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Association between wet-bulb globe temperature with peptic ulcer disease in different geographic regions in a large Taiwanese population study

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Abstract

Background Peptic ulcer disease (PUD) is a common and important cause of morbidity worldwide, with a large impact on healthcare costs. Little research has been conducted on the association between wet-bulb globe temperature (WBGT) and PUD. The aim of this study was to explore this association among different geographical regions of Taiwan in a large sample of participants.

Methods This is a cross-sectional study. The study participants ($n = 120{,}424$) were enrolled from the Taiwan Biobank (TWB) and resided across northern, central, southern and eastern Taiwan. Self-reported questionnaires were used to ascertain the occurrence of PUD. Average WBGT values were recorded during working hours (8:00 AM to 5:00 PM) and the noon period (11:00 AM to 2:00 PM) for each participant at 1, 3, and 5 years before the TWB survey year. The association between WBGT and PUD was examined with logistic regression analysis.

Results The 1-year and 5-year noon WBGT values per 1℃ increase were significantly associated with a low prevalence of PUD in northern Taiwan (odds ratio [OR], 0.960, 95% confidence interval [CI], 0.925–0.955; OR, 0.962, 95% CI, 0.929–0.997; respectively). In contrast, there were no significant associations between WBGT and PUD in central Taiwan. In southern Taiwan, the 1-, 3-, and 5-year WBGT values per 1℃ increase during the noon period (OR, 0.875, 95% CI, 0.873–0.909; OR, 0.860, 95% CI, 0.825–0.896; OR, 0.848, 95% CI, 0.812–0.885; respectively) and working period (OR, 0.852, 95% CI, 0.825–0.880; OR, 0.845, 95% CI, 0.816–0.876; OR, 0.832, 95% CI, 0.0.801–0.863; respectively) were significantly associated with a low prevalence of PUD. However, in eastern Taiwan, the 1-, 3-, and 5-year WBGT values per 1℃ increase during the noon period (OR, 1.074, 95% CI, 1.022–1.127; OR, 1.058, 95% CI, 1.013–1.104; OR, 1.058, 95% CI, 1.013–1.105; respectively), and the 3- and 5-year WBGT values per 1℃ increase during the working period were significantly associated with a high prevalence of PUD (OR, 1.049, 95% CI, 1.003–1.097; OR, 1.047, 95% CI,

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1.001–1.095; respectively). Based on nonlinear trend analysis, WBGT was categorized into three groups for the noon period or work period, and the results were similar to and generally consistent with those in linear models.

Conclusion The associations between WBGT and PUD differed across the geographical regions of Taiwan. In northern and southern Taiwan, increases in average WBGT values were significantly associated with a low prevalence of PUD. In addition, this relationship was much stronger in southern Taiwan than in northern Taiwan. Of note, there was a reverse relationship between WBGT and PUD during the noon and working periods in eastern Taiwan. Further studies are needed to elucidate the effects of WBGT on PUD.

Keywords Wet-bulb Globe temperature, Peptic ulcer disease, Different geographic region, Taiwan biobank

Introduction

Peptic ulcer disease (PUD) is defined as a defect in the gastric or duodenal mucosal lining due to persistent gastric acid secretion with insufficient mucosal defense [1]. Helicobacter pylori (H. pylori) infection and the use of medications such as nonsteroidal anti-inflammatory drugs (NSAIDs) and aspirin are important causes of PUD [2]. Patients with PUD may have epigastric pain, nausea, vomiting, or even more severe symptoms such as peptic ulcer bleeding or perforation requiring hospitalization [3, 4]. PUD is associated with morbidity and high healthcare costs [5, 6]. In addition to H. pylori infection and the use of NSAIDs, other known risk factors for PUD include family history, male sex, older age, lower socioeconomic status, chronic medical conditions, psychological stress, and the use of alcohol and tobacco [2, 7–10]. The prevalence of asymptomatic PUD in Taiwan is 9.4% [11], compared to around 8.4% in the United States [7]. Although the incidences of PUD has decreased in the past 30 years due to H pylori eradication measures and the use of protein pump inhibitors [12], if PUD is not diagnosed and treated promptly, the complications can be serious, especially in countries with a lower sociodemographic index [10, 13].

Changes to the global climate and increasing ambient heat levels are a threat to human health. Previous studies have shown that exposure to high ambient temperatures has a negative influence on health-associated issues, including increases in emergency room visits and hospitalizations, increased mortality from cardiorespiratory and other diseases, mental health issues, adverse pregnancy and birth outcomes, and increased healthcare costs [14, 15]. Extreme heat exposure can cause adverse health consequences such as heat stress and heat stroke, worsening heart disease, acute kidney injury, and even mortality [15, 16]. On the other hand, there is also considerable evidence regarding cold-related health issues [17], including hypothermia [18], cardiovascular disease [18, 19], acute coronary syndrome [20, 21], respiratory mortality [22], and alcohol and substance use [18]. Of these health issues, the association between cold exposure and a higher risk of cardiovascular disease is the most well-studied, and the effect has been shown to vary according to disease type and climate zone [19].

Wet bulb globe temperature (WBGT) was devised by the United States Armed Services in the early 1950s to combat serious heat-related issues [23]. WBGT is now an International Standards Organization approved metric of heat stress in humans, and also the most widely used index of heat stress [24]. WBGT combines measurements of natural wet bulb temperature and globe temperature with air temperature, thus considering transfer phenomena including evaporation, convection, and radiation [24]. The WBGT has been shown to be a feasible health evidence-based approach to determine appropriate heat-warning thresholds with various heat indicators and health outcomes in Taiwan [25, 26]. Climate change impacts human health, and extreme heat may cause food insecurity and increase infectious diseases [27]. Heat waves or hot temperatures have also been shown to increase infectious gastroenteritis and inflammatory bowel disease hospitalizations [28, 29]. Seasonality or meteorological factors may play a role in the onset of PUD. A study conducted in Nanning in China reported that the detectable rate of PUD was lower in summer than in winter [30]. In addition, a retrospective observational cohort study from South Korea reported the highest incidence of PUD during winter [31]. Previous studies had revealed that a trend for an increase in injury occurrence in male football (soccer) leagues in higher WBGT [32], higher WBGT are associated with pregnancy duration and newborn size [33], and high WBGT are associated with impaired renal function [34]. However, there is limited data on the relationship between WBGT and PUD.

The main island of Taiwan can be divided into four geographical regions; northern, central, southern and eastern Taiwan. The dramatic topography of Taiwan and differences in latitude give rise to the diversity in climate, as well as WBGT. Taiwan is located in subtropical and tropical zones, so a relatively low temperature is still higher compared to other countries. Therefore, WBGT was used as the evaluation method in this study. In this study, we used data from the Taiwan Biobank (TWB) and WBGT data obtained from the Central Weather Bureau

(CWB) to investigate associations between WBGT and PUD in the four geographical regions of Taiwan.

