

# Associations of Ambient Temperature with Mortality Rates of Cardiovascular and Respiratory Diseases in Taiwan: A Subtropical Country

Li-Tan Yang,<sup>1,2,3</sup> Yao-Mao Chang,<sup>4,5</sup> Tsung-Han Hsieh,<sup>6</sup> Wen-Hsuan Hou<sup>7,8,9,10#</sup> and Chung-Yi Li<sup>2,11#</sup>

**Background:** We conducted a time-series analysis of daily ambient temperature and all-cause, cardiovascular, and respiratory disease mortality in Taiwan, which is generally neither extremely hot nor cold.

**Methods:** Data on all-cause daily mortality rates (excluding accidents, suicide, and homicide), and mortality rates due to respiratory and cardiovascular diseases between 2008 and 2010 were obtained from the Taiwan Death Registry. The daily temperature for that period was averaged from 33 monitoring stations nationwide. A generalized least square model was constructed to assess the relationship between the time-series trends of temperature and mortality, and the cross-correlation function was used to determine the possible time lag for the effect of temperature on mortality.

**Results:** As the average temperature increased, the daily all-cause ( $\beta = -0.006$ ) and respiratory disease ( $\beta = -0.012$ ) mortality rates decreased. On the other hand, an inverse relationship ( $\beta = -0.028$ ) between average daily temperature and cardiovascular disease mortality was observed only for a temperature between 12.91 °C and 26.36 °C. The time lag for all-cause and cardiovascular disease mortality was similar at 4–6 days, while the lag for respiratory disease was longer at 13–16 days.

**Conclusions:** We found inverse associations between average temperature and all-cause and respiratory mortality. An inverse association between temperature and cardiovascular disease mortality was observed only from 12.91 °C to 26.36 °C.

**Key Words:** Cardiovascular disease • Epidemiology • Mortality

Received: May 22, 2017

Accepted: November 1, 2017

<sup>1</sup>Division of Cardiology, Department of Internal Medicine, National Cheng Kung University Medical College and Hospital; <sup>2</sup>Department of Public Health, College of Medicine, National Cheng Kung University; <sup>3</sup>Department of Internal Medicine, Tainan Hospital, Ministry of Health and Welfare, Tainan; <sup>4</sup>School of Health Care Administration, College of Management; <sup>5</sup>Health Policy and Care Research Center, College of Public Health, Taipei Medical University, Taipei; <sup>6</sup>Department of Public Health, Fu-Jen Catholic University, New Taipei City; <sup>7</sup>Cochrane Taiwan; <sup>8</sup>Master Program in Long-Term Care, College of Nursing; <sup>9</sup>School of Gerontology Health Management, College of Nursing, Taipei Medical University; <sup>10</sup>Department of Physical Medicine and Rehabilitation, Taipei Medical University Hospital, Taipei; <sup>11</sup>Department of Public Health, College of Public Health, China Medical University, Taichung, Taiwan.

Corresponding author: Dr. Chung-Yi Li, Department of Public Health, College of Medicine, National Cheng Kung University, No. 138, Sheng-Li Road, Tainan 704, Taiwan. Tel: 886-6-235-3535 ext. 4184; Fax: 886-6-275-3083; E-mail: cyli99@mail.ncku.edu.tw

# These authors contributed equally to this work.

## INTRODUCTION

Global warming is an ongoing process, and the frequency and intensity of the accompanying extreme climate events are anticipated to increase accordingly. This poses a threat to human health and has become a challenge for public health professionals.<sup>1</sup> Thus, the need to investigate the consequences of ambient temperature on human health is urgent.<sup>1</sup>

Extremely hot and cold spells affect cardiovascular and respiratory mortality.<sup>2–4</sup> However, the majority of ambient temperature-mortality studies have been conducted in European and North American cities, and very few have looked at subtropical areas where extreme temperatures occur less often.<sup>5</sup> Son et al.<sup>6</sup> reported dif-

ferent effects of cold and heat on mortality from 1996-2010 in São Paulo, a subtropical city in Brazil, where cold posed more of a threat than heat on mortality, especially cardiovascular deaths. Another study<sup>7</sup> in Changsha, a subtropical city in China, reported higher cold-related cardiovascular mortality with longer lags of heat-related cardiovascular mortality between 2008 and 2011. However, these observations might not reflect the unique island climate in Taiwan, a subtropical country (22-25 degrees N, 120-122 degrees E) near the southeast coast of mainland China. Taiwan is in the East Asia monsoon region, and experiences typhoons (a hurricane south of the equator) and a mixture of both continental and marine climates.<sup>8</sup> In addition, the unique geographic landscape (mountains constitute two-thirds of Taiwan's land mass) and great topographic variation (sea level to 4000 m in altitude) also affect Taiwan's climate.

