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Seasonal variations in peptic ulcer disease incidence in Taiwan, a country spanning both tropical and subtropical regions: a real-world database analysis

Yi-Chen Lai,[1] Yu-Han Chen,[2] Chien-An Chen,[3] Chung-Han Ho ,[4,5] Yu-Cih Wu,[6] Jhi-Joung Wang,[6,7] Shih-Feng Weng,[8,9] Yuan Kao[10,11]

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Y-CL and Y-HC contributed equally.

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For numbered affiliations see end of article.

Correspondence to
Dr Yuan Kao;
vincentkao6703@gmail.com

ABSTRACT

Objective Previous studies have shown that the incidence of peptic ulcer disease (PUD) exhibits seasonal variations. This study aimed to investigate the seasonal variation in PUD incidence in Taiwan, which spans both tropical and subtropical regions, using a nationwide database.

Methods A cross-sectional study was conducted using real-world claims data from Taiwan, which includes a representative sample of 2 million individuals. Patients hospitalised with a primary diagnosis of PUD between 2001 and 2019 were identified using International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) and International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) codes for gastric ulcers (GUs), duodenal ulcers (DUs) and unspecified peptic ulcers. Descriptive statistics were used to present the seasonal variations in PUD incidence. Patients' gender, age, PUD type, geographical region and non-steroidal anti-inflammatory drugs (NSAIDs) usage across the four seasons (spring, summer, fall, winter) were compared using Pearson's χ^2 test.

Results Among the 13 022 patients, new-onset PUD cases varied annually, peaking at 771 cases in 2004 and reaching a low of 614 cases in 2018. PUD incidence was higher in males than in females, and more common in elderly individuals aged ≥65 (59.5%). GU had the highest prevalence (56.1%), followed by DU (36.3%) and unspecified ulcers (7.7%). PUD incidence peaked in winter (26.8%), followed by spring (25.1%), fall (24.2%) and summer (23.9%). This seasonal trend was consistent across gender and age groups, with no significant impact on latitude, NSAID usage or PUD type.

Conclusion Across the tropical and subtropical regions of Taiwan, seasonal variation in PUD incidence is observed with the highest rates occurring in winter, regardless of age or sex. However, NSAID usage tends to obscure this trend. The seasonal variation in DU incidence showed no significant differences between north and south Taiwan, suggesting that factors other than temperature may affect DU incidence compared with their effect on GU incidence.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ The incidence of peptic ulcer disease (PUD) exhibits seasonal variations in high-latitude countries; however, seasonal variations in the regions of tropical and subtropical are poorly understood.

WHAT THIS STUDY ADDS

⇒ Across the tropical and subtropical regions of Taiwan, seasonal variation in PUD incidence was observed with the highest rates occurring in winter, but this finding was not statistically significant.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Our results provide a reference for health management agencies to plan preventive health education programmes for PUD and effectively use medical personnel and facilities.

INTRODUCTION

Seasonal variations in various medical conditions have been well established in the literature. For instance, cardiovascular diseases,[1] stroke,[2] cardiac arrest,[3] pulmonary disorders[4 5] and sepsis[6] commonly peak during winter. Understanding seasonal variations in diseases can help explain the nature of illnesses and aid in predicting demands for hospital resources. This knowledge is valuable for policy-makers in planning the appropriate allocation of medical resources and ensuring the presence of backup personnel during peak periods.[7 8]

Peptic ulcer disease (PUD), a major public health disease affecting millions of individuals worldwide annually,[9 10] exhibits seasonal variations.[8 11–15] A higher incidence of PUD during cold or winter seasons has been previously reported.[8 12 14 15] The mechanism underlying may be related to the thinner mucosa of the gastric antrum during cold weather and the decreased level of heat shock protein 70.[14] However, several studies have reported contradictory results. A nationwide cohort study conducted in the USA by Kanotra *et al* showed a peak for PUD incidence during

the spring and a trough in fall,[11] whereas another large-scale study in Italy reported three peak periods (autumn, winter and spring) for the incidence of PUD.[16] Therefore, the existing conclusions regarding the seasonal variability in PUD incidence remain inconclusive. Moreover, most of these studies were conducted in Western or Northeast Asian countries with distinct seasonal climatic changes. Research on PUD incidence in Southeast Asian and tropical countries is limited.

To address this gap, we aimed to conduct a nationwide population study to investigate the seasonal variation in PUD incidence in Taiwan, a country that spans both tropical and subtropical regions. Additionally, we further analysed factors, such as age, sex, non-steroidal anti-inflammatory drug (NSAID) usage and latitudinal differences, to explore their association with seasonal variability in PUD incidence. Our goal was to obtain comprehensive data to assist in planning medical resource allocation, thereby achieving better patient care.