Materials and methods

Study participants

The Taiwan Ministry of Health and Welfare initiated the TWB project to enhance healthcare and reduce the incidence of chronic diseases, particularly in light of the aging population. Further information can be found at https://www.twbiobank.org.tw/. We collected medical, genetic, and lifestyle data on the enrolled participants, who were middle-aged (30–70 years), resided around Taiwan, and had never been diagnosed with cancer [35, 36]. The establishment and operation of the TWB are overseen and approved by its Ethics and Governance Council and Institutional Review Board on Biomedical Science Research at Academia Sinica. Eligible participants were required to be of Taiwanese ethnicity, and provide written informed consent. Informed consent to participate was obtained from all of the participants in the study. The present study was approved by the IRB of our institute (KMUHIRB-E(I)-20240338), and it was performed in accordance with the Helsinki Declaration.

All participants in the TWB provide written informed consent before enrollment. Thereafter, the following data are obtained through questionnaires and physical examinations: clinical history (including hypertension and diabetes mellitus), age, sex, height, weight, body mass index, and lifestyle factors (tobacco/alcohol habits). In addition, fasting blood tests are performed to examine levels of uric acid, glucose, hemoglobin, triglycerides, total cholesterol, and estimated glomerular filtration rate (eGFR, calculated using the 2021 Chronic Kidney Disease Epidemiology Collaboration creatinine equation) [37].

Blood pressure readings were also performed following standard protocols by a trained member of staff, and the average of three readings (systolic and diastolic) were utilized in the analysis.

This is a cross-sectional study. In this study, we utilized baseline data, and obtained data on 121,364 participants in the TWB. After excluding those who lived outside the main island of Taiwan ($n = 940$) as they did not have WBGT data, the remaining 120,424 participants were enrolled (Fig. 1). The participants were geographically distributed across four major areas of Taiwan: northern, central, southern, and eastern regions (Fig. 2). The climate in these areas differs slightly, with that in the south being tropical, and that in the north and center being subtropical. Due to the shape of the eastern region, there are both subtropical and tropical climate areas. Regarding urbanization, there are five cities/counties in the south, seven cities/counties in the north, four cities/counties in the center, and five counties in the east.

Definition of PUD

Self-reported questionnaires were used to ascertain the presence of PUD. The participants were asked, “Have you been diagnosed with PUD?”, and those who replied “Yes” were considered to have PUD. The participants were classified into PUD and non-PUD groups accordingly.

Assessment of WBGT

There are 453 weather stations around Taiwan managed by the CWB [38], from which we recorded hourly temperature data from 2000 to 2020. The WBGT was calculated for each station as $0.7t_{nw} + 0.2t_g + 0.1t_a$, where t_{nw} is the natural wet-bulb temperature, t_g the globe temperature, and t_a the dry bulb temperature. These WBGT values were then categorized into those recorded during the working period (8:00 AM to 5:00 PM), and those recorded during the noon period (11:00 AM to 2:00 PM). Highly spatial-temporal differences in the hourly WBGT values were then examined using a land use-based spatial machine learning model. As solar declination, rainfall, wind speed, and relative humidity can affect WBGT, these data were also included, along with data on land use including recreational areas, industrial and residential areas, lakes and reservoirs, roads and places of interest such as religious centers and restaurants. SHapley Additive exPlanation values were used to select important predictors, along with a light gradient boosting machine algorithm to build the prediction model. This combination of WBGT and land use resulted in the model showing a high level of predictive accuracy, with an R^2 value as high as 0.99 [39]. In addition, the model yielded spatial-temporal WBGT values with a high-resolution grid of 50 m × 50 m.

Linking data from the TWB and WBGT

To estimate heat exposure, TWB and WBGT data were linked at the township level by the participants' residential individual addresses, detailed to the district. Annual average WBGT values were calculated for each participant, and also those for 1, 3, and 5 years before TWB enrollment. These WBGT values were used in the analysis of short- and long-term environmental exposure.

Statistical analysis

Data analysis was conducted with SPSS version 25 (IBM Inc., Armonk, NY). Data were expressed as percentage or mean ± standard deviation. Independent t-tests were used to compare continuous data between groups, while chi-square tests were used for categorical data. One-way analysis of variance (ANOVA) with Bonferroni correction was used for multiple comparisons among groups. The association between WBGT and PUD was examined with logistic regression analysis. Variables that showed significance in univariable analysis for PUD in Table 1