It is believed that different regions are influenced differently by global warming, and that the health stress associated with so-called "extreme climates" should be examined in regions individually, primarily because of people's adaptations to the climate.<sup>5</sup> Several Taiwanese studies<sup>5,9-12</sup> have investigated the effect of climate change on people's health in Taiwan. Unfortunately, these studies were limited by a number of problems, including a small sample sizes, restriction to specific regions, and evaluation of only cold seasons. Hence, population-based nationwide studies evaluating the association between ambient temperature and the health of the whole population of Taiwan are essential. The present study used national mortality registration data and meteorological data from 2008 to 2010 and (1) investigated the time-series associations of daily average temperature with all-cause mortality and deaths due to cardiovascular and respiratory diseases; and (2) identified the lag, if any, related to the effect of the average daily temperature on all-cause, cardiovascular, and respiratory disease mortality.

## MATERIALS AND METHODS

### Sources of data

Daily mortality data from 2008 to 2010 (n = 1095 days) were obtained from the Taiwan Death Registry. The Taiwan Death Registry is considered to be accurate

and complete because it is mandatory to register all deaths in Taiwan, and all death certificates must be completed by physicians.<sup>13</sup> We retrieved information on the date of death and underlying cause of death for each deceased individual. There were 126,667, 126,936, and 129,878 deaths in 2008, 2009, and 2010, respectively [excluding external causes of accidents (ICD-9-CM (International Classification of Diseases, Ninth Revision, Clinical Modification) codes: E800-E999)]. In addition to the analysis of all-cause mortality, we also examined the associations between daily average temperature and deaths due to cardiovascular diseases (including coronary artery disease (ICD-9-CM codes: 410, 411, 413, and 428) and cerebral vascular attack (ICD-9-CM codes: 430-436)), and respiratory diseases (ICD-9-CM codes: 460-519). To calculate the daily all-cause and cause-specific mortality rates, we obtained data on the size of the population from the 2008-2010 volumes of the *Taiwan-Fukien Demographic Fact Book*.<sup>14</sup>

Meteorological data were provided by the Central Weather Bureau of Taiwan. There are 46 meteorological monitoring stations in Taiwan, and each of these stations records a variety of meteorological data every hour including temperature, relative humidity, wind velocity, and precipitation, of which the average values are reported. Daily temperature (3.3-31.0 °C) during the study period was averaged from only 33 meteorological monitoring stations. Data from the other 13 meteorological monitoring stations were excluded because they were located in mountainous areas or on remote islands with few residents. We chose nationwide analysis instead of city-level analysis because Taiwan has a relatively narrow range of longitude and latitude (22-25 degrees N, 120-122 degrees E) and a relatively homogeneous climate. In addition, previous epidemiological studies conducted in Taiwan have also assessed the nationwide association between temperature and various health end-points such as unintentional carbon monoxide poisoning,<sup>15</sup> sudden infant death,<sup>16</sup> and enterovirus 71 infections.<sup>17</sup>

### Statistical analysis

We first constructed a scatter plot describing the graphic relationship between daily average temperature (X-axis) and the natural logarithm ( $\ln$ ) of the daily mortality rate (Y-axis). The scatter plots showed reverse

J-shaped curves (Figure 1A, B) for the associations between daily average temperature and daily all-cause and cardiovascular mortality rates, which suggested a non-linear relationship. However, a linear pattern (Figure 1C) was shown for the association between daily average temperature and daily mortality rate from respiratory diseases, thus suggesting a linear relationship. We then used a generalized least square model to assess the relationship between the two time-series trends of temperature and mortality, and to test whether there was a linear (square or cubic) relationship between daily average temperature and mortality. We also used smoothing functions in the models to further elucidate the relationship between daily temperature and mortality. A maximum cross-correlation function was used to determine the possible time lag for the influence of daily average temperature on mortality, which allowed for the number of “lag days” explored to range from 0 to the maximum number of days during the study period (i.e., 2008 to 2010).<sup>18,19</sup> In time delay analysis, cross-correlations are useful to determine the time delay between two signals. After calculating the cross-correlation between the two signals, the maximum (or minimum if the signals are negatively correlated) of the cross-correlation function indicates the point in time where the signals are best aligned.<sup>19</sup>

The models also took into account the relative humidity, as one previous Taiwanese study noted a negative dose-gradient relationship between relative humidity and the risk of mortality.<sup>15</sup> Thus, the initial model was constructed as follows:

$$\ln(Y_i) = \beta_0 + \beta_1(dT_{i-1}) + \beta_2(dT_{i-1})^2 + \beta_3(dT_{i-1})^3 + \beta_4(dH_{i-1}) + \beta_5(dH_{i-1})^2 + \beta_6(dH_{i-1})^3 + \varepsilon_i \quad (\text{Eq 1})$$

where  $Y_i$  = no. of deaths on day  $i$ ;  $dT_{i-l}$  = difference between mean temperature on day  $i$  and annual mean temperature;  $dH_{i-l}$  = difference between mean relative humidity on day  $i$  and annual mean relative humidity;  $l$  = lag time in days; and error term ( $\varepsilon_i$ ) ~ autoregressive-moving-average (ARMA) (p,q).