METHODS

Data source

The data for this study were obtained from the Health and Welfare Data Science Centre (HWDC) of the Ministry of Health and Welfare in Taiwan, using the longitudinal National Health Insurance Research Database (LHID2005). LHID2005 is a random sample of two million individuals from 2005, and it reflects the demographic characteristics of Taiwan according to the distribution of gender, age and region.[17 18] Therefore, the population distribution in LHID2005 accurately reflects the demographic characteristics of Taiwan, where the western region is significantly more populated than the eastern region.[19] Additionally, LHID2005 included the detailed medical and prescription records from 2001 to 2019. The accuracy of the diagnosis codes in the National Health Insurance Research Database has been evaluated in several validation studies, demonstrating the reliability of this claims database.[17] To protect personal information, the HWDC effectively manages deidentified patient data by linking the relative dataset. This study adhered to the Strengthening the Reporting of Observational Studies in Epidemiology statement[20] (online supplemental material).

Selection of patients

This study focused on PUD incidence in Taiwan, with specific attention paid to gastric ulcers (GUs), duodenal ulcers (DUs) and unspecified peptic ulcers, as classified by ICD-9-CM codes 531–534 and the corresponding ICD-10-CM codes K25–K28. Additionally, the study included data on NSAID usage, identified by the Anatomical Therapeutic Chemical (ATC) code M01A*. Patients with PUD were classified into three groups according to the use of the medication. Non-users were those who did not use NSAIDs in the 6 months before the diagnosis. Non-long-term users were patients who used NSAIDs at least once in the 6 months prior but did not meet the criteria for long-term use. Long-term users were those who used NSAIDs continuously for 14 days or accumulated 28 days of use within 3 months before the diagnosis.

Initially, 44 967 patients hospitalised for PUD between 2001 and 2019 were included. After excluding patients aged less than 20 years (n=465), 44 502 adult patients were included in the study. Patients whose first diagnosis code was PUD were selected from this group, resulting in a final sample size of 13 022.

Measurements

The incidence of PUD refers to the number of new cases diagnosed within a specific period. In this study, the incidence was defined as the number of patients who were first hospitalised with a diagnosis of PUD between 2001 and 2019. To reflect the overall burden of the disease, PUD prevalence was defined as the total number of existing cases of PUD at a given point in time or over a specified period.

Additionally, Taiwan is located between 21°45' and 25°56' north latitude, spanning both tropical and subtropical regions, with seasonal changes ranging from cool to hot, and a consistently humid climate throughout the year. The Central Weather Bureau defines spring as March–May, summer as June–August, fall as September–November and winter as December–February. The seasonal variation in average temperatures across Taiwan forms a symmetrical distribution. The lowest temperatures occur in late January to early February, with an average of around 18°C, followed by a gradual rise, reaching a peak in July with an average temperature of approximately 33°C. There is a notable difference in sunshine hours between northern and southern Taiwan. For instance, in 2019, Taipei in the north had an average sunshine duration percentage of 29.2%, while Kaohsiung in the south had 52.4%. Humidity levels, however, were similar, with Taipei at 76% and Kaohsiung at 75%.[21] This geographical and climatic information is intended to provide relevant context for understanding the potential influence of seasonal changes on PUD incidence. Seasonal variations in PUD incidence among patients using different types of NSAIDs and those suffering from different PUD types were observed. Considering the association between area and temperature, PUD incidence in different areas of Taiwan was measured throughout the study.

Statistical analysis

Descriptive statistics were used to summarise baseline characteristics, including age, sex, PUD type, area, NSAID use and season, with frequency distributions. Temporal trends were assessed according to the annual prevalence and incidence rates, and seasonal variations were analysed by comparing the number of cases across the four seasons. Trends in annual prevalence and incidence rates were estimated using a linear trend test. To identify significant patterns, we used Pearson's χ^2 test and estimated the differences among PUD incidence in the

