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# Associating emergency room visits with first and prolonged extreme temperature event in Taiwan: A population-based cohort study

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# ABSTRACT

The present study evaluated emergency room visit (ERV) risks for all causes and cardiopulmonary diseases associated with temperature and long-lasting extreme temperatures from 2000 to 2009 in four major cities in Taiwan. The city-specific daily average temperatures at the high 95th, 97th, and 99th percentiles, and the low 10th, 5th, and 1st percentiles were defined as extreme heat and cold. A distributed lag non-linear model was used to estimate the cumulative relative risk (RR) of ERV for morbidities associated with temperatures (0 to 3-day lags), extreme heat and cold lasting for 2 to 9 days or longer, and with the annual first extreme heat or cold event after controlling for covariates. Low temperatures were associated with slightly higher ERV risks than high temperatures for circulatory diseases. After accounting for 4-day cumulative temperature effect, the ERV risks for all causes and respiratory diseases were found to be associated with extreme cold at the 5th percentile lasting for >8 days and 1st percentile lasting for >3 days. The annual first extreme cold event of 5th percentile or lower temperatures was also significantly associated with ERV, with RRs ranging from 1.09 to 1.12 for all causes and from 1.15 to 1.26 for respiratory diseases. The annual first extreme heat event of 99th percentile temperature was associated with higher ERV for all causes and circulatory diseases. Annual first extreme temperature temperature event and intensified prolonged extreme cold events are associated with increased ERVs in Taiwan.

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### 1. Introduction

The temperature–mortality association has been widely evaluated worldwide for various weather conditions appearing with U-, V-, and J-shaped relationships (Basu, 2009; Curriero et al., 2002; Huynen et al., 2001). On the other hand, studies on the morbidity–temperature association are limited (Knowlton et al., 2009; Kovats et al., 2004; Lin et al., 2009; Linares and Diaz, 2008; Mastrangelo et al., 2007; Michelozzi et al., 2009; Rocklov and Forsberg, 2009; Theoharatos et

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al., 2010; Tong et al., 2010). Previous studies have shown that temperature has strong and acute effects on mortality from circulatory diseases (Keatinge and Donaldson, 1995; Lin et al., 2011; Medina-Ramon et al., 2006). The morbidities of respiratory diseases are more likely associated with extreme heat (Kovats et al., 2004; Lin et al., 2009; Linares and Diaz, 2008; Michelozzi et al., 2009; Rocklov and Forsberg, 2009) and its long-lasting event (Mastrangelo et al., 2007; Theoharatos et al., 2010).

Because of the trend of increasing extreme temperatures, the additional mortality risk associated with prolonged extreme heat and cold has attracted attentions. (Anderson and Bell, 2009, 2011; D'Ippoliti et al., 2010; Gasparrini and Armstrong, 2011; Hajat et al., 2006; Huynen et al., 2001; Knowlton et al., 2009; Lin et al., 2011; Tong et al., 2010; Wang et al., 2011). Studies generally define the temperatures at the high 99.5th, 99th, 97th, 95th, and 90th percentiles as extreme heat and those at the low 10th, 5th, and 1st percentiles as extreme cold (Anderson and Bell, 2009; 2011; Braga et al., 2002; D'Ippoliti et al., 2010; Diaz et al., 2002; Hajat et al., 2002, 2006;

Abbreviations: CI, confidence interval; CWB, Central Weather Bureau; DLNM, distributed lag non-linear model; ERV, emergency room visit; Flu, influenza; NHRI, National Health Research Institute; PM<sub>10</sub>, particulate matter less than 10 µm in aerodynamic diameter; RR, relative risk; RH, relative humidity; TCDC, Taiwan Centers for Disease Control; TEPA, Taiwan Environmental Protection Administration; WS, wind speed.

