's about time: a comparison of Canadian and American time–activity patterns. Journal of Exposure Science Environmental Epidemiology. 2002;12(6):427.

10. Jung C-C, Hsu N-Y, Su H-J. Temporal and spatial variations in IAQ and its association with building characteristics and human activities in tropical and subtropical areas. Build Environ. 2019;163:106249.

11. McCormack MC, Belli AJ, Waugh D, Matsui EC, Peng RD, Williams DAL, Paulin L, Saha A, Aloe CM, Diette GB. Respiratory effects of indoor heat and the interaction with air pollution in chronic obstructive pulmonary disease. Annals of the American Thoracic Society. 2016;13(12):2125–31.

12. Sexton K, Hattis D. Assessing cumulative health risks from exposure to environmental mixtures—three fundamental questions. Environmental health
perspectives. 2007;115(5):825–32.

13. Frank A, Belokopytov M, Shapiro Y, Epstein Y. The cumulative heat strain index—a novel approach to assess the physiological strain induced by exercise-heat stress. European journal of applied physiology. 2001;84(6):527-32.

14. Papakostas K, Kyriakis N. Heating and cooling degree-hours for Athens and Thessaloniki, Greece. Renewable Energy. 2005;30(12):1873-80.

15. Satman A, Yalcinkaya N. Heating and cooling degree-hours for Turkey. Energy. 1999;24(10):833-40.

16. Gasparrini A, Armstrong B, Kovats S, Wilkinson P. The effect of high temperatures on cause-specific mortality in England and Wales. Occup Environ Med. 2012;69(1):56-61.

17. Khajavi A, Khalili D, Azizi F, Hadaegh F. Impact of temperature and air pollution on cardiovascular disease and death in Iran: A 15-year follow-up of Tehran Lipid and Glucose Study. Sci Total Environ. 2019;661:243-50.

18. Wallmüller C, Spiel A, Sterz F, Schober A, Hubner P, Stratil P, Testori C. Age-dependent effect of targeted temperature management on outcome after cardiac arrest. Eur J Clin Invest. 2018;48(12):e13026.

19. United Nations. World Population Aging. In.: United Nations; 2017.

20. Ministry of the Interior. Statistical report of Ministry of the Interior. In. Taipei: Ministry of the Interior; 2018.

21. Xiong J, Lian Z, Zhou X, You J, Lin Y. Investigation of gender difference in human response to temperature step changes. Physiol Behav. 2015;151:426-40.

22. Mehnert P, Bröde P, Griefahn B. Gender-related difference in sweat loss and its impact on exposure limits to heat stress. Int J Ind Ergon. 2002;29(6):343-51.

23. Matz CJ, Stieb DM, Davis K, Egyed M, Rose A, Chou B, Brion O. Effects of age, season,
gender and urban-rural status on time-activity: Canadian Human Activity Pattern Survey 2 (CHAPS 2). Int J Environ Res Public Health. 2014;11(2):2108–24.

24. Jung C-C, Hsia Y-FH, Hsu N-YH, Wang Y-CW, Su H-J. Cumulative effect of indoor temperature on cardiovascular disease–related emergency department visits among older adults in Taiwan. Science of the Total Environment 2020. Accepted.

25. Lo Y-C. Effects of estimated indoor temperature on cardiovascular and respiratory morbidities. Tainan: National Cheng Kung University; 2017.

26. National Health Insurance: National Health Insurance Annual Report 2014 – 2015

National Health Insurance: National Health Insurance Annual Report 2014–2015. Taiwan ROC In. Taipei: National Health Insurance Administration, Ministry of Health and Welfare; 2015.

27. Liao Y-H, Wang G-S, Wang C-H, Lee Y-H, Lu K-C, Hsiao CK. Impact of area-specific temperature extremes on health outcomes in seven regions in Taiwan–using cerebrovascular and ischemic heart diseases as examples. Taiwan Gong Gong Wei Sheng Za Zhi. 2015;34(6):616.

28. Wang Y-C, Lin Y-K. Temperature effects on outpatient visits of respiratory diseases, asthma, and chronic airway obstruction in Taiwan. Int J Biometeorol. 2015;59(7):815–25.