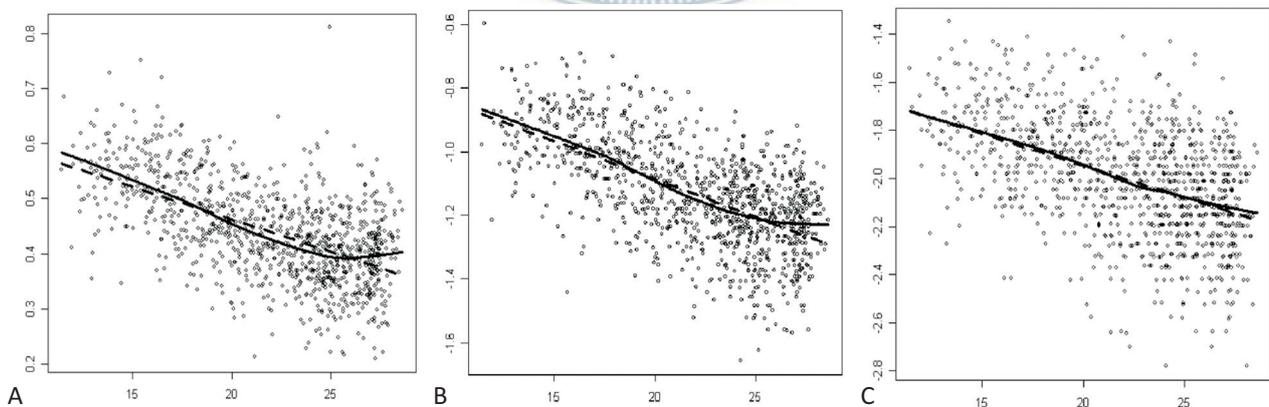
The model was fitted and tested in a stepwise manner by removing the terms from the model until the best fit was achieved. In each step, we removed only one independent variable for which the regression coefficient had the greatest p-value and was also > 0.05. The model was continuously fitted with first degree residuals until all of the independent variables were statistically significant (p-value < 0.05). The final models for all-cause mortality (Equation 2), cardiovascular disease mortality (Equation 3), and respiratory disease mortality (Equation 4) were:

$$\ln(Y_i) = \beta_0 + \beta_1(dT_{i-4}) + \beta_2(dH_{i-3}) + \varepsilon_i; \varepsilon_i \sim \text{ARMA}(2,2) \quad (\text{Eq 2})$$

$$\ln(Y_i) = \beta_0 + \beta_1(dT_{i-4}) + \beta_2(dT_{i-4})^2 + \beta_3(dT_{i-4})^3 + \beta_4(dH_{i-2}) + \varepsilon_i; \varepsilon_i \sim \text{ARMA}(0,0) \quad (\text{Eq 3})$$

$$\ln(Y_i) = \beta_0 + \beta_1(dT_{i-16}) + \beta_2(dH_{i-4}) + \varepsilon_i; \varepsilon_i \sim \text{ARMA}(2,2) \quad (\text{Eq 4})$$

Figure 2 shows the cross-correlation function values for all-cause, cardiovascular, and respiratory disease, respectively. The maximum cross-correlation function was



**Figure 1.** Scatter plots of daily temperature (X-axis, °C) and daily mortality rates (Y-axis, in  $1/10^5$ ) for (A) all-cause, (B) cardiovascular, and (C) respiratory diseases. The solid and dashed lines are derived from the linear regression model with generalized least square method, and the generalized additive models with smoothing functions of independent variables.

noted at the 4th day following the  $i^{\text{th}}$  day for both all-cause mortality (A) and cardiovascular disease mortality (B). The maximum cross-correlation function appeared at the 16th day for respiratory disease mortality (C). Because the final model showed a non-linear relationship between daily average temperature and cardiovascular disease mortality, the cardiovascular disease mortality data were split according to appropriate inflection points, which were the sign of changes in curvature. For a cubic curve, the first derivative test can sometimes distinguish inflection points from extrema for differentiable functions  $f(x)$ . The second derivative test is also sometimes useful. A necessary condition for  $x$  to be an inflection point is  $f''(x) = 0$ , and a sufficient condition requires  $f''(x + \varepsilon)$  and  $f''(x - \varepsilon)$  to have opposite signs in the neighborhood of  $x$ .<sup>20</sup> As the cardiovascular data were split into three parts according to the two inflection points, we performed three independent first degree linear regression models in the stratified analyses. The three equations also showed that relative humidity was associated with the risk of mortality and thus should be adjusted in the models. To address the potential for effect-modification by age, we also performed statistical testing for the interaction of daily temperature with age (0-14, 15-64, and  $\geq 65$  years).