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Lin et al., 2011; Pattenden et al., 2003; Tong et al., 2010). Studies have investigated mortality risks associated with extreme temperatures lasting for 2 days, 4 days, and more than 3 days (Anderson and Bell, 2009, 2011; Hajat et al., 2006; Tong et al., 2010; Wang et al., 2011), but there are only a few studies that have evaluated their association with extreme temperatures lasting for 8 days and longer (Gasparrini and Armstrong, 2011; Hemon et al., 2003; Lin et al., 2011). Further, there are fewer studies on the association of morbidity with the first long-lasting extreme temperature in the year. Studies conducted in Greece (Theoharatos et al., 2010) and Italy (Mastrangelo et al., 2007) found significant association between hospitalization, emergency room visit (ERV), and longer duration of heat waves and its early occurrence in the year.

Taiwan is an island located on the western part of the Pacific Ocean, with an area of 150 km wide and 350 km long, stretching from 22 to 25° north latitude. With subtropical climate, the island has an average mean temperature of 24 °C, but varies from north to south, and the mean daily temperature ranges from 8 °C in winter to 33 °C in summer in urban cities. Approximately 13.6 million people of the 23 million population inhabit in four major cities, namely, Taipei, Taichung, Tainan, and Kaohsiung.

How the extreme weather may trigger disease exacerbations for the population living in this subtropical island is of interest. This ecological study aims to evaluate the association between emergency room visit for all causes and cardiopulmonary diseases and temperature change, prolonged extreme temperature events, and the annual occurrence of the first extreme temperature event. We used population-based representative insurance claims data for the population residing in the four major cities to evaluate the cumulative relative risk (RR) of ERV for all causes and cardiopulmonary diseases.

#### 2. Materials and methods

#### 2.1. Data source

The present study used daily meteorological records obtained from the Central Weather Bureau (CWB), universal health insurance claims from the National Health Research Institute (NHRI), daily air pollution monitoring records from the Taiwan Environmental Protection Administration (TEPA), and daily virological surveillance data from the Taiwan Centers for Disease Control (TCDC). The study period was from 2000 to 2009. The four cities included in the present study are located from Northern to Southern Taiwan.

The CWB provided 24-hour weather data (average temperature, maximum temperature, minimum temperature, relative humidity, and barometric pressure) from 25 real-time weather monitoring stations in Taiwan (Central Weather Bureau, 2011a). The present study used daily weather measurements from Taipei, Taichung, Tainan, and Kaohsiung weather stations from 2000 to 2009 (Central Weather Bureau, 2011b).

Over 96% of the 23 million population in Taiwan have been covered under the Taiwan National Health Insurance program since 1996 (Bureau of National Health Insurance, 2001). The Taiwan NHRI established a cohort with the electronic reimbursement claim records, consisting of a national representative population of one million people randomly sampled from all insured residents (Taiwan National Health Insurance Research Database, 2011). In the year 2000, approximately 58.7% of the one million people resided in the study cities. The dataset contained scrambled identification numbers of citizens and information on gender, birth dates, health care received, physicians' diagnoses for outpatient visits, inpatient admissions and discharges, and emergency services, and medical care providers. Disease diagnoses were coded according to the 9th revision of the International Classification of Diseases with Clinical Modification (ICD9 CM). The records of ERV for all causes (excluding injuries and external causes (ICD9 CM 800-999)), circulatory diseases (ICD9 CM 390–459), and respiratory diseases (ICD9 CM 460–519) during the study period were retrieved.

The Taiwan Air Quality Monitoring Network established by TEPA in 1993 included 74 stationary monitoring stations distributed throughout the island (Taiwan Environmental Protection Administration, 2011; Taiwan Governmental Information Office, 2008). Concentrations of ambient air pollutants, such as particulate matters less than 10  $\mu$ m in aerodynamic diameter (PM<sub>10</sub>), nitrogen oxides (NOx), and ozone (O<sub>3</sub>), were determined and recorded hourly at each station. The present study analyzed the daily average data for PM<sub>10</sub>, O<sub>3</sub>, and NOx monitored at 32 general ambient stations, 13 in Taipei, 5 inTaichung, 4 inTainan, and 10 in Kaohsiung.