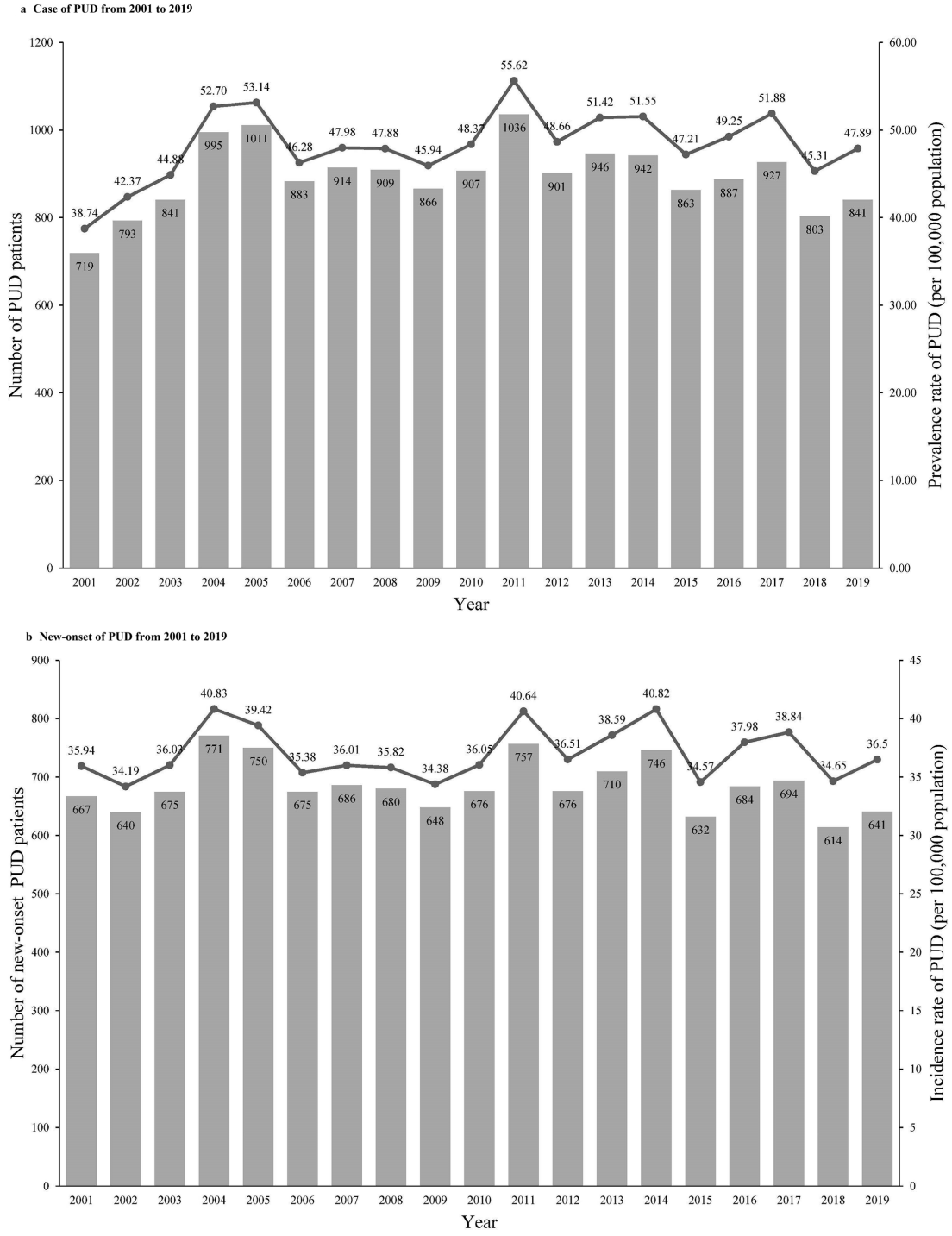

Figure 1 The annual PUD prevalence and incidence from 2001 to 2019. PUD, peptic ulcer disease.

four seasons throughout the study. All statistical analyses were performed by using SAS statistical software V.9.4 (SAS Institute), and statistical significance was set as a p value of less than 0.05.

RESULTS

Figure 1 shows the annual trends of PUD prevalence and incidence from 2001 to 2019. PUD prevalence during this period ranged from 719 cases in 2001 to 1036 cases (the peak of PUD prevalence) in 2011, with annual fluctuations. Similarly, the trend of new-onset PUD showed annual variations, ranging from a peak of 771 cases in 2004 to a minimum of 614 cases in 2018. However, these two trends were not statistically significant.

Table 1 presents the baseline information for the overall and seasonal variations. The number of peptic ulcers was higher in males than in females. Additionally, the incidence was higher in the elderly (age ≥65) compared with younger individuals. Among the different types of peptic ulcers, the proportion was highest for

Table 1 The overall and subgroup of selected variables among PUD patients in different seasons