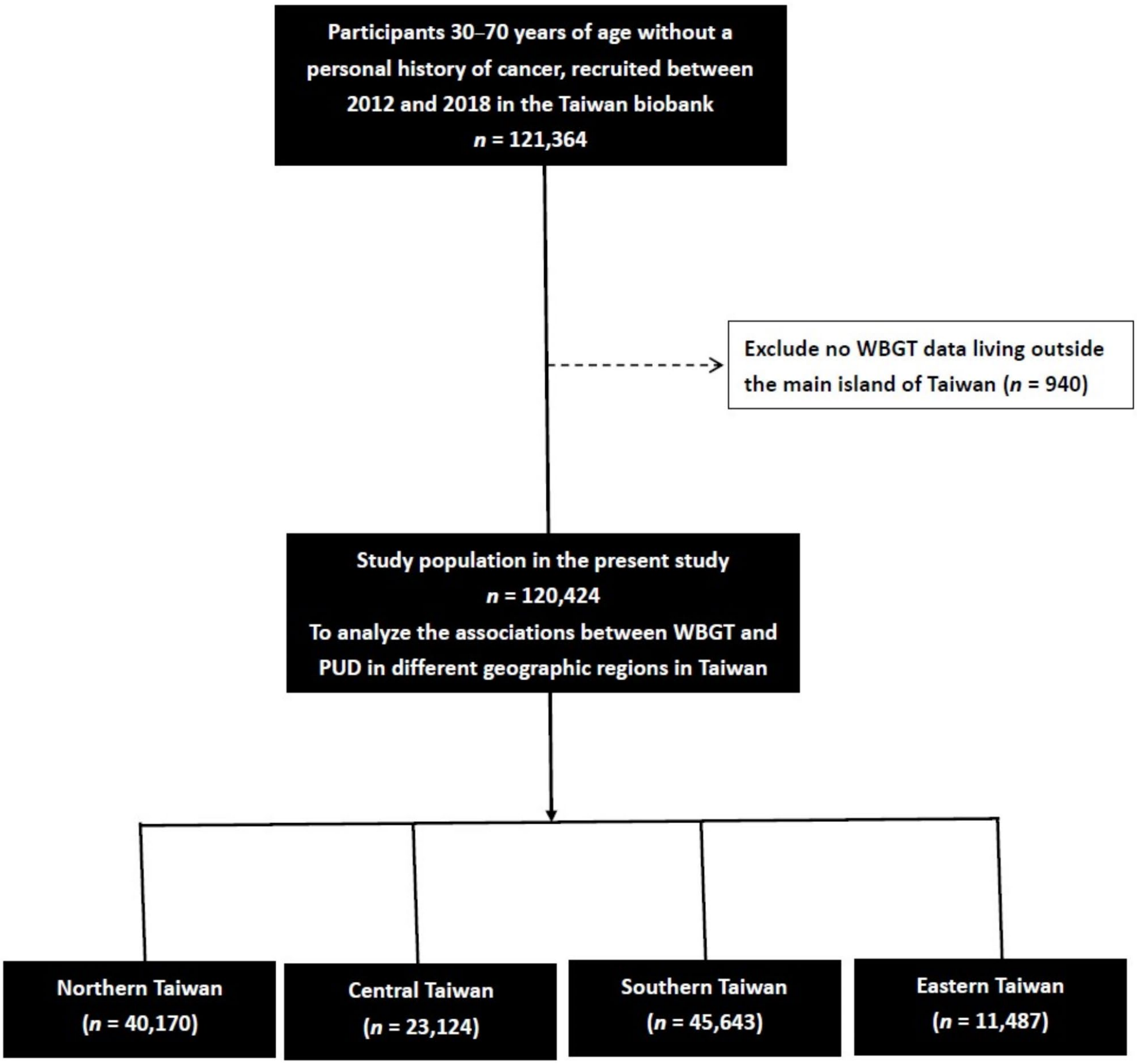

Fig. 1 Flowchart of study population

(including WBGT, age, sex, smoking and alcohol history, diabetes, hypertension, systolic blood pressure, body mass index, fasting glucose, hemoglobin, triglycerides, total cholesterol, eGFR and uric acid) were subsequently included in multivariable analysis. A p value < 0.05 was considered to indicate a statistically significant difference.

Results

Of the 120,424 enrolled participants (43,250 men and 77,174 women), the mean age was 49.9 ± 11.0 years, 17,508 (14.5%) had PUD, and 102,916 (85.5%) did not. In addition, 37.9% of the participants lived in southern Taiwan, 9.5% in eastern Taiwan, 33.4% in northern Taiwan, and 19.2% in central Taiwan. The average 1-, 3-, and 5-year WBGT values during the noon period were 27.25 ± 1.08, 27.11 ± 1.10, and 26.97 ± 1.10℃, respectively, compared to 25.02 ± 1.17, 24.93 ± 1.16, and 24.80 ± 1.16℃, respectively, during the working period.

Clinical characteristics of the PUD groups

The clinical characteristics of the PUD and non-PUD groups are compared in Table 1. Compared to the non-PUD group, the PUD group were predominantly male and older, had higher prevalence of diabetes mellitus, hypertension, smoking history and alcohol use, higher uric acid, systolic blood pressure, fasting glucose, hemoglobin, triglycerides and total cholesterol, and lower eGFR and body mass index.

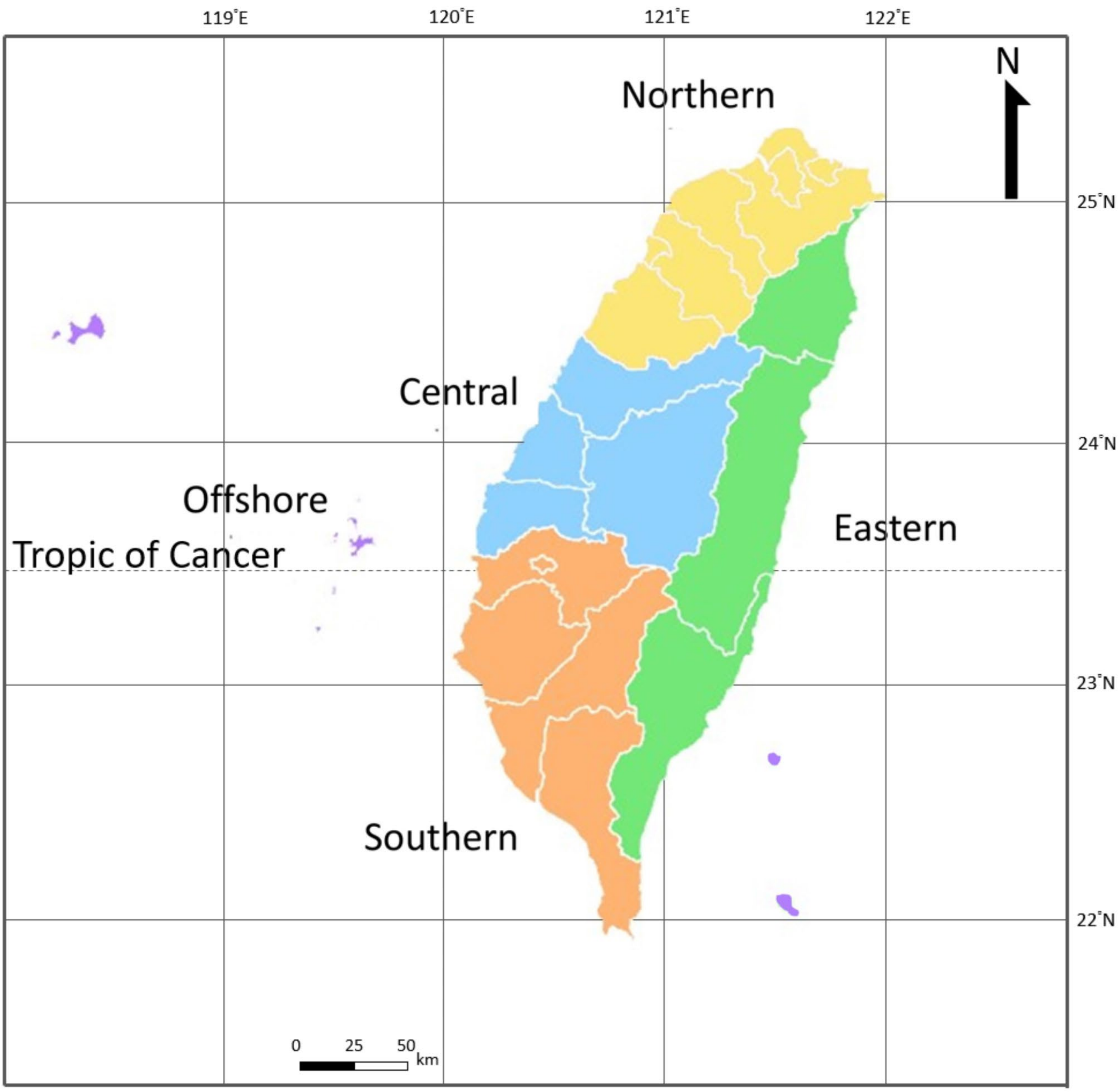

Fig. 2 The distribution of different regions in Taiwan

Comparisons of the participants' clinical characteristics by region

Compared to the participants living in northern, central and southern Taiwan, those living in eastern Taiwan had the highest prevalence of PUD (Table 2). In addition, the highest average WBGT values during both the noon and working periods at all yearly time points occurred in southern Taiwan compared to the other regions. *Associations between WBGT and PUD in the four geographical regions.*