The TCDC launched a nationwide virus surveillance network in 1999 (Taiwan Centers for Disease Control, 2011). Information on specimen collection and viral identification was described elsewhere (Shih et al., 2005). Briefly, nasal and/or throat samples from patients with one or more symptoms of respiratory tract infections, including cough, sore throat, tonsillitis, pharyngitis, pneumonia, and bronchiolotis, were collected by sentinel physicians in communities. This study used laboratory-based viral surveillance data from 2000 to 2009 in each city, which contained information on scrambled patient identifications, gender, birthday, residential area, dates of disease diagnosis and admission, results of viral isolation, and medical caregivers providing services. Influenza A virus (Flu A), influenza B virus (Flu B), and adenovirus (AV) were identified from viral surveillance. Daily city-virus-specific isolation rates were calculated using the number of positive identified respiratory infections specimens divided by the total specimens from regional reference virology laboratories.

#### 2.2. Definition of temperature extremes

The intensity, the duration, and the timing of extreme temperature events are the key factors in evaluating their health impacts (Anderson and Bell, 2011; D'Ippoliti et al., 2010). Daily temperatures during the entire study period were classified into normal or extreme heat/cold based on the city-specific daily average temperatures. A detailed method was described in a previous report (Lin et al., 2011). This study evaluated ERV risks associated with 16 extreme temperatures of the 97th, 95th, 10th, and 5th percentiles lasting for 3–5, 6–8, and >8 days, and of the 99th and 1st percentiles lasting for 2–3 days and >3 days.

In addition, the annual first extreme temperatures of the 97th, 95th, 10th, and 5th percentiles lasting more than 2 days, and of the 99th and 1st percentiles lasting more than 1 days were coded as an extra categorical dummy variable (*First*) to assess adverse effects for populations exposed to the annual first extreme temperature event.

#### 2.3. City-specific relative risk estimate

Poisson regression had been widely used in the health risk studies associated with the ambient temperature and air pollutants, which used time-series numbers of events from a cohort to estimate the relative risks (McCullagh and Nelder, 1989; Thomas, 2009). Therefore, for each city, the associations between the daily average temperatures and daily ERVs for all causes, circulatory diseases, and respiratory diseases were evaluated using a distributed lag non-linear model (DLNM) with Poisson distribution (Armstrong, 2006; Gasparrini et al., 2010).

This study used the natural cubic spline (NS) function for average temperature in the DLNM models, so the relative risk of ERV per 1 °C temperature change would not be favorably reported. In Taiwan, 18 °C is approximately 5th–20th percentiles of the average temperature, and 30 °C is approximately 95th–97th percentiles of the average temperature across these cities. Therefore, the cumulative 4-day (from 0 to 3-day lags) ERV risks and 95% confidence intervals (CI) associated with specific temperature (18 °C and 30 °C) were estimated

by comparing with the mean temperature of the city-disease-specific lowest ERV temperature (the centered value of temperature basis variables).

The previously defined extreme temperature events and the annual first extreme temperature events were set as the categorical covariates and risks were estimated by comparing with the nonconsecutive days of extreme temperature and days of normal temperatures. A linear relationship was assumed between ERV and air pollutants, such as PM<sub>10</sub>, O<sub>3</sub>, and NOx, with zero thresholds and 5-day maximum lag.