	Overall	Spring	Summer	Fall	Winter	P value
Overall	13022	3317 (25.47)	3143 (24.14)	3072 (23.59)	3490 (26.8)	
Gender						
Male	8392 (64.44)	2146 (25.57)	2035 (24.25)	1959 (23.34)	2252 (26.84)	0.8391
Female	4630 (35.56)	1171 (25.29)	1108 (23.93)	1113 (24.04)	1238 (26.74)	
Age						
<65	5273 (40.49)	1342 (25.45)	1299 (24.63)	1250 (23.71)	1382 (26.21)	0.5473
≥65	7749 (59.51)	1975 (25.49)	1844 (23.8)	1822 (23.51)	2108 (27.2)	
PUD type						
GU	7306 (56.11)	1822 (24.94)	1814 (24.83)	1750 (23.95)	1920 (26.28)	0.0816
DU	4720 (36.25)	1256 (26.61)	1090 (23.09)	1078 (22.84)	1296 (27.46)	
Others	996 (7.65)	239(24)	239(24)	244 (24.5)	274 (27.51)	
Area						
North	4953 (38.04)	1269 (25.62)	1175 (23.72)	1159 (23.4)	1350 (27.26)	0.6972
Central	3244 (24.91)	825 (25.43)	791 (24.38)	792 (24.41)	836 (25.77)	
South	4292 (32.96)	1086 (25.3)	1056 (24.6)	1010 (23.53)	1140 (26.56)	
East	472 (3.62)	121 (25.64)	107 (22.67)	99 (20.97)	145 (30.72)	
Others	61 (0.47)	16 (26.23)	14 (22.95)	12 (19.67)	19 (31.15)	
NSAIDs use						
Non-NSAIDs users	4065 (31.22)	1049 (25.81)	941 (23.15)	909 (22.36)	1166 (28.68)	0.0194
NSAIDs users (non-long term)	5111 (39.25)	1304 (25.51)	1239 (24.24)	1242 (24.3)	1326 (25.94)	
NSAIDs users (long term)	3846 (29.53)	964 (25.07)	963 (25.04)	921 (23.95)	998 (25.95)	

DU, duodenal ulcer; GU, gastric ulcer; NSAIDs, non-steroidal anti-inflammatory drugs; PUD, peptic ulcer disease.

GUs, followed by DUs and unspecified peptic ulcers. More than half of the individuals had used NSAIDs within 6 months before developing peptic ulcers. Additionally, the currently observed seasonal distribution of PUD was highest in winter, followed by spring, summer and autumn (figure 2).

Table 2 presents the number of new patients with peptic ulcers across all seasons in the NSAID-use group and across different subgroups, including sex, age, PUD type and area. Among non-NSAID users, the seasonal trend for PUD incidence was highest in winter, followed by spring. However, NSAID use exhibited different seasonal variations. Long-term NSAID users presented higher rates of PUD incidence during winter among males (25.96%), females (25.93%), the elderly (age ≥65) (26.11%), those suffering from DUs (27.78%) and those residing in north (26.75%) and central (25.67%) Taiwan.

Table 3 presents the categorised data by PUD type and shows the number of new PUD cases across different subgroups (sex and age) by season. In these subgroups, patients in the GU and DU subgroups presented higher rates of PUD in winter, particularly among patients older than 65 years (27.98%).

DISCUSSION

Studies on the seasonal variability in PUD incidence have primarily been conducted in Western and Northern Asian countries with distinct seasons. Many studies have suggested a peak incidence during winter; however, their results are inconclusive. Ours is the first large, real-world database study on the seasonal variability of PUD incidence conducted in Taiwan, which spans both tropical and subtropical zones. This study provides clinically important reference data to assist in planning the appropriate allocation of medical resources to address their availability during peak seasons. The findings indicated that males and elderly individuals (age ≥65) exhibited a higher incidence of peptic ulcers. The frequency of peptic ulcer occurrences and the number of new cases peaked during winter. These results were consistent across all age and sex groups, with no significant effect of differences in latitude, NSAID usage or PUD type. However, subtle differences were observed when analysed further, which are discussed in detail below.

Demographics

According to a previous study, the global prevalence of PUD decreased from 143.4 per 100000 population in 1990 to 99.4 in 2019. Countries with low to middle Socio-Demographic Index (SDI) experienced a more significant decline, while the trend in countries with high SDI remained relatively stable.[22] In the current study, the prevalence of PUD in Taiwan was 38.74 per 100000 population in 2001 and 47.89 in 2019, which is similar to the trends observed in other high SDI countries. Consistent with previous studies, the present results indicated a