29. Lam HC-y, Li AM, Chan EY-y, Goggins WB. The short-term association between asthma hospitalisations, ambient temperature, other meteorological factors and air pollutants in Hong Kong: a time-series study. Thorax. 2016;71(12):1097–109.

30. Buckeridge DL. Outbreak detection through automated surveillance: a review of the determinants of detection. J Biomed Inform. 2007;40(4):370–9.
31. Michelozzi P, Accetta G, De Sario M, D'Ippoliti D, Marino C, Baccini M, Biggeri A, Anderson HR, Katsouyanni K, Ballester F. High temperature and hospitalizations for cardiovascular and respiratory causes in 12 European cities. Am J Respir Crit Care Med. 2009;179(5):383–9.

32. Medina-Ramon MaS J. Temperature, temperature extremes, and mortality: a study of acclimatization and effect modification in 50 United States cities. Occup Environ Med. 2007;64:827–33.

33. Koskela HO. Cold air-provoked respiratory symptoms: the mechanisms and management. Int J Circumpolar Health. 2007;66(2):91–100.

34. Brenner I, Castellani J, Gabaree C, Young A, Zamecnik J, Shephard R, Shek P. Immune changes in humans during cold exposure: effects of prior heating and exercise. J Appl Physiol. 1999;87(2):699–710.

35. Zhang B, Li G, Ma Y, Pan X. Projection of temperature-related mortality due to cardiovascular disease in Beijing under different climate change, population, and adaptation scenarios. Environmental research. 2018;162:152–9.

36. Waugh J, Gardner D, Vines D. Differences in capnography and pulse oximetry measurements related to gender. Chest. 2012;142(4):939A.

37. Bain E, Pierides KL, Clifton VL, Hodyl NA, Stark MJ, Crowther CA, Middleton P. Interventions for managing asthma in pregnancy. Cochrane Database of Systematic Reviews 2014(10).

38. Pinkerton KE, Harbaugh M, Han MK, Jourdan Le Saux C, Van Winkle LS, Martin WJ, Kosgei RJ, Carter EJ, Sitkin N, Smiley-Jewell SM. Women and lung disease. Sex differences and global health disparities. Am J Respir Crit Care Med. 2015;192(1):11–6.

39. Regitz-Zagrosek V, Seeland U: Sex and gender differences in clinical medicine:
40. Yu K-P, Yang KR, Chen YC, Gong JY, Chen YP, Shih H-C. Lung S-CC: Indoor air pollution from gas cooking in five Taiwanese families. Build Environ. 2015;93:258–66.

41. Stabile L, Fuoco F, Marini S, Buonanno G. Effects of the exposure to indoor cooking-generated particles on nitric oxide exhaled by women. Atmos Environ. 2015;103:238–46.

42. McArdle W, Magel J, Spina R, Gergley T, Toner M. Thermal adjustment to cold-water exposure in exercising men and women. J Appl Physiol. 1984;56(6):1572–7.

43. Liu H, Tan Q, Li B-z, Tan M-l. Ma X-l: Impact of cold indoor thermal environmental conditions on human thermal response. Journal of Central South University of Technology. 2011;18(4):1285–92.

44. Yamashita Y, Hamatani Y, Esato M, Chun Y-H, Tsuji H, Wada H, Hasegawa K, Abe M, Lip GY, Akao M. Clinical characteristics and outcomes in extreme elderly (age ≥ 85 years) Japanese patients with atrial fibrillation: the Fushimi AF registry. Chest. 2016;149(2):401–12.

45. Lin Y-K, Ho T-J, Wang Y-C. Mortality risk associated with temperature and prolonged temperature extremes in elderly populations in Taiwan. Environmental research. 2011;111(8):1156–63.

46. Gender Equality Committee of the Executive Yuan. Percentage of alcohol drinking in adult in Taiwan. Taipei: Gender Equality Committee of the Executive Yuan; 2018.

47. Health Promotion Administration. Adult Smoking Behavior Surveillance System. Taipei: Health Promotion Administration, Ministry of Health and Welfare; 2019.

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