After adjusting for the significant variables shown in Table 1, multivariable logistic regression analysis was performed to examine the associations between WBGT and PUD in the four geographical regions (Table 3). The results showed that in northern Taiwan, the 1-year and 5-year average noon WBGT values per 1℃ increase were significantly associated with PUD (odds ratio [OR], 0.960, $p = 0.026$; OR, 0.962, $p = 0.033$, respectively). No significant association between WBGT and PUD was found in central Taiwan during either the noon or working period. In southern Taiwan, the 1-, 3-, and 5-year average WBGT values per 1℃ increase were significantly associated with a low prevalence of PUD during both the noon period (OR, 0.875, $p < 0.001$; OR, 0.860, $p < 0.001$; OR,

Table 1 Comparison of clinical characteristics among participants according to PUD in study participants

Characteristics	PUD (-) ($n = 102,916$)	PUD (+) ($n = 17,508$)	p
Age (year)	49.3 ± 11.0	53.2 ± 10.1	< 0.001
Male sex (%)	35.1	40.7	< 0.001
DM (%)	9.3	11.0	< 0.001
Hypertension (%)	24.0	27.2	< 0.001
Smoking history (%)	26.3	32.6	< 0.001
Alcohol history (%)	8.1	10.5	< 0.001
Systolic BP (mmHg)	120.3 ± 18.7	121.2 ± 18.3	< 0.001
Diastolic BP (mmHg)	73.8 ± 11.4	73.9 ± 11.1	0.110
BMI (kg/m^2)	24.2 ± 3.8	24.1 ± 3.7	< 0.001
Laboratory parameters			
Fasting glucose (mg/dL)	95.8 ± 20.8	96.8 ± 20.0	< 0.001
Hemoglobin (g/dL)	13.7 ± 1.6	13.9 ± 1.6	< 0.001
Triglyceride (mg/dL)	115.2 ± 94.9	117.7 ± 88.5	0.001
Total cholesterol (mg/dL)	195.5 ± 35.9	196.5 ± 35.6	< 0.001
eGFR (mL/min/1.73 m^2)	105.8 ± 13.7	102.3 ± 14.4	< 0.001
Uric acid (mg/dL)	5.42 ± 1.43	5.46 ± 1.40	< 0.001
Residence			< 0.001
Northern Taiwan (%)	33.6	31.9	
Central Taiwan (%)	19.3	18.4	
Southern Taiwan (%)	37.8	38.2	
Eastern Taiwan (%)	9.2	11.4	
WBGT during noon period*			
1-year average of WBGT (per 1 ℃)	27.26 ± 1.08	27.22 ± 1.09	< 0.001
3-year average of WBGT (per 1 ℃)	27.11 ± 1.10	27.08 ± 1.11	< 0.001
5-year average of WBGT (per 1 ℃)	26.97 ± 1.10	26.94 ± 1.11	< 0.001
WBGT during work period*			
1-year average of WBGT (per 1 ℃)	25.02 ± 1.17	24.99 ± 1.17	0.002
3-year average of WBGT (per 1 ℃)	24.93 ± 1.16	24.90 ± 1.17	0.004
5-year average of WBGT (per 1 ℃)	24.80 ± 1.16	24.78 ± 1.16	0.007

*Noon period is defined as 11 am to 2 pm, and work period is defined as 8 am to 5 pm

Abbreviations. PUD, peptic ulcer disease; DM, diabetes mellitus; BP, blood pressure; BMI, body mass index; eGFR, estimated glomerular filtration rate; WBGT, wet-bulb globe temperature

Table 2 Comparison of clinical characteristics among participants in different geographic regions

Characteristics	Northern Taiwan ($n = 40,170$)	Central Taiwan ($n = 23,124$)	Southern Taiwan ($n = 45,643$)	Eastern Taiwan ($n = 11,487$)	ANOVA p
PUD (%)	13.9	14.0*	14.7*†	17.4$^{*†\#}$	< 0.001
WBGT during noon period*					
1-year average of WBGT (per 1 ℃)	26.38 ± 0.77	27.40 ± 0.82*	28.10 ± 0.69*†	26.68 ± 1.02$^{*†\#}$	< 0.001
3-year average of WBGT (per 1 ℃)	26.23 ± 0.81	27.23 ± 0.79*	27.98 ± 0.63*†	26.44 ± 1.15$^{*†\#}$	< 0.001
5-year average of WBGT (per 1 ℃)	26.08 ± 0.80	27.10 ± 0.78*	27.86 ± 0.60*†	26.23 ± 1.14$^{*†\#}$	< 0.001
WBGT during work period*					
1-year average of WBGT (per 1 ℃)	24.83 ± 1.06	23.83 ± 0.74*	25.82 ± 0.78*†	24.87 ± 1.14$^{*†\#}$	< 0.001
3-year average of WBGT (per 1 ℃)	24.76 ± 1.09	23.75 ± 0.74*	25.73 ± 0.72*†	24.69 ± 1.11$^{*†\#}$	< 0.001
5-year average of WBGT (per 1 ℃)	24.63 ± 1.10	23.63 ± 0.76*	25.61 ± 0.68*†	24.51 ± 1.10$^{*†\#}$	< 0.001

*Noon period is defined as 11 am to 2 pm, and work period is defined as 8 am to 5 pm

Abbreviations. PUD, peptic ulcer disease; WBGT, wet-bulb globe temperature

$^*p < 0.05$ compared with northern Taiwan; $^†p < 0.05$ compared with central Taiwan; $^\#p < 0.05$ compared with southern Taiwan

0.848, $p < 0.001$, respectively) and working period (OR, 0.852, $p < 0.001$; OR, 0.845, $p < 0.001$; OR, 0.832, $p < 0.001$, respectively). In contrast, in eastern Taiwan, the 1-, 3-, and 5-year average WBGT values per 1℃ increase were significantly associated with high prevalence of PUD during the noon period (OR, 1.074, $p = 0.005$; OR, 1.058, $p = 0.011$; OR, 1.058, $p = 0.011$, respectively), and the 3- and 5-year average WBGT values per 1℃ increase were significantly associated with a high prevalence of PUD

Table 3 Association of WBGT with PUD in different geographic regions using multivariable logistic regression analysis