The model for the expected disease-specific ERV count at day (t) in each city (c) is

$$\begin{split} LogE[Y_t^c] &= \beta_0 + \sum_{t=0}^5 X_{i,t}^c + \sum_{t=0}^3 NS(T_t^c, 5; lag, 2) + Extremes_t^c + First_t^c \\ &+ NS(RH_t^c, 4) + NS(WS_t^c, 5) \\ &+ NS(Time, ^7/year) + covariates, \end{split}$$

where  $Y_t^c$  is the expected disease-specific ERV for city c on day t;  $\beta_0$  is the model intercept;  $X_{i,t}^c$  represents the linear effects of air pollutants  $(i = 1-3 \text{ for PM}_{10}, O_3, \text{ and NOx})$  for city c; and  $NS(T_t^c, 5; lag, 2)$  is the natural cubic splines of the daily average temperature. The temperatures for city c were set at 5 degrees of freedom (df) and their effects were totaled for 4 days (from 0 to 3-day lags) under a 2 df lag stratification. *Extremest*<sup>c</sup> are the categorical variables representing extreme temperature events for city c on day t. *First*<sup>c</sup> indicates the annual cityspecific first-occurrence extreme heat or cold event. Natural cubic splines were also applied in the daily measurements of relative humidity (RH, 4 df) and wind speed (WS, 5 df). The smoother time term (Time) was set at 7 df per year. Other covariates, such as holidays, day of the week, and the daily viral isolation rates of Flu A, Flu B, and AV were also adjusted in the models.

Sensitivity analysis was used to evaluate df, which ranged from 3 to 6 for the temperature–morbidity curves and from 0 to 2 for the coefficient–lag curves. Time smoothing with various df=4, 7, and 14 per year was also performed. The Akaike's information criterion was used for model selection (Akaike, 1973).

#### 2.4. Random-effect meta-analysis

City-specific relative risks of ERV associated with temperature, extreme temperature events and the annual first extreme temperature events were further evaluated for combined effects using metaanalysis (Viechtbauer, 2010). The restricted maximum likelihood was set as an estimator of the amount of heterogeneity. We estimated RR and 95% CI of factors associated with ERV using exponential of model coefficient. All data manipulation and statistical analyses were performed using SAS version 9.1 (SAS Institute Inc., Cary, NC, USA) and Statistical Environment R 2.12.

#### 3. Results

Table 1 describes the latitude of location, the population size, and the characteristics of temperatures and air pollutants for the four cities. Compared with other Taiwan cities, Taipei is hotter in summer but colder in winter. The numbers of days with extreme temperature, in general, are similar among these 4 cities. There were more extreme low temperatures than extreme high temperatures (596–598 days vs. 350–356 days). Among the four cities, the  $PM_{10}$  concentration was the highest in Kaohsiung, and the NOx level was the highest in Taipei. The  $O_3$  levels in Tainan and Kaohsiung were likely higher than the other cities.

From 2000 to 2009, a total of 317,343 insured population in the 4study cities made 867,306, 54,560 and 170,005 ERVs for all causes, circulatory diseases and respiratory diseases, respectively (data not shown). The male-to-female ratio is 1.01, and 16.5% patients were

#### Table 1

Latitude of location, population size, and characteristics of temperatures and air pollutants of the four cities in Taiwan, 2000–2009.

	Taipei	Taichung	Tainan	Kaohsiung
Latitude, °N	25.0	24.2	23.1	23.0
Population in millions	6.41	2.60	1.87	2.76
Population aged $65 + years$ , %	9.74	8.13	10.8	9.56
Daily atmospheric environment				
Average temperature, °C				
Mean	23.4	23.7	24.7	25.3
Minimum	8.3	8.5	9.3	11.6
25th	19.3	20.0	21.1	22.5
50th	23.9	24.9	26.0	26.4
75th	28.0	27.7	28.7	28.4
Maximum	33.0	32.0	31.7	32.0
$PM_{10}, \mu g/m^3$				
Minimum	10.7	13.2	12.3	17.9
25th	31.4	38.5	42.2	45.1
50th	43.6	55.1	65.9	75.2
75th	60.1	77.6	93.0	104
Maximum	286	255	410	218
NOx, ppb				
Minimum	3.90	3.20	1.80	5.00
25th	23.1	19.3	13.9	18.0
50th	30.1	24.9	19.2	25.0
75th	39.5	34.0	26.2	36.2
Maximum	119	108	64.8	76.9
$O_3$ of 24 h, ppb				
Minimum	4.50	3.80	4.70	3.00
25th	19.0	19.0	20.7	20.0
50th	24.9	24.7	27.9	28.8
75th	31.2	31.8	36.1	38.4
Maximum	73.1	77.8	76.5	73.4
Days with extreme temperature				
1th percentile	41	39	38	37
5th percentile	187	188	187	185
10th percentile	368	371	369	375
95th percentile	200	189	198	189
97th percentile	114	111	111	122
99th percentile	37	51	41	45