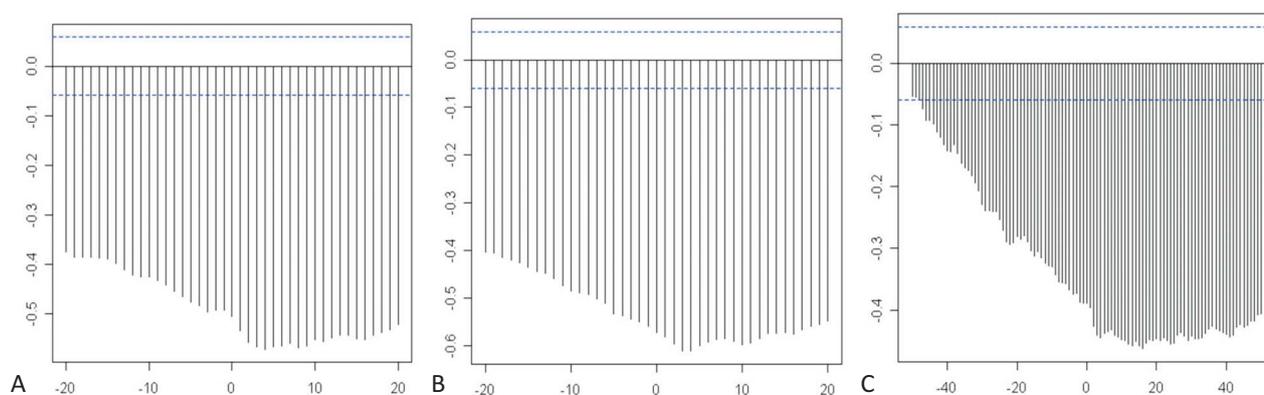
Both R 2.4.1 (Free Software Foundation, Boston, MA, USA) and ASTSA (Aladdin Enterprises, Menlo Park, CA, USA) were used for the analyses. Ethical approval was waived by the Institutional Review Board for this analysis because the personal identification numbers of the deceased are encrypted and all associated data are de-identified.

## RESULTS

As the daily average temperature increased, the daily all-cause ( $\beta = -0.006$ ) and respiratory disease ( $\beta = -0.012$ ) mortality rates linearly decreased with a time lag of 4 and 16 days, respectively. However, two inflection points (12.91 °C and 26.36 °C) were identified by the generalized least square model for the analysis of cardiovascular disease mortality, justifying further analysis according to three different temperature ranges (Table 1). Although "humidity" was also significantly associated with all-cause, cardiovascular disease, and respiratory disease mortality in the three final models of interest, the strength of association, as indicated by the sizes of the regression coefficients, of all three study outcomes with humidity were considered too small to be of clinical significance.

The apparently inverse relationship ( $\beta = -0.028$ ) between daily average temperature and cardiovascular disease mortality was observed only for a temperature ranging from 12.91 °C to 26.36 °C, with a relative risk (RR) estimate of 0.972 [95% confidence interval (CI) = 0.963-0.982]. The potential effects of a daily average temperature  $< 12.91$  °C and  $> 26.36$  °C were positively associated with the risk of mortality from cardiovascular disease, with slightly elevated RRs of 1.010 (95% CI = 0.995-1.026) and 1.106 (95% CI = 0.951-1.287), respectively (Table 2).

The interactive effect of daily mean temperature and age was statistically significant ( $p < 0.001$ ) for all three study end-points. Further stratified analyses with the same lag days as reported above indicated that a 1



**Figure 2.** The cross-correlation function values (Y-axis) versus day following the  $i^{\text{th}}$  day (X-axis) for (A) all-cause, (B) cardiovascular, and (C) respiratory disease mortality.

**Table 1.** Relative risk estimated from the generalized least square models

Cause of death	Regression <sup>a</sup>	Inflection points <sup>b</sup>	$\beta$	RR
All causes	$\ln(Y_i) = \beta_0 - 0.006 (dT_{i-4}) - 0.001 (dH_{i-3}) + \varepsilon_i$ $\varepsilon_i \sim ARMA(2,2)$		-0.006	0.994
Cardiovascular disease	$\ln(Y_i) = \beta_0 + 0.248 (dT_{i-4}) - 0.014 (dT_{i-4})^2 + 0.0002 (dT_{i-4})^3 + 0.0002 (dH_{i-2}) + \varepsilon_i$ $\varepsilon_i \sim ARMA(0,0)$	12.91 °C, 26.36 °C		
Respiratory disease	$\ln(Y_i) = \beta_0 - 0.012 (dT_{i-16}) - 0.002 (dH_{i-4}) + \varepsilon_i$ $\varepsilon_i \sim ARMA(2,2)$		-0.012	0.988

ARMA, autoregressive moving average; RR, relative risk.

<sup>a</sup>  $T_{i-j}$ : daily temperature;  $H_{i-j}$ : daily humidity;  $\ln$ : natural logarithm;  $Y_i$ :  $\ln$  (daily mortality rate) ( $1/10^5$ );  $\varepsilon_i$ : error term; ARMA: autoregressive-moving-average; <sup>b</sup> Relationship between daily temperature and daily cardiovascular disease mortality varied with the temperature range.

**Table 2.** Relative risk estimates of cardiovascular disease mortality based on various daily temperature ranges

Range of daily temperature	Sample size	Regression model	$\beta$	RR (95% CI)
$dT_{i-4} > 26.36$ °C	210	$\ln(Y) = \beta_0 + 0.010 (dT_{i-4}) + 0.0001 (dH_{i-2})$	0.010	1.010 (0.995-1.026)
$26.36$ °C $\geq dT_{i-4} \geq 12.91$ °C	870	$\ln(Y) = \beta_0 - 0.028 (dT_{i-4}) + 0.0002 (dH_{i-2})$	-0.028	0.972 (0.963-0.982)
$dT_{i-4} < 12.91$ °C	15	$\ln(Y) = \beta_0 + 0.101 (dT_{i-4}) - 0.0001 (dH_{i-2})$	0.101	1.106 (0.951-1.287)
Total	1095			

CI, confidence interval;  $\ln$ , natural logarithm; RR, relative risk.