WBGT	PUD	p
	Odds ratio (95% CI)	
Noon period	Northern Taiwan (n = 40,170)	
1-year average of WBGT (per 1 ℃)	0.960 (0.925–0.955)	0.026
3-year average of WBGT (per 1 ℃)	0.967 (0.934–1.001)	0.059
5-year average of WBGT (per 1 ℃)	0.962 (0.929–0.997)	0.033
Work period		
1-year average of WBGT (per 1 ℃)	1.002 (0.976–1.030)	0.857
3-year average of WBGT (per 1 ℃)	1.002 (0.976–1.028)	0.888
5-year average of WBGT (per 1 ℃)	1.002 (0.976–1.028)	0.909
Noon period	Central Taiwan (n = 23,124)	
1-year average of WBGT (per 1 ℃)	0.974 (0.930–1.019)	0.254
3-year average of WBGT (per 1 ℃)	0.966 (0.922–1.012)	0.148
5-year average of WBGT (per 1 ℃)	0.969 (0.924–1.017)	0.201
Work period		
1-year average of WBGT (per 1 ℃)	0.972 (0.924–1.022)	0.261
3-year average of WBGT (per 1 ℃)	0.967 (0.920–1.018)	0.199
5-year average of WBGT (per 1 ℃)	0.974 (0.928–1.023)	0.294
Noon period	Southern Taiwan (n = 45,643)	
1-year average of WBGT (per 1 ℃)	0.875 (0.873–0.909)	< 0.001
3-year average of WBGT (per 1 ℃)	0.860 (0.825–0.896)	< 0.001
5-year average of WBGT (per 1 ℃)	0.848 (0.812–0.885)	< 0.001
Work period		
1-year average of WBGT (per 1 ℃)	0.852 (0.825–0.880)	< 0.001
3-year average of WBGT (per 1 ℃)	0.845 (0.816–0.876)	< 0.001
5-year average of WBGT (per 1 ℃)	0.832 (0.801–0.863)	< 0.001
Noon period	Eastern Taiwan (n = 11,487)	
1-year average of WBGT (per 1 ℃)	1.074 (1.022–1.127)	0.005
3-year average of WBGT (per 1 ℃)	1.058 (1.013–1.104)	0.011
5-year average of WBGT (per 1 ℃)	1.058 (1.013–1.105)	0.011
Work period		
1-year average of WBGT (per 1 ℃)	1.037 (0.993–1.083)	0.103
3-year average of WBGT (per 1 ℃)	1.049 (1.003–1.097)	0.037
5-year average of WBGT (per 1 ℃)	1.047 (1.001–1.095)	0.047

Values expressed as odds ratio and 95% confidence interval (CI). Abbreviations. WBGT, wet-bulb globe temperature

*Noon period is defined as 11 am to 2 pm, and work period is defined as 8 am to 5 pm

Multivariable model: adjusted for age, sex, smoking and alcohol history, diabetes, hypertension, systolic blood pressure, body mass index, fasting glucose, hemoglobin, triglycerides, total cholesterol, eGFR and uric acid (significant variable in Table 1)

during the working period (OR, 1.049, $p = 0.037$; OR, 1.047, $p = 0.047$, respectively).

The associations between WBGT and PUD at 1, 3, and 5 years during the noon and working periods by area are displayed in Figs. 3 and 4, respectively.

To assess the potential nonlinear relationship between the 1-year, 3-year, and 5-year average WBGT (during both noon and work periods) and the risk of PUD across different geographic regions, a restricted cubic spline analysis with five knots was conducted using a logistic regression model (Fig. 5). The analysis adjusted for multiple covariates, including age, sex, smoking and alcohol history, diabetes, hypertension, systolic blood pressure, BMI, fasting glucose, hemoglobin, triglycerides, total cholesterol, eGFR, and uric acid. The spline knots were placed at the 5th, 27.5th, 50th, 72.5th, and 95th percentiles of the WBGT distribution in the study sample. The relationship between the 1-year, 3-year, and 5-year average WBGT (during both the noon and work periods) and the risk of PUD exhibite nonlinear effects, with statistical significance observed for both the noon period ($p < 0.001$) and the work period ($p < 0.001$).

A restricted cubic spline analysis showed statistically significant nonlinearity across different regions, indicating that WBGT may have varying risk trends across different temperature ranges. Based on nonlinear trend analysis, WBGT was categorized into three groups for the noon period or work period (see Supplementary Tables 1 and 2).

Based on nonlinear trend analysis for noon period, WBGT was categorized into three groups: < 26 °C, 26–27 °C, and > 27 °C. The results (supplementary Table 1) showed that in northern Taiwan, WBGT < 26 °C was associated with a lower PUD risk (OR ≤ 0.905; $p \leq 0.014$ for the 1-year, 3-year, and 5-year average WBGT), while WBGT of 26–27 °C was associated with a higher PUD risk (OR = 1.184; $p = 0.020$) only for the 1-year average of WBGT. In southern Taiwan, WBGT of 26–27 °C was linked to a higher PUD risk (OR = 2.039; $p = 0.007$ only for the 5-year average of WBGT), whereas WBGT > 27 °C was associated with a lower PUD risk (OR ≤ 0.920; $p \leq 0.002$ for the 1-year, 3-year, and 5-year average WBGT). In eastern Taiwan, a WBGT of 26–27 °C was associated with an increased PUD risk (OR = 1.432; $p = 0.046$ for only the 5-year average of WBGT and OR = 1.386; $p < 0.001$ for only the 1-year average of WBGT).

Based on nonlinear trend analysis for work period, WBGT was categorized into three groups: < 24 °C, 24–25 °C, and > 25 °C. The results (supplementary Table 2) showed that in northern Taiwan, WBGT < 24 °C was associated with a lower PUD risk (OR ≤ 0.921; $p \leq 0.032$) only for the 3-year and 5-year average WBGT. In southern Taiwan, WBGT of 24–25 °C was linked to a lower PUD risk (OR ≤ 0.751; $p \leq 0.022$) only for the 3-year and 5-year average WBGT. In eastern Taiwan, a WBGT of > 25 °C was associated with an increased PUD risk (OR ≤ 1.154; $p \leq 0.049$) for the 1-year, 3-year, and 5-year average WBGT.