aged 65 years and above. Among all ERVs for circulatory diseases, cerebrovascular disease (ICD9 CM 430–439) accounted for 40.2% and ischemic heart disease (ICD9 CM 410–414) for 29.6%. Among ERVs for respiratory cares, 62.8% of visits were for pneumonia (ICD9 CM 480–486) and 20.2% for chronic airway obstruction, not else classified (ICD9 CM 496). In addition, 83,200 biological specimens were collected for viral determinations at the same stated period.

Fig. 1 shows the daily means of pooled temperatures and causespecific ERVs by month in the 4-study cities. The daily mean ERVs were the highest in February for all causes and circulatory diseases



Fig. 1. Daily average of pooled temperatures and cause-specific emergency room visits by month in study cities during 2000–2009.

(72.6 and 4.21 visits per day, respectively), and in January for the respiratory diseases (18.2 visits per day).

# 3.1. Adverse temperature effects

The ERV risks associated with city-specific average temperatures and extreme temperature events were estimated using DLNM after controlling for the daily city-specific average levels of  $PM_{10}$ , NOx,  $O_3$ , RH, WS, daily viral isolation rates for Flu A, Flu B and AV, holidays, day of the week, and long-term trends. Fig. 2 shows city-specific association between daily mean temperatures and ERVs. The lowest ERV was associated with an average temperature of approximately 24 °C for the four cities in general.

Fig. 3 summarizes the cumulative 4-day ERV risk estimates of random-effect meta-analyses at temperatures of 30 °C and 18 °C. Risk patterns for low temperatures were somewhat different from those for high temperatures. In the 18 °C environment, only the pooled ERV risks for circulatory diseases were significantly elevated (RR = 1.07, 95% CI: 1.01–1.13). The ERV risks for all causes and respiratory diseases increased as the city location was at lower latitude. In the 30 °C environment, the cumulative 4-day RR of ERVs for all causes was 1.05 (95% CI: 0.98–1.13) in the pooled estimates of the four cities. RRs were higher in Taichung (1.13, 95% CI: 1.09–1.18) and Tainan (1.11, 95% CI: 1.05–1.17).

#### 3.2. Adverse effects from consecutive days of extreme temperatures

Fig. 4 shows the pooled ERV risks for diseases in the 4-study cities associated with occurrences of extreme heat and cold events by the extreme levels and durations. The ERV risk estimates for all causes and respiratory diseases increased as durations of the 5th and the 1st percentiles cold extremes increased. The RR of ERVs for all causes was 1.18 (95% CI: 1.10–1.27) for populations exposed to the 5th percentile extreme temperature for 9 days or longer. The RR increased to 1.31 (95% CI: 0.94–1.84) for populations exposed to the 1st percentile extreme temperature for 4 days or longer. The corresponding RRs of ERVs for respiratory diseases were 1.28 (95% CI: 1.08–1.52) and

1.77 (95% CI: 0.97–3.22). Sensitivity analyses showed that the added effects of consecutive extreme temperatures were robust to the alternative models (data not shown).

