

Letter to the Editor

**Quantifying the Temperature Effects on the Morbidity of Digestive Diseases In an Inland Plateau-Valley City***

Pan Ma^{1,2}, Yang Yang¹, Ning Zhou^{3,#}, Xinzi Wang⁴, Yulu Wang⁵, Wenjuan Feng⁵,
Zhaoqin Bai^{3,5}, and Shigong Wang¹

Extreme air temperature and increased weather oscillations caused by climate change have been threatening global health. Meteorological conditions are external inducers that may trigger the onset of gastrointestinal diseases, in addition to bacterial infection or behavioral factors including smoking, alcohol consumption, and hot food consumption^[1,2]. The global age-standardised incidence and prevalence of digestive diseases during 1990–2019 showed little to no decrease, with 95,582 and 35,106 cases per 100,000 individuals in 2019, respectively^[2]. In China, digestive diseases ranked seven in the disease spectrum of death in 2021, which has maintained an overall rising trend since 2015 (China Health Statistics Yearbook 2022, www.zgtjnj.org). The susceptibilities of gastrointestinal diseases to climate alterations and weather changes have gained wide recognition. Higher morbidities of peptic ulcer and gastrointestinal bleeding in winter or during cold weather have been reported in Europe and China^[3,4]. However, quantitative evidence on the effects of universal temperature indicators, obtained from routine monitoring, is still very limited. The daily minimum temperature (T_{\min}) reveals the effects of the coldest climate condition in a day instead of the 24-hour means. To large extent, it represents the coldest thermal stress. Further, weather instability or temperature fluctuation could be another trigger for gastrointestinal diseases. It has been shown that the diurnal temperature range (DTR) added an additional risk of multiple chronic diseases^[5]. Large temperature variations may also

lead to a decrease in digestive function, the abnormal secretion of digestive enzymes, as well as decreased human immunity. However, the quantitative evidence on relations between DTR and digestive morbidity was insufficient, particularly in northwest China. As the capital of Gansu Province, Lanzhou is on the Loess Plateau and has a semi-arid continental climate, with distinct seasons and prominent weather changes. Therefore, the objectives of the current study were: i) explore the exposure-response associations between digestive risk and typical temperature indicators (T_{\min} and DTR) in Lanzhou, Gansu; ii) compare temperature effects in the warm (April to September) and cold (October to March) seasons; and iii) investigate the synergistic effects of T_{\min} and DTR.

Daily data on hospitalizations for digestive disease from March 1, 2016 to May 1, 2021, were collected from the Lanzhou First People's Hospital, which covered all records in the Department of Gastroenterology and the Department of Infectious Diseases. The admission date, age, sex, and primary diagnosis were obtained, and a continuous time-series of daily admissions was established. Patients with incomplete data and those who lived outside Lanzhou were excluded. For quality control, logical checks were implemented in the medical data to identify data entry errors and missing information. A total of 10,944 cases classified by the tenth revision of the International Classification of Diseases (K00–K93) were analyzed. A confidentiality agreement has been signed and submitted to the hospital. The

doi: [10.3967/bes2024.140](https://doi.org/10.3967/bes2024.140)

*This research was supported by the National Natural Science Foundation of China [42205185]; the Natural Science Foundation of Sichuan Province [2024NSFSC0773]; the Key Research and Development Plan of Gansu Province [21YF5FA169]; and China Meteorological Administration "Research on value realization of climate ecological products" Youth Innovation Team Project [CMA2024QN15].

1. Plateau Atmosphere and Environment Key Laboratory of Sichuan Province, College of Atmospheric Science, Chengdu University of Information Technology, Chengdu 610225, Sichuan, China; 2. Chengdu Plain Urban Meteorology and Environment Observation and Research Station of Sichuan Province, Chengdu 610225, Sichuan, China; 3. The Infectious Disease Department, The First People's Hospital of Lanzhou, Lanzhou 730050, Gansu, China; 4. Meteorological Bureau of Jinnan District, Tianjin 300350, China; 5. Gansu University of Chinese Medicine, Lanzhou 730000, Gansu, China

surface meteorological observations of Lanzhou were obtained from the National Meteorological Science Data Center of China (<http://data.cma.cn/>). In temperate cities, such as Lanzhou, the six months (April - September) dominated by warm temperature were defined as the warm season, and the remaining half-year was defined as the cold season (October - March).