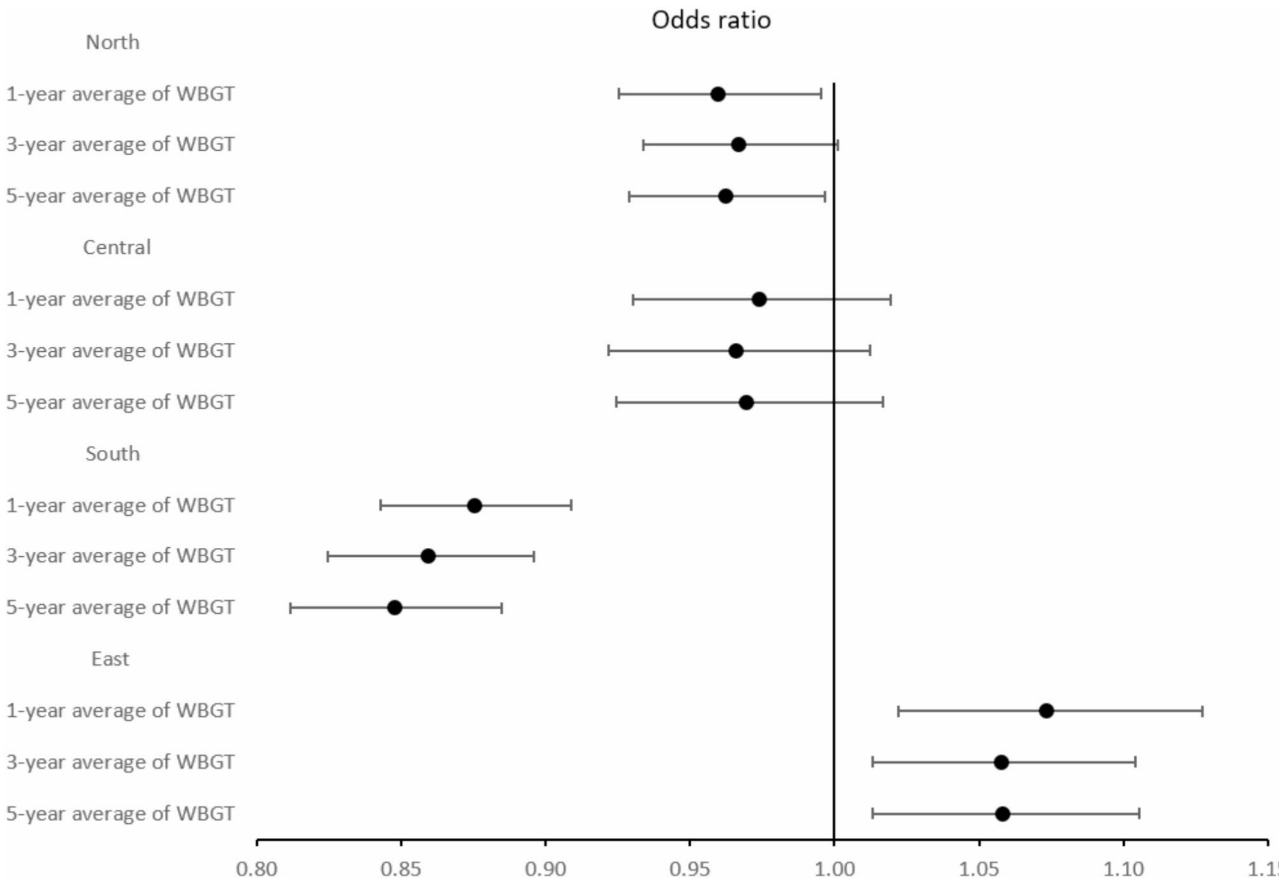

Fig. 3 Forest plots of the association of WBGT in noon period with PUD using multivariable logistic regression analysis stratification by geographic regions

Discussion

Our results demonstrated differences in the association between WBGT and PUD across the different geographical regions of Taiwan. We found that increases in average WBGT values were significantly associated with a low prevalence of PUD in northern and southern Taiwan, and that this association was much stronger in southern Taiwan compared to northern Taiwan. Interestingly, a reverse relationship between WBGT and PUD was found in eastern Taiwan.

There are several key findings in this study. First, the 1- and 5-year average WBGT values per 1℃ increase during the noon period were significantly associated with a low prevalence of PUD in northern Taiwan, and the 1-, 3-, and 5-year average WBGT values per 1℃ increase during both the noon and work period were significantly associated with a low prevalence of PUD in southern Taiwan. Variations in seasonality and meteorological factors such as ambient temperature have been shown to play a role in the development of PUD [30, 31, 40, 41]. A retrospective study in the United States from 1986 to 1989 including nationwide data from the Department of Veterans Affairs, Health Care Financing Administration, and Vital Statistics found that hospitalizations secondary to PUD appeared to peak around March and October, with a dip during the summer months [42]. In addition, a study conducted in China from 1992 to 1997 reported that the rate of PUD was highest in winter (26.5%), then decreased from spring to summer, with the lowest rate in June (20.0%) [30]. A retrospective observational study conducted from 2012 to 2016 using Health Insurance Review and Assessment-National Patient Samples database in South Korea found that the incidence of PUD was higher in winter (28.5–32.8%) than in autumn (19.8–21.5%) in a cohort of 14,626 patients [31]. Another retrospective study in Italy with 26,848 PUD patients reported that the lowest rate of PUD hospital admissions occurred in the summer compared to other seasons [41]. Moreover, a study conducted in Tokyo from 1996 to 1999 of 441 patients with hematemesis, including 275 (62.4%) with gastric ulcer, reported highly significant monthly fluctuations and seasonal variations in hematemesis events related to gastric ulcer. The mean number of hematemesis events decreased in summer and increased in winter, and significant differences were found between summer and winter, and autumn [43]. The mechanism underlying the association between cold temperatures and an increase in PUD is still unclear. For coronary