Fig. 5 shows that the ERV risks for all causes and respiratory diseases were significantly associated with the exposure to the annual first extreme cold event of the 5th and the 1st percentiles. The RRs for all causes were 1.12 (95% CI: 1.05–1.20) and 1.09 (95% CI: 1.04–1.13), and 1.26 (95% CI: 1.08–1.48) and 1.15 (95% CI: 1.06–1.26) for the respiratory diseases. Moreover, exposure to the first extreme heat event of the 99th percentile temperature was moderately associated with ERV for all causes and circulatory diseases, with RRs of 1.08 (95% CI: 1.01–1.15) and 1.23 (95% CI: 0.98–1.54), respectively.

# 3.3. Risks from other covariates

Exposure to  $PM_{10}$  was significantly associated with ERVs of all causes with a 6-day (0 to 5-day lags) cumulative RR of 1.03 (95% CI: 1.02–1.04) in Taipei and 1.01 (95% CI: 1.00–1.02) in Kaohsiung, as  $PM_{10}$  increased for 1 µg/m<sup>3</sup> (data not shown). The association between  $PM_{10}$  and ERVs for respiratory diseases was the strongest in Taipei with a RR of 1.06 (95% CI: 1.04–1.08) as  $PM_{10}$  increased for 1 µg/m<sup>3</sup>. In contrast, exposure to ozone, with an increase of 1 ppb, the 6-day cumulative risk of ERVs for respiratory diseases was the highest in Taichung (RR = 1.16 (95% CI: 1.09–1.24)).

Further analysis on circulating respiratory viruses reveals that ERV risk had stronger association with Flu A than with Flu B and AV. These associations were statistically significant only in Taichung. ERVs for all causes were associated with per 10% Flu A isolation with a RR of 1.01 (95% CI: 1.00–1.01). In addition, RRs of ERVs were 1.01 (95% CI: 1.01–1.02) for all causes and 1.03 (95% CI: 1.02–1.05) for respiratory diseases associated with 10% increase in the isolation rate of Flu B.

#### 4. Discussion

Single extreme temperature event has been evaluated for sudden morbidity effects (Knowlton et al., 2009; Kovats et al., 2004; Lin et al., 2009; Linares and Diaz, 2008; Michelozzi et al., 2009; Rocklov and



Fig. 2. Associations between cause-specific emergency room visits and daily average temperatures in studied cities. Relative risks were estimated using DLNM, controlling for consecutive temperature extremes, daily city-specific averages of PM<sub>10</sub>, NOx, O<sub>3</sub>, relative humidity, wind speed, daily isolation rate for influenza A, influenza B, and adenovirus, holiday effects, day of the week, and long-term trends.



**Fig. 3.** City-specific and pooled risk estimates for overall 4-day effects at 18 °C and 30 °C temperatures, compared with the average temperature with the lowest emergency room visits at 24 °C. Relative risks by city-specific average temperature were estimated using DLNM, controlling for consecutive temperature extremes, daily city-specific averages of PM<sub>10</sub>, NOx, O<sub>3</sub>, relative humidity, wind speed, daily isolation rate for influenza A, influenza B and adenovirus, holiday effects, day of the week, and long-term trends. The pooled risk estimates were obtained using random-effect meta-analysis.

Forsberg, 2009; Wang et al., 2011). The present study is the first to evaluate how intensified long-duration extreme temperature events and how annual first extreme temperature events are associated with ERV risks for all causes and cardiopulmonary diseases in a sub-tropical island in Southeastern Asia. The climate of the 4-study cities is somewhat hot and humid. However, associations between the morbidities in residents and the weather changes vary among the 4 cities.

The first extreme cold temperature in a year, longer duration, and higher intensity of extreme cold events are associated with higher ERV risks for all causes and respiratory diseases. Furthermore, heat extremes are associated with higher ERV risks for respiratory diseases, but not for all causes and circulatory diseases, which are more likely associated with the annual first extreme heat event. The present study shows that temperature–ERV associations are very



Fig. 4. Four city pooled relative risks of emergency room visits from all causes, circulatory diseases, and respiratory diseases associated with consecutive extreme temperatures lasting for 3–5 days, for 6–8 days, and >8 days by random-effect meta-analysis.