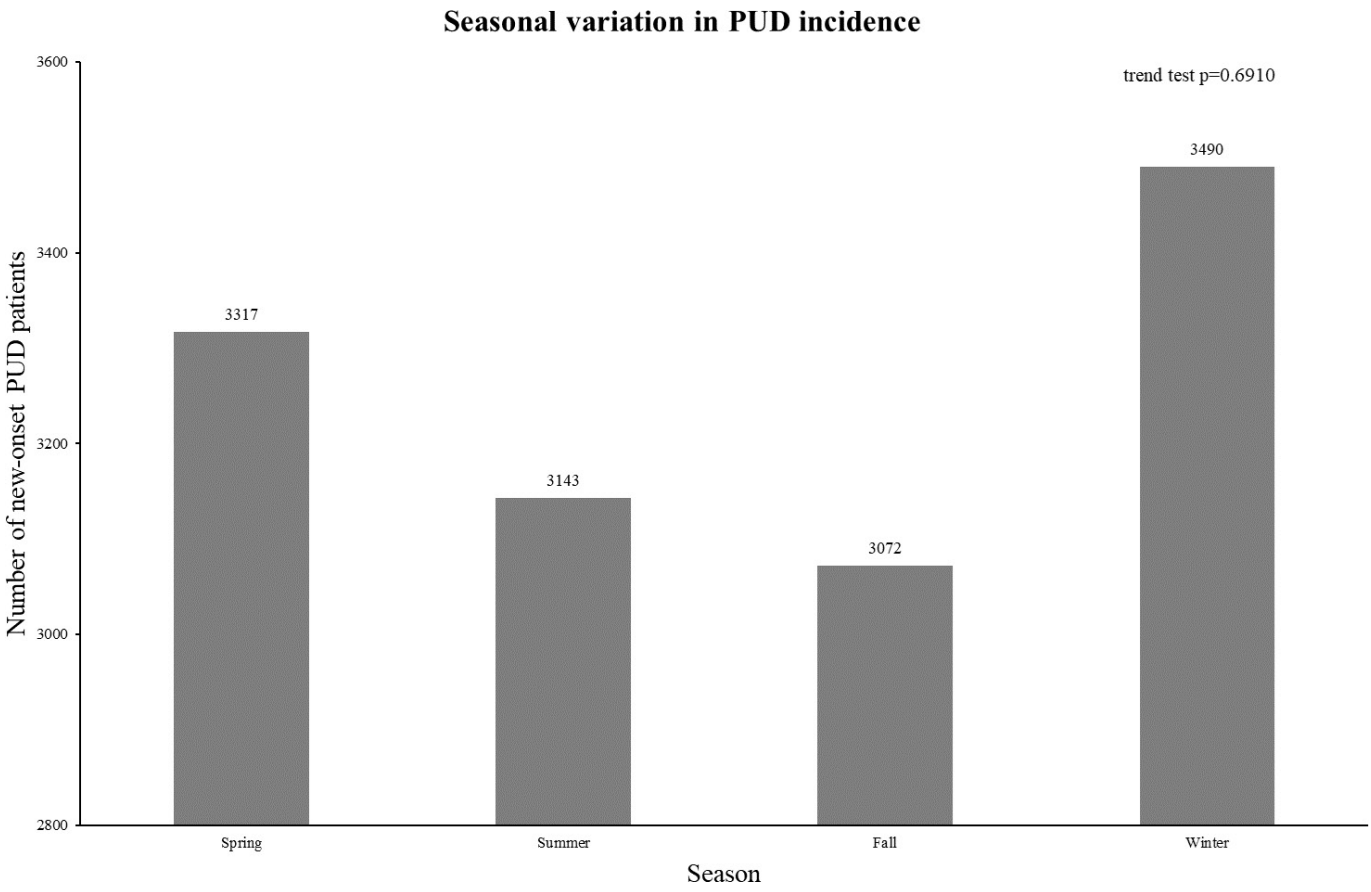

Figure 2 The seasonal variation in PUD incidence. PUD, peptic ulcer disease.

higher incidence of ulcers in males than in females.[23 24] This was attributed to the significantly higher smoking rates among males in Taiwan,[25] the higher global prevalence of *Helicobacter pylori* infection among males,[25 26] and sex-related differences in gastroduodenal mucosal defence mechanisms.[27 28] Additionally, PUD incidence was higher in older adults than in younger ones. Both the incidence of PUD and the frequency of hospitalisations due to PUD-related complications are increasing in elderly populations.[23 29] This trend may be associated with several factors such as a higher rate of *H. pylori* infection among older individuals,[30] an increased use of aspirin and other NSAIDs by older individuals owing to specific medical conditions,[31] and a weakening of gastric and duodenal mucosal defence mechanisms in this age group. Gastric and duodenal mucosal defence mechanisms include reduced bicarbonate secretion,[32] lower prostaglandin concentrations in the stomach and duodenum and altered prostaglandin responses of the mucosa to injuries.[33]