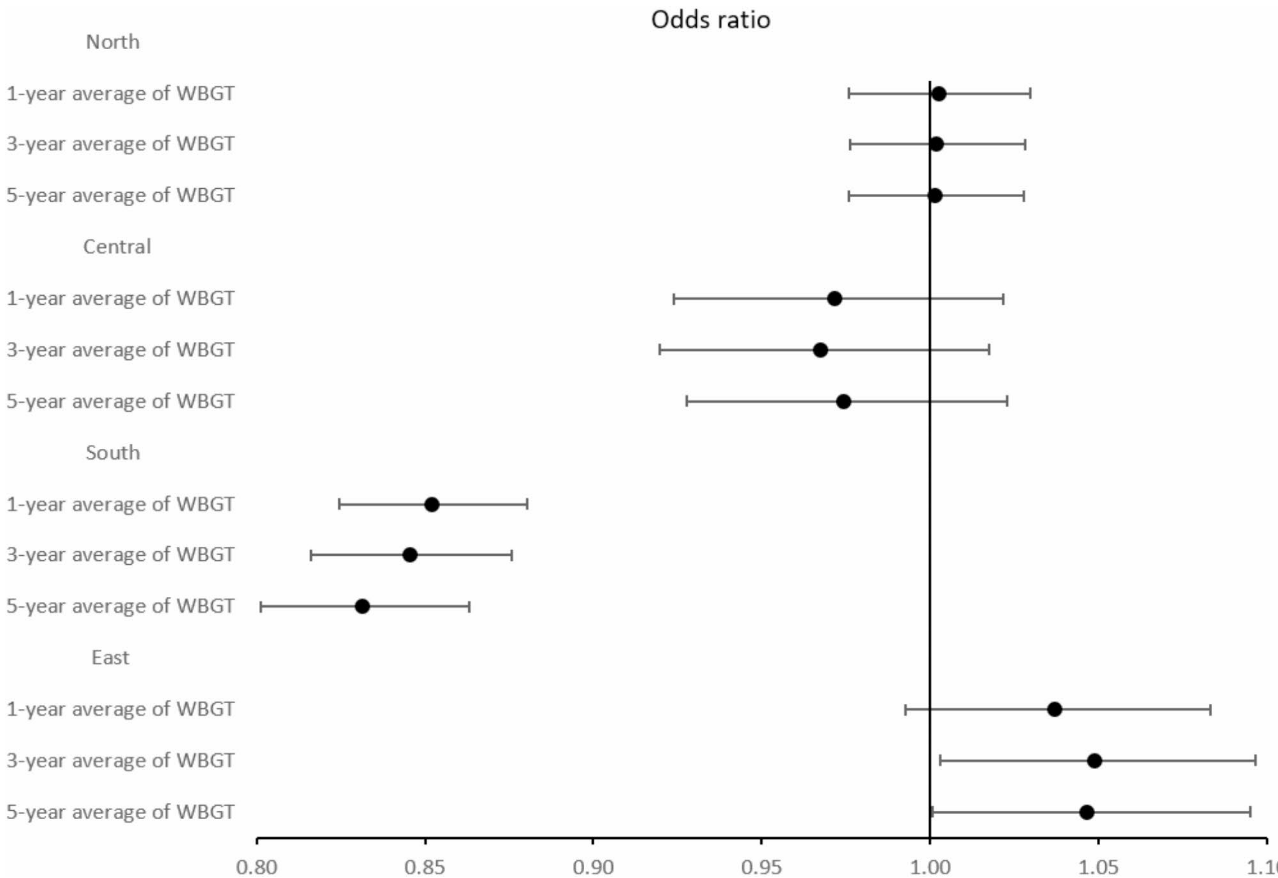

Fig. 4 Forest plots of the association of WBGT in work period with PUD using multivariable logistic regression analysis stratification by geographic regions

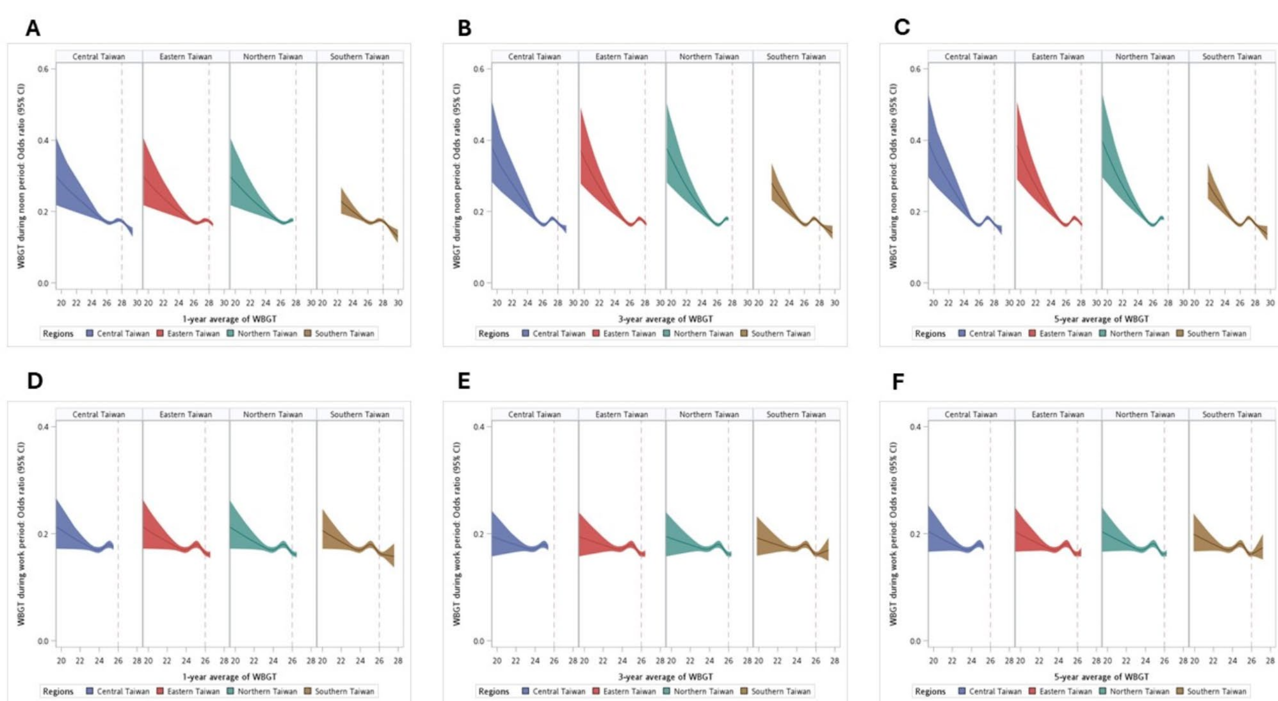

Fig. 5 Nonlinear relationship between the noon period: 1-year (**A**), 3-year (**B**), and 5-year (**C**), and work period: 1-year (**D**), 3-year (**E**), and 5-year (**F**) average WBGT and the risk of PUD across different geographic regions

artery disease, the winter months have been associated with a higher incidence of myocardial infarction [21, 44], probably due to cold-induced sympathetic nervous system stimulation and increase in plasma catecholamine levels [20, 21, 45]. Previous studies have reported that extreme changes in meteorological factors can result in a series of stressful conditions (fight or flight response), causing excitation of the sympathetic nervous system and increased adrenal activity with catecholamine, epinephrine and norepinephrine secretion, finally leading to PUD [40, 45–47]. In addition, the level of norepinephrine has been shown to increase after whole body or hand exposure to cold water [45]. One clinical study analyzed gastric juice and biopsy specimens from 176 patients with PUD, and found that an extremely cold climate was associated with significantly thinner mucosa of the gastric antrum and significantly lower heat shock protein (HSP) 70 expression compared to a hot climate [40]. HSPs, including HSP90, HSP70, and HSP27 are known to play roles in gastric defense mechanisms at the intracellular level, in the maintenance of normal cell integrity, and in improving cellular recovery and ulcer healing [48, 49].

In southern Taiwan, the increases in 1-, 3-, and 5-year average WBGT values per 1℃ had a more pronounced influence on the prevalence of PUD compared to northern Taiwan. Unexpectedly, the higher increases in WBGT values in southern Taiwan seemed to have a more protective effect on PUD than those in northern Taiwan. Most epidemiological studies have reported associations between extreme heat with direct heat-related morbidity and mortality [50–52], along with higher rates of cardiovascular, respiratory, and renal diseases [53]. However, the development of new physiological and biophysical models has provided new opportunities to assess how humans might live and work in a global warming future [54], and they have suggested that human thermoregulatory responses to extreme heat or heat strain could be more powerful than previously conceived heat tolerance thresholds [54, 55]. Furthermore, protective factors against heat strain, such as fitness [56], heat acclimatization [57], and behavioral adaptations [58], may reduce the impact of extremely hot environments. The key thermoregulatory responses to heat stress in humans include redistributing blood flow to the skin (vasodilation) to improve heat transfer to the environment, and secreting sweat, which evaporates and removes body heat [59, 60]. Although there are limited data regarding the association between higher environment temperatures and the lower prevalence of PUD, our results may suggest that people living in areas with a higher WBGT may develop more heat acclimatization and adaptation measures, resulting in a protective effect against PUD.