°C increase in daily mean temperature was significantly associated with reduced RR estimates of 0.9836, 0.9732, and 0.9800 for all-cause, cardiovascular, and respiratory mortality, respectively, in people aged 65 years and over. Significantly reduced RR estimates were also observed for cardiovascular (0.9902) and respiratory (0.9956) disease mortality in people aged 15-64 years. However, for children aged < 15 years, significantly reduced risks of mortality were observed for all-cause (0.9934) and respiratory disease (0.9451) mortality.

## DISCUSSION

We confirmed an inverse relationship between ambient temperature and all-cause mortality in Taiwan, where the subtropical climate means there are no extreme climate events such as heat waves or snowstorms. We also found that a higher daily average temperature had a greater beneficial effect on cardiovascular disease mortality than on respiratory disease mortality. A lower daily average temperature appeared to have a short-term (4-6 days) effect on the risk of all-cause and cardiovascular disease mortality. However, a lower daily temperature may have been associated with a higher risk of

respiratory disease mortality within a 13- to 16-day lag. This information may help to prevent deaths from weather-related causes.

Contrary to the U- or V-shaped relationship between ambient temperature and mortality seen in northern areas of the Earth, we found a reverse J-shaped or linear relationship between daily temperature and all-cause mortality, which became flat when the temperature was  $\geq 24$ - $26$  °C. This suggests that the threat of cold weather might include days with a daily average temperature below 24 °C in Taiwan, which is consistent with other reports.<sup>21,22</sup> According to our data, about 165 days per year (45.2%) had a daily average temperature < 24 °C in Taiwan between 2008 and 2010. Although 24 °C would not be considered to be extremely cold in most cold climates, Curriero et al.<sup>23</sup> reported that people living in warm climates are generally more vulnerable to cold. Exposure to warm or hot weather seemed to have a lesser effect on all-cause mortality. Our findings are in agreement with results from several previous studies that included data from Taiwan. A recently multinational study by Gasparrini et al. showed that the effect of cold on mortality was more prominent than heat.<sup>24</sup> In addition, Guo et al. reported that although both cold and hot temperatures can have adverse effects on mortality,

cold appears to have a higher relative risk compared to heat in Taiwan.<sup>25</sup> Chung et al. studied three cities in Taiwan from 1994-2007, six cities in Korea from 1992-2010, and six cities in Japan from 1972-2009, and found that the effect of cold was greater for cities in Taiwan whereas the effect of heat was greater for cities in Korea.<sup>26</sup> One plausible explanation for the reduced effect of warm weather or heat in Taiwan could be a greater use of central air conditioning and people's better adaptation to the warmer climate.<sup>1,22</sup> Similar observations have also been reported in cities with comparable climates, such as London, Shanghai, and the southern part of the USA.<sup>21-23</sup> Interestingly, compared with the reverse S-shaped curve in our study for cardiovascular disease and linear curve for respiratory disease, research conducted in Norway<sup>27</sup> and Denmark<sup>28</sup> has shown similar curves for the relationship between daily average temperature and cardiovascular mortality, but a U-shaped curve for the relationship between daily average temperature and respiratory mortality. Additional studies are needed to clarify whether latitude moderates the relationship between daily temperature and cardiovascular mortality. Moreover, we did not find an association between a higher risk of mortality from respiratory disease and high temperatures, unlike other studies<sup>27-29</sup> conducted in cold weather areas. Whether the lower rate of heat-related respiratory deaths in Taiwan or in other tropical or subtropical areas is due to a greater use of air conditioning on hot days or greater adaptation warrants additional investigations.

We found an inverse relationship between daily mean temperature and cardiovascular disease mortality in the temperature range from 12.91 °C to 26.36 °C. The upper limit of this range can be considered to be a daily mean temperature with the lowest risk of cardiovascular disease mortality, which is essentially consistent with the temperature range in Taiwan associated with a lower risk of cardiovascular mortality (26-29 °C) reported by Pan et al.,<sup>7</sup> and is also consistent with that found in cities at similar latitudes, such as Jacksonville (24.86 °C), Tampa (27.06 °C), and Miami (27.18 °C), Florida. With respect to the reduction in mortality from all causes and cardiovascular disease per 1 °C increase, our results are similar to the findings of Martens<sup>31</sup> (0.6-1.3% vs. 1.0%). However, the reduction in respiratory disease mortality per 1 °C increase was lower in our study (1.2-2.5% vs.

3.8%). This may be due to regional differences in the effects of temperature, or to the different types of respiratory diseases prevalent in different areas. For example, Braga et al.<sup>29</sup> reported different effects of daily average temperature on deaths from pneumonia and chronic obstructive pulmonary disease.