A generalized additive model (GAM) with a quasi-Poisson family of distributions and a distributed-lag nonlinear model (DLNM) were used to estimate temperature effects on digestive risk^[6]. First, the model was adjusted for trends by including a counter variable for each day of the time series and a smoothing spline was fitted. As long-term trends were usually controlled with seven degrees of freedom (*df*) per year, three *df* for time was selected in each half-year. *Holidays* and *day of the week* (*DOW*) were marked by dummy categorical variables. Second, the cross-basis functions of T_{\min} and DTR were built by the DLNMs, a natural cubic spline was employed for daily T_{\min} and DTR (*df* = 4), and a polynomial spline (*df* = 4) was used to capture their lag effects. The maximum lags of T_{\min} and DTR were set to 14 d and 10 d in the warm season, respectively, to capture all the effects and achieve maximum model stability. Meanwhile, the lags of T_{\min} and DTR in the cold season were adjusted to 20 d and 14 d, respectively. Given the potential impacts on human physiology, confounders including relative humidity and wind speed were controlled in the GAMs through the fitting of spline functions (*df* = 4). To avoid collinearity among climate variables, their correlation coefficients were checked before being adopted in the models (Supplementary Table S1, available in www.besjournal.com). Finally, non-parametric binary models were built to explore the co-effects of T_{\min} and DTR. T_{\min} was smoothed on varied lags (0–3 d, 0–6 d, and 0–9 d) to capture its lag effects. Relative risk (*RR*) was defined as the risk of onset caused by a unit change in T_{\min} (or DTR), relative to its reference value, along with 95% confidence intervals. R 3.6.1 software (<http://www.r-project.org>) was used for model fitting. The “mgcv” and “dlnm” packages in R were used.

The number of patients admitted daily ranged from 0 to 25, with a mean of 5.8. There were more males than females (1.23 vs. 1) (Supplementary Table S2, available in www.besjournal.com). The annual mean temperature in Lanzhou was 11.4 °C, with an annual variety up to 42 °C (-12.4 °C–30.8 °C). In this plateau-valley city, the mean DTR was large (11.3 °C), mean humidity was moderately low

(48.3%), and mean wind speed was low (1.1 m/s). There were more morbidities from November to January and from April to August, while there were lower admission rates in February and September (Supplementary Figure S1, available in www.besjournal.com). The lowest hospitalisation rate in February, was probably due to the Chinese Spring Festival and the return of migrant workers^[7]. The complex pathogenesis of digestive disease and non-meteorological confounders may also contribute to the insignificant seasonal variations^[3].

Figure 1 and Supplementary Table S3 (available in www.besjournal.com) show the comparison of temperature effects under opposite background climates, by typical percentiles of T_{\min} . T_{\min} ranged from -4 °C–26 °C and -16 °C–16 °C in the warm and cold seasons, respectively. Supplementary Figure S2 (available in www.besjournal.com) displays the detailed three-dimensional T_{\min} -morbidity associations. The cumulative *RR* was bimodal in the warm season, with the highest digestive risks occurring at 3 °C–10 °C and 17 °C–21 °C, respectively (Figure 1A). A strong and immediate effect was revealed for cold T_{\min} (e.g., 5.1 °C, P_5), while a delayed effect of high T_{\min} (21.7 °C, P_{95}) was found (Figure 1C, Supplementary Table S3). In the cold season, an unexpected higher risk at warm T_{\min} was found (Figure 1B), which was inconsistent with previous studies^[3,4]. Besides, prominently high *RR*s were observed for moderate (3 °C, P_{75}) and relatively high (8.7 °C, P_{95}) temperatures (Figure 1D, Supplementary Table S3). In northwest China, the sudden enhancement and northward movement of warm air masses, is common in spring and autumn. Abnormal warming processes could lead to increased superficial blood circulation, weak gastrointestinal peristalsis, and reduced secretion of gastric juice^[8,9]. Increased water demand may also dilute stomach acid and lead to indigestion. We previously revealed high-temperature effects on the number of emergency room visits for digestive disease in Beijing^[9]. The low humidity of inland Lanzhou may effectively reduce the heat stress of hotter weather.