**Fig. 5.** Pooled ERV risk for all causes, circulatory diseases, and respiratory diseases associated with the annual occurrence of the first extreme temperature event (the 99th, 97th, 95th, 10th, 5th, and 1st percentile temperatures).

different from temperature–mortality associations (Anderson and Bell, 2009; Gasparrini and Armstrong, 2011; Hajat et al., 2006; Kovats et al., 2004; Lin et al., 2011).

Only a few studies have reported varying threshold temperatures associated with morbidity. Lin et al. (2009) found that temperature threshold ranging from 28.9 °C to 29.4 °C is critical for the hospitalization of patients with respiratory and cardiovascular diseases in New York City (Lin et al., 2009). Kovats et al. (2004) reported that thresholds varied with admission causes ranging from 6 °C to 24 °C in Greater London, UK (Kovats et al., 2004). Linares and Díaz also reported in 2007 that there were more hospital admissions for residents above 75 years old, with a 34 °C as the threshold maximum temperature in Madrid, Spain (Linares and Díaz, 2008). Tong et al. reported that 27 °C was threshold temperature for ERV and death in Brisbane (Tong et al., 2010).

In Taiwan, the threshold temperature varies with the disease causes, ranging from 25 °C to 27 °C in temperature–mortality association (Lin et al., 2011). In the present study, the threshold ranges from 10 °C to 33 °C for the temperature–ERV association. Residents in cities located at the lower latitude (Tainan and Kaohsiung) are more sensitive to the exposure to low temperatures. They are likely to have higher mortality risks from circulatory and respiratory diseases (Lin et al., 2011) and higher ERV risks for all causes and respiratory diseases. Similar to a previous study (Kovats et al., 2004), the risks of high temperatures are significantly associated with mortality, but not with emergency room visits in Taiwanese population.

The intensity, the duration, and the timing of extreme temperature events are the key factors for evaluating the mortality impact of extreme weather conditions (D'Ippoliti et al., 2010). A Czech Republic study found an excess mortality from cardiovascular always appears in the first winter cold spell for population (Kysely et al., 2009). However, there are limited studies on the association between morbidity and the first or prolonged extreme temperature in the year. Studies on morbidity have reported that a hot humid weather that lasts longer than 4 days is significantly associated with an increase in hospital admissions (Mastrangelo et al., 2007). Heat waves that occur in early summer seem to cause greater health effects in Attica, Athens (Theoharatos et al., 2010). Our previous mortality analysis showed that the increase of mortality risk is associated with stronger and prolonged heat extremes, but there is no significant association observed for prolonged extreme cold event (Lin et al., 2011; Kysely et al., 2009). The present study has identified different patterns for associations between ERVs and extreme temperatures. Both annual first extreme heat and extreme cold events cause noticeable ERV risks. To the best of our knowledge, this study is the first report that the first day of cold temperatures in the year has the greatest impact on ERVs. This phenomenon is probably a unique for population residing on a subtropical island. They have generally accustomed themselves to mainly warm weather. We suspect that the first extreme cold weather is associated with the interruption of medical care for chronic conditions, triggering patients with chronic cardiovascular and respiratory conditions at risk for a greater disease exacerbation. It is probably more important to establish a warning system for the first cold extreme than heat extreme, particularly for the emergency care facilities.