We found a 4-6 day time lag in the effects of cold weather on all-cause and cardiovascular disease mortality, while the lag for respiratory disease was longer at 13-16 days. This finding is consistent with the study by Braga et al.<sup>29</sup> who investigated the relationship between the weather and mortality in 12 USA cities and found that the effect of cold, but not heat, persisted for days. Onozuka et al.<sup>32</sup> investigated the association between extreme temperatures and mortality from 1973-2012 in Japan, and they also found that heat extremes (30.7-32.2 °C) had 0-1 days of lag associated with mortality, but that cold extremes (2.5-4.7 °C) had a lag of 0-25 days. Chung et al. also reported that the effect of cold had a longer time lag (5-11 days) than heat, for which the effects were immediate (1-3 days).<sup>26</sup> The findings of the study by Seposo et al.<sup>33</sup> conducted from 2006 to 2010 in Manila (latitude: 14° 35' N), not far from Kaohsiung in southern Taiwan (latitude: 23° 0' N), also support our findings, as they found a shorter lag for cardiovascular disease-related deaths and a longer lag for respiratory disease-related deaths. Hence, timely preventative measures are important to reduce the risk of mortality risk from extremely high temperatures, and several days of protection are needed to reduce the risk of mortality from cold.

The present study broadens the current understanding of ambient temperature-related health problems in subtropical countries such as Taiwan. Several clinical and preventive implications can be drawn from this study. First, information obtained from this analysis is crucial in predicting the occurrence of weather-related mortality, and may help public healthcare systems to mitigate extreme temperature-related mortality, including healthcare system preparedness, timely warnings, medical advice, housing and urban planning improvements, and health education. Second, we found that an increase in daily average temperature may protect against mortality from respiratory disease, but that a similar beneficial effect associated with a higher temperature for cardiovascular disease was only noted in a specific

range (12.91-26.36 °C), which justifies different preventive strategies targeting a reduction in mortality from these two types of diseases. Third, the short cold weather lag effect (4-6 days) on cardiovascular disease implies a potentially faster body responses to cold weather for the residents of Taiwan. Hence, immediate precautions are required when the daily average temperature falls below 26 °C. Furthermore, when the daily temperature falls, it is mandatory to pay attention to the risks for respiratory disease mortality for up to 2 weeks. The longer lag time (13-16 days) observed for the relationship between daily mean temperature and respiratory disease mortality could be due to a higher admission rate for respiratory diseases, which could lower, at least to some extent, the likelihood of sudden death for people with respiratory diseases. However, we were unable, based on the current mortality data, to confirm or refute this hypothesis. In addition, the appropriateness of disease management for patients with cardiovascular disease may have an effect on the risk of mortality.<sup>34</sup> Due to a lack of information on clinical interventions and treatment for the patients with cardiovascular or respiratory disease, it is not possible to fully attribute the observed effects on mortality to ambient temperature per se. Further, we used mortality data rather than incidence data as an end-point. Therefore, the concepts of risk and prognosis are mixed, which limits the interpretation of our study findings. Finally, our findings suggest that people living in a warm climate are more vulnerable to cold weather, which is consistent with a study comparing the effect of temperature on mortality among Taiwan, Korea, and Japan (three countries with similar socioeconomic and cultural aspects, but slightly different weather conditions) by Chung et al.<sup>26</sup> Their and other studies also indicated that people in northern (cooler) areas are less able to adapt to hot weather.<sup>26,35,36</sup>

This study has some limitations. First, the locations of the meteorological monitoring stations may not necessarily reflect temperatures in inhabited areas, which may have biased our study results and attenuated the true relationship between daily temperature and mortality. Although we managed to reduce that bias by excluding meteorological monitoring stations in mountainous and remote areas with few residents, we cannot entirely exclude bias. Second, we found a greater risk of mortality from cardiovascular disease on days with tem-

peratures > 26.36 °C and < 12.91 °C. However, this risk was based on limited sample sizes (210 days and 15 days), which reduced its statistical power. Third, although we considered relative humidity in our analysis, we were unable to take into account a comprehensive list of environmental and lifestyle risk factors for cardiovascular and respiratory diseases such as ambient air pollutants, which have been reported to affect mortality<sup>4,37-39</sup> and also to have an interactive effect with temperature on the risk of mortality. Specifically, Qian et al. found that associations between daily temperature and mortality from all natural causes ( $p = 0.014$ ), cardiovascular disease ( $p = 0.007$ ), and cardiopulmonary ( $p = 0.014$ ) causes were significantly related to the level of particulate matter.<sup>40</sup> Fourth, because different types of cardiovascular and respiratory diseases may be differently affected by temperature,<sup>22</sup> we treated all cardiovascular diseases and all respiratory diseases as a single disease category in this analysis. This may have masked some diseases with a stronger association with daily average temperature, and limited specific interpretations of the association between daily temperature and cardiovascular and respiratory diseases.