Before or after the period when central heating is used, frequent weather changes accompanied by significant cooling, might explain the increased risk at moderately low T_{\min} . Physiologically, cold stimulation could excite the sympathetic nervous system, increase the secretion of catecholamines, cause constriction of peripheral blood vessels in the abdominal organs and the skin, and reduce the secretory functions of the digestive glands^[3,4,10].

Nonetheless, the effects of extremely low T_{\min} were significantly reduced by the use of central heating (from October to March), the climate adaptability of the human body, reduced outdoor exposure, and the

limited stability of the model under severe conditions^[9].

Figure 2 shows the effects of small, large, and extreme DTRs (the 25th, 90th, and 99th percentiles) on

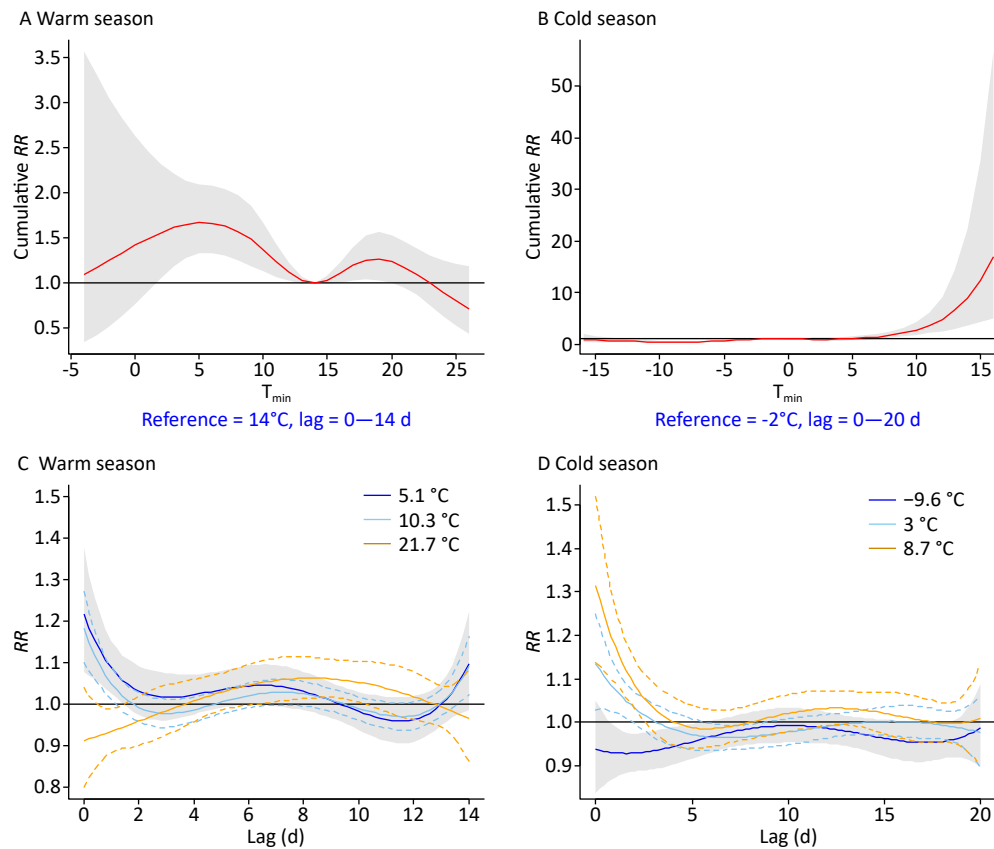


Figure 1. The overall and specific effects of the daily minimum temperature (T_{\min}) on digestive morbidity under opposite climate backgrounds. P_5 , P_{25} , and P_{95} in the warm season, P_5 , P_{75} , and P_{95} in the cold season were selected, respectively. RR, relative risk.