Our results showed that the frequency of hospitalisation due to peptic ulcers in Taiwan did not significantly change from 2001 to 2019. Recent studies using the Global Burden of Disease database have shown that the incidence and mortality rates of PUD have remained stable over the past decade. A noticeable decrease observed once attributed to the use of proton pump inhibitors as well as to the treatment for *H. pylori* infection was no longer apparent. This stability may be related to a shift in primary risk factors for peptic ulcers from *H. pylori* infection to NSAID use, along with the ageing of the global population.[10 22]

Seasonal variations in PUD incidence and related determinants

Taiwan has an insular climate, with the Tropic of Cancer passing through Chiayi County, the northernmost part of southern Taiwan, placing most of southern Taiwan in the tropical zone. Furthermore, temperatures remain high throughout the year, with moderate seasonal temperature variance of about 8°C. In contrast, central and northern Taiwan has a subtropical climate, characterised by more distinct seasonal changes, with temperature differences between winter and summer around 12°C.

The present findings indicated that DU, GU and other types of PUD exhibited the highest prevalence and incidence in winter, followed by spring, with more pronounced seasonal variation observed for DU. Similarly, Tsai *et al* conducted a cross-sectional study in Taiwan and found a higher incidence of symptomatic DU during colder months, from November to March.[34] Xirasagar *et al* adjusted for meteorological factors and found an inverse correlation between the rates of hospitalisation for DU and temperature in Taiwan.[35] However, the present study revealed that seasonal variations in DU incidence between northern and southern Taiwan were

Table 2 The new PUD cases in different seasons among various subgroups (gender and age Groups) based on the usage of NSAIDs

	Non-NSAIDs users				NSAIDs users (non-long term)				NSAIDs users (long term)			
	Spring	Summer	Fall	Winter	Spring	Summer	Fall	Winter	Spring	Summer	Fall	Winter
Gender												
Male	719 (24.9)	683 (23.65)	650 (22.51)	836 (28.95)	885 (26.23)	807 (23.92)	819 (24.27)	863 (25.58)	542 (25.45)	545 (25.59)	490(23)	553 (25.96)
Female	330 (28.04)	258 (21.92)	259 (22.01)	330 (28.04)	419 (24.12)	432 (24.87)	423 (24.35)	463 (26.66)	422 (24.59)	418 (24.36)	431 (25.12)	445 (25.93)
Age												
<65	501 (26.01)	459 (23.83)	444 (23.05)	522 (27.1)	605 (25.99)	573 (24.61)	550 (23.63)	600 (25.77)	236 (23.16)	267 (26.2)	256 (25.12)	260 (25.52)
≥65	548 (25.62)	482 (22.53)	465 (21.74)	644 (30.11)	699 (25.12)	666 (23.93)	692 (24.87)	726 (26.09)	728 (25.75)	696 (24.62)	665 (23.52)	738 (26.11)
PUD type												
GU	532 (24.72)	508 (23.61)	485 (22.54)	627 (29.14)	726 (25.41)	702 (24.57)	711 (24.89)	718 (25.13)	564 (24.55)	604 (26.3)	554 (24.12)	575 (25.03)
DU	436 (27.82)	343 (21.89)	352 (22.46)	436 (27.82)	485 (25.87)	455 (24.27)	430 (22.93)	505 (26.93)	335 (26.21)	292 (22.85)	296 (23.16)	355 (27.78)
Others	81 (23.41)	90 (26.01)	72 (20.81)	103 (29.77)	93 (24.54)	82 (21.64)	101 (26.65)	103 (27.18)	65 (23.99)	67 (24.72)	71 (26.2)	68 (25.09)
Area												
North	418 (25.66)	373 (22.9)	361 (22.16)	477 (29.28)	470 (25.54)	437 (23.75)	457 (24.84)	476 (25.87)	381 (25.67)	365 (24.6)	341 (22.98)	397 (26.75)
Central	255 (25.97)	227 (23.12)	224 (22.81)	276 (28.11)	332 (25.7)	319 (24.69)	330 (25.54)	311 (24.07)	238 (24.54)	245 (25.26)	238 (24.54)	249 (25.67)
South	334 (25.93)	302 (23.45)	293 (22.75)	359 (27.87)	462 (25.62)	445 (24.68)	418 (23.18)	478 (26.51)	290 (24.15)	309 (25.73)	299 (24.9)	303 (25.23)
East	36 (24.66)	37 (25.34)	28 (19.18)	45 (30.82)	36 (23.53)	28 (18.3)	31 (20.26)	58 (37.91)	49 (28.32)	42 (24.28)	40 (23.12)	42 (24.28)
Others	6 (30)	2 (10)	3 (15)	9 (45)	4 (17.39)	10 (43.48)	6 (26.09)	3 (13.04)	6 (33.33)	2 (11.11)	3 (16.67)	7 (38.89)

DU, duodenal ulcer; GU, gastric ulcer; NSAIDs, non-steroidal anti-inflammatory drugs; PUD, peptic ulcer disease.