Fifth, we only used daily mean temperature in the present study and did not assess the effect of other temperature-related parameters. In addition to the effect of daily mean temperature, comparisons of mortality between cold spells and non-cold spells are also important, as they may reveal the potential effects of the cold spell characteristics (e.g., duration and intensity) on the risk of mortality.<sup>41</sup> In addition, variability of temperature is another parameter suspected of being associated with the risk of mortality. Cheng et al.<sup>42</sup> conducted a lag non-linear analysis in China to investigate whether a sudden temperature change, calculated as the current day's temperature minus the previous day's temperature, between neighboring days had a significant impact on mortality. They found that a temperature change (both increase and decrease) was significantly associated with an elevated risk of mortality from non-accidental and cardiovascular causes, and that males and people aged 65 years or older appeared to be more vulnerable to the impact of such temperature changes. Another study by Zhang et al.<sup>43</sup> also from China assessed associations between intra-day and inter-day changes in temperature and the risk of mortality. They noted that

temperature variation was an independent risk factor for non-accidental mortality, and that such temperature variation-related effects were more prominent in warm than in cold seasons, as well as in older than in younger populations. Finally, although Taiwan is a small country, regional variations in the relationship between daily average temperature and mortality are possible because different regions have different altitudes and latitudes. Additional studies that include more data by covering a longer study duration are necessary to assess whether the relationships between temperature and mortality found in this study vary by region.

## CONCLUSIONS

Our findings from Taiwan, a subtropical area, showed an apparent inverse relationship between daily average temperature and all-cause mortality, and higher temperatures had a more beneficial effect on cardiovascular disease mortality than on respiratory disease mortality. Moreover, we found that lower daily average temperatures had a short-term (4-6 days) effect on all-cause and cardiovascular disease mortality, compared to a 13- to 16-day time lag for the greatest risk in respiratory disease mortality. Since cardiovascular disease may affect both old and young adults in Taiwan,<sup>44</sup> our findings have important implications with respect to formulating public health warning strategies to mitigate temperature-related deaths.

## FUNDING

This study was supported by grant from the R.O.C. Ministry of Science and Technology (MOST 106-2629-B-006-002).

## CONFLICTS OF INTEREST

None.

## REFERENCES

1. Kenney WL, Craighead DH, Alexander LM. Heat waves, aging, and human cardiovascular health. *Med Sci Sports Exerc* 2014;46:1891-9.
2. Åström DO, Forsberg B, Rocklöv J. Heat wave impact on morbidity and mortality in the elderly population: a review of recent studies. *Maturitas* 2011;69:99-105.
3. Cheng X, Su H. Effects of climatic temperature stress on cardiovascular diseases. *Eur J Intern Med* 2010;21:164-7.
4. Basu R. High ambient temperature and mortality: a review of epidemiologic studies from 2001 to 2008. *Environ Health* 2009; 8:40.
5. Lin YK, Ho TJ, Wang YC. Mortality risk associated with temperature and prolonged temperature extremes in elderly populations in Taiwan. *Environ Res* 2011;111:1156-63.
6. Son JY, Gouveia N, Bravo MA, et al. The impact of temperature on mortality in a subtropical city: effects of cold, heat, and heat waves in São Paulo, Brazil. *Int J Biometeorol* 2016;60:113-21.
7. Huang J, Wang J, Yu W. The lag effects and vulnerabilities of temperature effects on cardiovascular disease mortality in a subtropical climate zone in China. *Int J Environ Res Public Health* 2014;11:3982-94.
8. Lin CY, Chua YJ, Sheng YF, et al. Altitudinal and latitudinal dependence of future warming in Taiwan simulated by WRF nested with ECHAM5/MPIOM. *Int J Climatol* 2015;35:1800-9.
9. Wang YC, Lin YK, Chuang CY, et al. Associating emergency room visits with first and prolonged extreme temperature event in Taiwan: a population-based cohort study. *Sci Total Environ* 2012; 416:97-104.
10. Chen VY, Wu PC, Yang TC, Su HJ. Examining non-stationary effects of social determinants on cardiovascular mortality after cold surges in Taiwan. *Sci Total Environ* 2010;408:2042-9.
11. Wu PC, Lin CY, Lung SC, et al. Cardiovascular mortality during heat and cold events: determinants of regional vulnerability in Taiwan. *Occup Environ Med* 2011;68:525-30.
12. Lin YK, Wang YC, Lin PL, et al. Relationships between cold-temperature indices and all causes and cardiopulmonary morbidity and mortality in a subtropical island. *Sci Total Environ* 2013;461-462:627-35.
13. Lu TH, Lee MC, Chou MC. Accuracy of cause-of-death coding in Taiwan: Types of miscoding and effects on mortality statistics. *Int J Epidemiol* 2000;29:336-43.
14. Department of Household Registration. *Household Registration Statistics Data Analysis*. Taipei: Taiwan Ministry of the Interior, 2008-2010.
15. Shei HG, Li CY. Population-based case-control study of risk factors for unintentional mortality from carbon monoxide poisoning in Taiwan. *Inhal Toxicol* 2007;19:905-12.
16. Chang HP, Li CY, Chang YH, et al. Socio-demographic and meteorological correlates of sudden infant death in Taiwan. *Pediatr Int* 2013;55:11-6.
17. Chang HL, Chio CP, Su HJ, et al. The association between enterovirus 71 infections and meteorological parameters in Taiwan. *PLoS One* 2012;7:e46845.
18. Shumway RH, Azari AS, Pawitan Y. Modelling mortality fluctuations in Los Angeles as functions of pollution and weather ef-