Short-term extreme temperatures cause greater adverse effects on mortality from circulatory diseases than the long-lasting extreme temperature event (Lin et al., 2011). Most studies on ERV for circulatory diseases fail to identify the positive association between temperature, extreme temperature event and hospital admission (Kovats et al., 2004; Linares and Diaz, 2008; Mastrangelo et al., 2007; Michelozzi et al., 2009; Rocklov and Forsberg, 2009). On the contrary, mortality from and morbidity for respiratory diseases are consistently sensitive to temperature changes and intensify prolonged extreme temperature events (Basu, 2009; Kovats et al., 2004; Lin et al., 2009, 2011; Linares and Diaz, 2008; Mastrangelo et al., 2007; Michelozzi et al., 2009; Rocklov and Forsberg, 2009). Linares and Díaz proposed that people die from circulatory diseases rapidly before they can be admitted to hospitals when they are exposed to high temperatures (Linares and Diaz, 2008). We observed a similar pattern in the population of Taiwan.

Studies have associated air pollutants, such as ozone and  $PM_{10}$ , with mortality from cardiovascular and respiratory diseases during heat waves (Anderson and Bell, 2009; Hajat et al., 2006; Medina-Ramon and Schwartz, 2007). Moreover, air pollutants like NO<sub>2</sub>, O<sub>3</sub>, and particulate matter were also reported correlated with the increased ERV of cardiopulmonary diseases (Peel et al., 2005; Tsai et al., 2009). The present study confirmed the significant association between ambient levels of  $PM_{10}$  and  $O_3$  and the ERV of respiratory diseases.

Some studies have linked the circulating respiratory viruses with ERV (Bourgeois et al., 2006; Olson et al., 2007). However, this study failed to identify the extraordinary risks for these respiratory viruses as we had expected. Previous studies reported that winter seems to have a higher positive rate of identifying the circulating respiratory viruses.(Denny, 1995; Diaz et al., 2007) In Taiwan, only Flu A and Flu B are more likely to have seasonal variation (data not shown). Cold air could enhance the susceptibility of sensitive population by increasing vasoconstriction in upper airways and depressing the clearance mechanism of infections (Chu et al., 2006; Shephard and Shek, 1998). Additionally, transmission of suspected infectious bioaerosol (e.g. influenza viruses) has been reported negatively related with ambient temperature (Lowen et al., 2007). The seasonal temperatures and the biological interactions deserve further study.

Lin et al. and Gasparrini and Armstrong used DLNM to evaluate the main effects of daily temperature and the additional effects of extreme heat events (Gasparrini and Armstrong, 2011; Lin et al., 2011). They found that the general temperature explains most of the excess risk of mortality, and that heat extremes contribute little additional effects even if it sustains for more than 4 days. Temperature-ERV association is different from temperature-mortality association (Kovats et al., 2004; Linares and Diaz, 2008; Michelozzi et al., 2009). Wargon et al. concluded in a study that using the weather condition to predict emergency room utilization is less practical (Wargon et al., 2009). Our study has conflicting findings. The annual first extreme temperature event and intensified long-duration extreme cold event demonstrate more significant association with ERV than the daily temperature. Therefore, improving the predictive ability of extreme temperatures and enhancing the warning system in advance to the public is important.

# 5. Conclusion

This population-based study used daily representative morbidity data and accurate well-matched day-to-day climate and air pollution data. Data analysis completed the concise measures. The present study is the first to evaluate how the intensity, the duration and the timing of extreme temperature events are associated with ERV for populations exposed to a subtropical climate, controlling for potential confounders. Intensified long-duration extreme cold events are significant conditions leading to higher ERV risks for all causes and respiratory diseases. ERV risk for respiratory diseases is also partially associated with extreme heat event. The annual first extreme heat event with the temperature of 99th percentile is associated with elevated ERV for all causes and cardiopulmonary diseases, which have to be included in the warning system as well. Therefore, establishing the predictive ability of extreme temperatures and enhancing the early warning system for the public, particularly on more vulnerable populations, are important.

# **Authors' contribution**

All authors have been involved in this study. YC Wang, YK Lin, CY Chuang, MH Li, CH Chou, CH Liao and FC Sung have designed and obtained funds. YC Wang analyzed data. YC Wang, YK Lin, and FC Sung drafted and finalized the manuscript. All authors have read and approved the final version of the manuscript.

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