Table 3 Incidence and number of new occurrences in different seasons among various subgroups (gender and age groups) by different PUD types

	GU				DU				Others			
	Spring	Summer	Fall	Winter	Spring	Summer	Fall	Winter	Spring	Summer	Fall	Winter
Gender												
Male	1105 (24.8)	1108 (24.87)	1072 (24.06)	1170 (26.26)	877 (27.03)	753 (23.2)	729 (22.47)	886 (27.3)	164 (23.7)	174 (25.14)	158 (22.83)	196 (28.32)
Female	717 (25.15)	706 (24.76)	678 (23.78)	750 (26.31)	379 (25.69)	337 (22.85)	349 (23.66)	410 (27.8)	75 (24.67)	65 (21.38)	86 (28.29)	78 (25.66)
Age												
<65	691 (24.47)	709 (25.11)	700 (24.79)	724 (25.64)	546 (27.06)	491 (24.33)	441 (21.85)	540 (26.76)	105 (24.36)	99 (22.97)	109 (25.29)	118 (27.38)
≥65	1131 (25.23)	1105 (24.65)	1050 (23.43)	1196 (26.68)	710 (26.28)	599 (22.17)	637 (23.58)	756 (27.98)	134 (23.72)	140 (24.78)	135 (23.89)	156 (27.61)
Area												
North	684 (24.64)	690 (24.86)	639 (23.02)	763 (27.49)	483 (26.98)	388 (21.68)	420 (23.46)	499 (27.88)	102 (26.36)	97 (25.06)	100 (25.84)	88 (22.74)
Central	449 (25.31)	441 (24.86)	442 (24.92)	442 (24.92)	322 (26.29)	283 (23.1)	294(24)	326 (26.61)	54 (22.04)	67 (27.35)	56 (22.86)	68 (27.76)
South	609 (24.93)	603 (24.68)	606 (24.81)	625 (25.58)	405 (26.15)	386 (24.92)	329 (21.24)	429 (27.7)	72 (24.08)	66 (22.07)	75 (25.08)	86 (28.76)
East	70 (25.45)	72 (26.18)	53 (19.27)	80 (29.09)	41 (28.87)	28 (19.72)	33 (23.24)	40 (28.17)	10 (18.18)	7 (12.73)	13 (23.64)	25 (45.45)
Others	10 (26.32)	8 (21.05)	10 (26.32)	10 (26.32)	5 (35.71)	5 (35.71)	2 (14.29)	2 (14.29)	1 (10.00)	2 (20.00)	0 (0.00)	7 (70.00)

DU, duodenal ulcer; GU, gastric ulce; PUD, peptic ulcer disease.

similar, suggesting that temperature may not be the sole affecting factor. Additionally, smoking may contribute to the seasonal prevalence of DUs during winter. Historically, smoking has been considered a primary causative factor for PUD.[36 37] Smokers in Taiwan tend to smoke more during the winter and rainy seasons,[35] with smoking rates significantly higher among men than women, mirroring the significantly higher incidence of DU among males observed in the present study. Seasonal variation in light exposure, which induces annual rhythms of melatonin, might also be a critical factor triggering DU, in addition to stress induced by harsh winter conditions.[35 38]

In contrast, the seasonal variations in GU incidence were more pronounced in northern and southern Taiwan. This discrepancy may be associated with the more distinct four-season climate and colder winters in the north. Cold weather and rapid temperature fluctuations can trigger an acute stress reaction, leading to the increased secretion of epinephrine, norepinephrine and endothelin, causing vasoconstriction in the gastrointestinal mucosa, reduced blood flow and damage to protective barriers due to insufficient oxygen. These factors increase gastric acid levels and accelerate PUD development.[39 40]

Seasonal differences in PUD incidence were most consistent among non-NSAID users, possibly because NSAID usage itself is a major risk factor for PUD, thereby obscuring seasonal variations. A study from Spain showed that DU bleeding was most frequent in autumn and winter; however, this trend was not observed in NSAID users.[41] Similarly, a study from Greece found that the seasonal distribution of acute upper gastrointestinal bleeding was only evident in patients who did not use NSAIDs.[42] The present results revealed that the peak of PUD prevalence in short-term NSAID users occurred during winter and spring. This may be related to the seasonal peaks of respiratory illnesses[43 44] and other diseases, such as osteoarthritis and rheumatic arthritis,[45 46] which are more prevalent in colder seasons. The increased likelihood of short-term NSAID use during these periods could affect the seasonal variation in PUD incidence. Although the overall incidence of PUD remained the highest in winter, the differences across seasons were minimal, and the results varied considerably among the subgroups. This inconsistency may be attributed to the strong effect of prolonged NSAID use on PUD incidence, which could overshadow any seasonal variation.