- fects. *Environ Res* 1988;45:224-41.
19. Alberdi JC, Díaz J, Montero JC, Mirón I. Daily mortality in Madrid community 1986-1992: relationship with meteorological variables. *Eur J Epidemiol* 1998;14:571-8.
  20. Bronshtein IN, Semendyayev KA, Musiol G, et al. *Handbook of Mathematics*, 4th ed. New York: Springer-Verlag, 2004, p. 231.
  21. Kan H, London SJ, Chen H, et al. Diurnal temperature range and daily mortality in Shanghai, China. *Environ Res* 2007;103:424-31.
  22. Keatinge WR, Donaldson GC, Cordioli E, et al. Heat related mortality in warm and cold regions of Europe: observational study. *BMJ* 2000;321:670-3.
  23. Curriero FC, Heiner KS, Samet JM, et al. Temperature and mortality in 11 cities of the eastern United States. *Am J Epidemiol* 2002;155:80-7.
  24. Gasparrini A, Guo Y, Hashizume M, et al. Mortality risk attributable to high and low ambient temperature: a multicountry observational study. *Lancet* 2015;386:369-75.
  25. Guo Y, Gasparrini A, Armstrong B, et al. Global variation in the effects of ambient temperature on mortality: a systematic evaluation. *Epidemiology* 2014;25:781-9.
  26. Chung Y, Lim YH, Honda Y, et al. Mortality related to extreme temperature for 15 cities in northeast Asia. *Epidemiology* 2015;26:255-62.
  27. Nafstad P, Skrondal A, Bjertness E. Mortality and temperature in Oslo, Norway, 1990-1995. *Eur J Epidemiol* 2001;17:621-7.
  28. Huynen MM, Martens P, Schram D, et al. The impact of heat waves and cold spells on mortality rates in the Dutch population. *Environ Health Perspect* 2001;109:463-70.
  29. Braga AL, Zanobetti A, Schwartz J. The effect of weather on respiratory and cardiovascular deaths in 12 U.S. cities. *Environ Health Perspect* 2002;110:859-63.
  30. Pan WH, Li LA, Tsai MJ. Temperature extremes and mortality from coronary heart disease and cerebral infarction in elderly Chinese. *Lancet* 1995;345:353-5.
  31. Martens WJ. Climate change, thermal stress and mortality changes. *Soc Sci Med* 1998;46:331-44.
  32. Onozuka D, Hagihara A. Variation in vulnerability to extreme-temperature-related mortality in Japan: a 40-year time-series analysis. *Environ Res* 2015;140:177-84.
  33. Seposo XT, Dang TN, Honda Y. Evaluating the effects of temperature on mortality in Manila City (Philippines) from 2006-2010 using a distributed lag nonlinear model. *Int J Environ Res Public Health* 2015;12:6842-57.
  34. Chiang CE, Wang TD, Lin TH, et al. The 2017 focused update of the guidelines of the Taiwan Society of Cardiology (TSOC) and the Taiwan Hypertension Society (THS) for the management of hypertension. *Acta Cardiol Sin* 2017;33:213-25.
  35. McMichael AJ, Wilkinson P, Kovats RS, et al. International study of temperature, heat and urban mortality: the 'ISOTHURM' project. *Int J Epidemiol* 2008;37:1121-31.
  36. Goggins WB, Chan EY, Yang C, Chong M. Associations between mortality and meteorological and pollutant variables during the cool season in two Asian cities with sub-tropical climates: Hong Kong and Taipei. *Environ Health* 2013;12:59.
  37. Houck PD, Lethen JE, Riggs MW, et al. Relation of atmospheric pressure changes and the occurrences of acute myocardial infarction and stroke. *Am J Cardiol* 2005;96:45-51.
  38. Hoek G, Krishnan RM, Beelen R, et al. Long-term air pollution exposure and cardio-respiratory mortality: a review. *Environ Health* 2013;12:43.
  39. Chien KL. Mini-review of the Chin-Shan Community Cardiovascular Cohort Study in population health research in Taiwan. *Acta Cardiol Sin* 2017;33:226-32.
  40. Qian Z, He Q, Lin HM, et al. Part 2. Association of daily mortality with ambient air pollution, and effect modification by extremely high temperature in Wuhan, China. *Res Rep Health Eff Inst* 2010;154:91-217.
  41. Wang L, Liu T, Hu M, et al. The impact of cold spells on mortality and effect modification by cold spell characteristics. *Sci Rep* 2016;6:38380.
  42. Cheng J, Zhu R, Xu Z, et al. Temperature variation between neighboring days and mortality: a distributed lag non-linear analysis. *Int J Public Health* 2014;59:923-31.
  43. Zhang Y, Yu C, Bao J, Li X. Impact of temperature variation on mortality: an observational study from 12 counties across Hubei Province in China. *Sci Total Environ* 2017;587-588:196-203.
  44. Tsai WC, Wu KY, Lin GM, et al. Clinical characteristics of patients less than forty years old with coronary artery disease in Taiwan: a cross-sectional study. *Acta Cardiol Sin* 2017;33:233-40.