In northern Taiwan, a negative association was found for the noon period and a marginally positive association was observed for the working period. The opposite association between WBGT and PUD at different time intervals in Northern Taiwan is an interesting finding. A negative association was found for the noon period and a marginally positive association was observed for the working period. The possible reason for this difference in the association between WBGT and PUD at different time intervals in Northern Taiwan may be that people stay indoors during noon period and the WBGT has less effect on health issue. On the other hand, people worked outdoors more during working period and make them more vulnerable to high WBGT. Why is this association only found in the Northern Taiwan is still not well-understood. Future research is needed to validate this issue.

Another interesting finding is that high WBGT values during both the noon period and working period were significantly associated with a high prevalence of PUD in eastern Taiwan. This result is in contrast to the association with a low prevalence of PUD in northern and southern Taiwan. The pathophysiologic responses to heat stroke are not due to the immediate effects of heat exposure, but are rather the result of systemic inflammatory responses following thermal injury [60]. Previous human and animal studies have suggested that host inflammatory and hemostatic responses to heat stress contribute to tissue and organ injuries in those who survive the initial deleterious effects of hyperthermia [61–63]. Previous studies have shown that splanchnic hypoperfusion may result in ischemia in gastrointestinal organs followed by injuries related to reperfusion during rapid splanchnic vasodilatation, and that this may be related to inappropriate nitric oxide (NO) production preceding the start of hemodynamic collapse and hyperthermia in conditions of environmental heat stress [64, 65]. NO and NO synthases have been shown to be involved in preserving the integrity of the gastrointestinal mucosal through the regulation of mucous secretion, gastric mucosal blood flow, and defense barriers [66, 67]. Therefore, an imbalance in NO production, lacking a protective effect, may occur during inflammatory conditions during heat stress, and lead to the development of PUD [66]. Eastern Taiwan has a unique topography, including the Coast Range, Longitudinal Valley and Central Range, along with a rocky shoreline. Despite the long coastline, the sea breeze has a limited cooling effect due to the Coastal and Central Mountain ranges, resulting in greater humidity in this area. Whether the high WBGT in eastern Taiwan causes more heat stroke events and subsequently a higher incidence of PUD due to inflammation status warrants further exploration. Previous studies have shown that high temperature and high humidity increase the risk of heat stress [68, 69]. Exposure to extreme heat can also result in a range of health consequences such as heat stroke, worsening heart disease, and acute kidney injury, leading to an increase in all-cause mortality, particularly in people aged over 65 years who are especially vulnerable to these effects [51, 52]. The estimated survivable limit for peak 6-hourly environmental wet-bulb temperature is considered to be around 35 °C for humans, depending on the concept of resting metabolic rate and assuming a normothermic resting body core temperature of approximately 37 °C [70]. Taking age, comorbidities, fitness, outdoor shade and the use of air conditioning into account, the effects of high WBGT on human health and PUD become more complicated, and depend to some extent on the characteristics of the region and socioeconomic status [26]. In other words, people, and especially older individuals, who live in vulnerable areas with high WBGT without appropriate heat adaptation such as housing optimized to improve indoor thermal comfort and reduce energy consumption, and in areas with fewer trees or shade will be at increasing risk of heat strain and mortality [54, 71–73].

The inclusion of a large population-based cohort living throughout the main island of Taiwan increases the power of our analysis. Nevertheless, several limitations should also be considered. First, temporal relationships between WBGT and PUD could not be evaluated due to the cross-sectional design of the study. The effect of seasonal changes on PUD could also not be evaluated. Further studies are required to validate our results. Second, as the participants self-reported their PUD status via questionnaire and the diagnosis was not verified, the type and severity of PUD could not be included in the analysis. Nevertheless, a previous study in Taiwan reported concordance between claims data and self-reported illnesses [74]. Third, we only analyzed outdoor but not indoor WBGT. The use of dehumidifiers and air conditioners and consequently lower humidity and temperature indoors may have resulted in underestimation of the association between WBGT and PUD. However, a previous study reported a strong association between outdoor and indoor temperatures when the outdoor temperature is higher than 12.7℃ [75]. This correlation may also be extended to WBGT, providing credibility to our approach of applying outdoor WBGT estimates to indoor environments. In addition, this version of TWB we apply lacks some important information influencing the prevalence of PUD, such as lifestyle factors, sociodemographics, socioeconomic status and genetic data, which may influence the results and interpretation. However, in this version of Taiwan biobank, there is no data of socioeconomic status. Finally, we enrolled more women than men in this study, possible due to their greater willingness to participate in research studies, and so our findings may not be generalizable to the general population.

In conclusion, this study showed that WBGT had varying impacts on the incidence of PUD in a large population-based cohort living in the four main geographical regions of Taiwan. High WBGT seemed to be a protective factor in northern and southern Taiwan, whereas it seemed to be harmful in eastern Taiwan. Previous studies have discussed the relationship between seasonality and PUD [30, 31, 40, 41, 76], however they did not further evaluate the impacts of meteorological factors such as solar radiation, ambient air temperature, humidity, or wind speed. Our study highlights the importance of heat protection, and especially in eastern Taiwan, where high WBGT was associated with a higher incidence of PUD. Further longitudinal studies are warranted to investigate the risk of WBGT for incident PUD, involving repeated measures of WBGT and PUD symptoms over time, and comprehensive information on lifestyle factors, sociodemographics, socioeconomic status and genetic data.

Supplementary Information

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Supplementary Material 1

Author contributions

Conceptualization, methodology, validation, formal analysis, writing—review and editing, and supervision: C-HK and S-CC. Software and investigation: C-DW and S-CC. Resources, project administration, and funding acquisition: S-CC. Data curation: Y-CG, C-YK, W-YS, W-LT, Y-JW, P-HW, M-YL, C-DW, C-HK and S-CC. Writing—original draft preparation: Y-CG and S-CC. Visualization: C-DW, C-HK and S-CC. All authors have read and agreed to the published version of the manuscript.

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Data availability

The data underlying this study are from the Taiwan Biobank. Due to restrictions placed on the data by the Personal Information Protection Act of Taiwan, the minimal data set cannot be made publicly available. Data may be available upon request to interested researchers. Please send data requests to: Szu-Chia Chen, PhD, MD. Division of Nephrology, Department of Internal Medicine, Kaohsiung Medical University Hospital, Kaohsiung Medical University.

Declarations

Ethical approval

The study was conducted according to the Declaration of Helsinki, and it was granted approval by the Institutional Review Board of Kaohsiung Medical University Hospital (KMUHIRB-E(I)-20240338), and the TWB was granted approval by the IRB on Biomedical Science Research, Academia Sinica, Taiwan and the Ethics and Governance Council of the TWB.

Consent to participate

Informed consent to participate was obtained from all of the participants in the study.

Consent to publish
Not applicable.

Conflicts of interest
The authors declare that they have no known competing financial interests.

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