Strengths and limitations

The primary strength of this study is the use of a nationwide population-based database that provides representative data to investigate seasonal variations in PUD incidence. Another strength is its location in Taiwan, which spans tropical and subtropical regions. The present subgroup analyses based on latitude helped us gain a deeper understanding of the seasonal variability in PUD incidence across regions with different climates.

Nevertheless, the study has several limitations. First, the LHID2005 lacks comprehensive clinical information,

making it impossible to assess and adjust for risk factors for PUD such as smoking, alcohol consumption, caffeine intake, *H. pylori* infection, gastric bypass surgery and stress.[47] Second, we did not adjust for individual meteorological factors such as atmospheric pressure, humidity, sunshine duration and rainfall, which may affect the seasonal variability in PUD incidence.[35] Third, some acute conditions related to seasonal changes, such as arthritis and acute respiratory illnesses, can lead to the short-term use of NSAIDs, thereby potentially affecting PUD incidence and seasonal variations in its incidence, and ultimately affecting the present results. Additionally, the exact season and dates of NSAID use as well as medication adherence among these patients could not be obtained from the LHID2005. Furthermore, the possibility of misclassification bias exists within this administrative claims data, which may affect the accuracy of the diagnosis codes used to identify diseases in this study. However, due to the large sample size and standardised coding practices in Taiwan's healthcare insurance system, the potential impact of this bias could be limited.

Across the tropical and subtropical regions of Taiwan, a significant seasonal variation in PUD incidence is observed, with the highest rates occurring in winter, regardless of age or sex. However, NSAID usage tends to obscure this trend. The seasonal variation in DU incidence showed no significant differences between north and south Taiwan, suggesting that factors other than temperature may affect DU incidence compared with their effect on GU incidence.

CONCLUSION

The current results provide a reference for medical institutions to plan health education programmes for preventing PUD. For example, encouraging the reduction of NSAID use and smoking during the winter months while adjusting the allocation of medical resources according to seasonal variations. Nevertheless, future large-scale prospective studies with comprehensive and precise clinical information on patients with PUD and adjustments for meteorological factors are warranted.

Author affiliations
[1]Emergency Department, Tainan Municipal An Nan Hospital, Tainan City, Taiwan
[2]Department of Family Medicine, Tainan Municipal An Nan Hospital, Tainan City, Taiwan
[3]Department of Hepato-Gastroenterology, DA-AN Women and Children Hospital, Tainan, Taiwan
[4]Medical Research, Chi Mei Medical Center, Tainan, Taiwan
[5]Department of Information Management, Southern Taiwan University of Science and Technology, Tainan, Taiwan
[6]Department of Medical Research, Chi Mei Medical Center, Tainan, Taiwan
[7]Department of Anesthesiology, Chi Mei Medical Center, Tainan, Taiwan
[8]Department of Healthcare Administration and Medical Informatics; Center for Medical Informatics and Statistics, Office of R&D, Kaohsiung Medical University, Kaohsiung, Taiwan
[9]Department of Medical Research, Kaohsiung Medical University Hospital, Kaohsiung, Taiwan
[10]Department of Emergency Medicine, Chi Mei Medical Center, Tainan, Taiwan
[11]Department of Nursing, National Tainan Junior College of Nursing, Tainan, Taiwan

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ORCID iD
Chung-Han Ho http://orcid.org/0000-0001-5925-8477

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STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	3-4
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	6-7
Objectives	3	State specific objectives, including any prespecified hypotheses	7
Methods			
Study design	4	Present key elements of study design early in the paper	8
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	7-9
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	8-9
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	9-10
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*7-9*
Bias	9	Describe any efforts to address potential sources of bias	11
Study size	10	Explain how the study size was arrived at	9
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	10
		(*b*) Describe any methods used to examine subgroups and interactions	
		(*c*) Explain how missing data were addressed	9-10
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	9
		(*e*) Describe any sensitivity analyses	

Continued on next page

Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	12
		(b) Give reasons for non-participation at each stage	12
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	12
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	*12-16*
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	13-16
Discussion			
Key results	18	Summarise key results with reference to study objectives	18
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	23-24
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	18-24
Generalisability	21	Discuss the generalisability (external validity) of the study results	18-24
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	26

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.