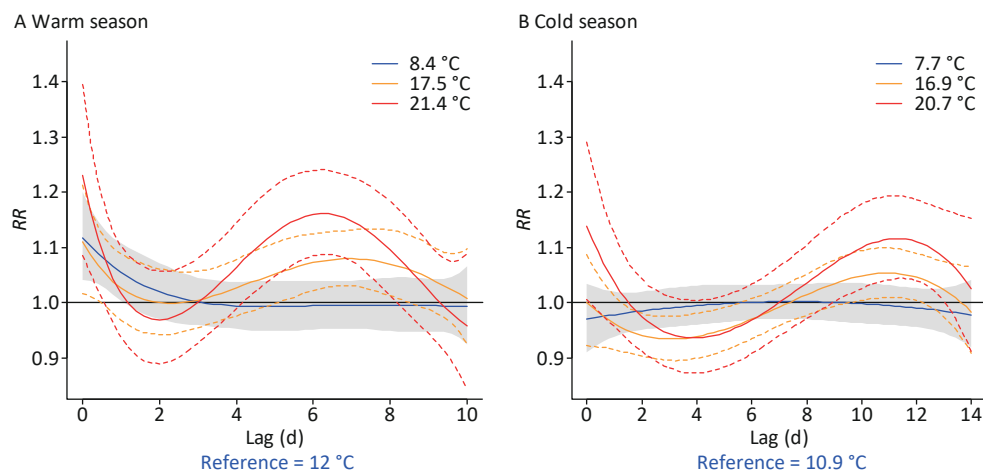


Figure 2. The lag effect of typical percentiles of diurnal temperature range (DTR) (P_{25} , P_{90} , and P_{99}) on digestive morbidity under opposite climate backgrounds. RR, relative risk.

digestive morbidity, for both half-years. [Supplementary Table S4](#) (available in www.besjournal.com) lists corresponding *RRs* for specific DTRs. Acute gastrointestinal risks were identified at both minor and major DTRs in the warm season, while weaker and more delayed DTR effects were found in the cold season ([Figure 2](#)). Overall, higher DTRs with more severe health impacts were identified in the warm season than in the cold season ([Supplementary Table S4](#)).

[Figure 3](#) shows the comprehensive effects of two temperature metrics. In the warm season, the coexistence of moderately low T_{\min} and large DTRs immediately increased digestive morbidity, whereas very low T_{\min} accompanying by large DTRs induced increased risk at diverse lags ([Figure 3](#), [Supplementary Figure S3](#)). This further reflects the persistent effects of low temperature and demonstrates a more dominant effect of T_{\min} than of DTR. In the cold season, increased risk on lag 0d was observed at low T_{\min} with high DTRs, while at varied lags, warm T_{\min} had a strong influence ([Figure 3](#),

[Supplementary Figure S3](#)). Abnormal warm weather with significant temperature fluctuations generally occurs in transitional periods from autumn to winter. A sharp peak in the mortality of variceal bleeding was also found in early winter in French public hospitals^[4]. In the northwest of China, the DTR is generally larger in the transition of seasons than in summer or midwinter, due to the north–south shift of the subsolar point and intensified activity of air masses. Moreover, due to thinner clouds and shorter atmospheric columns, the influence of solar radiation on surface temperature is stronger on plateaus than on the eastern plain areas. Therefore, a dramatic change in diurnal temperature could amplify the adverse effects of air temperature, thus more targeted preventive measures should be taken to reduce the burden of digestive diseases.

This study offers fresh perspectives on preventing digestive diseases and will enlighten future studies on the impact of climate on health in inland plateau areas. The study has some limitations. First, the collected medical data were

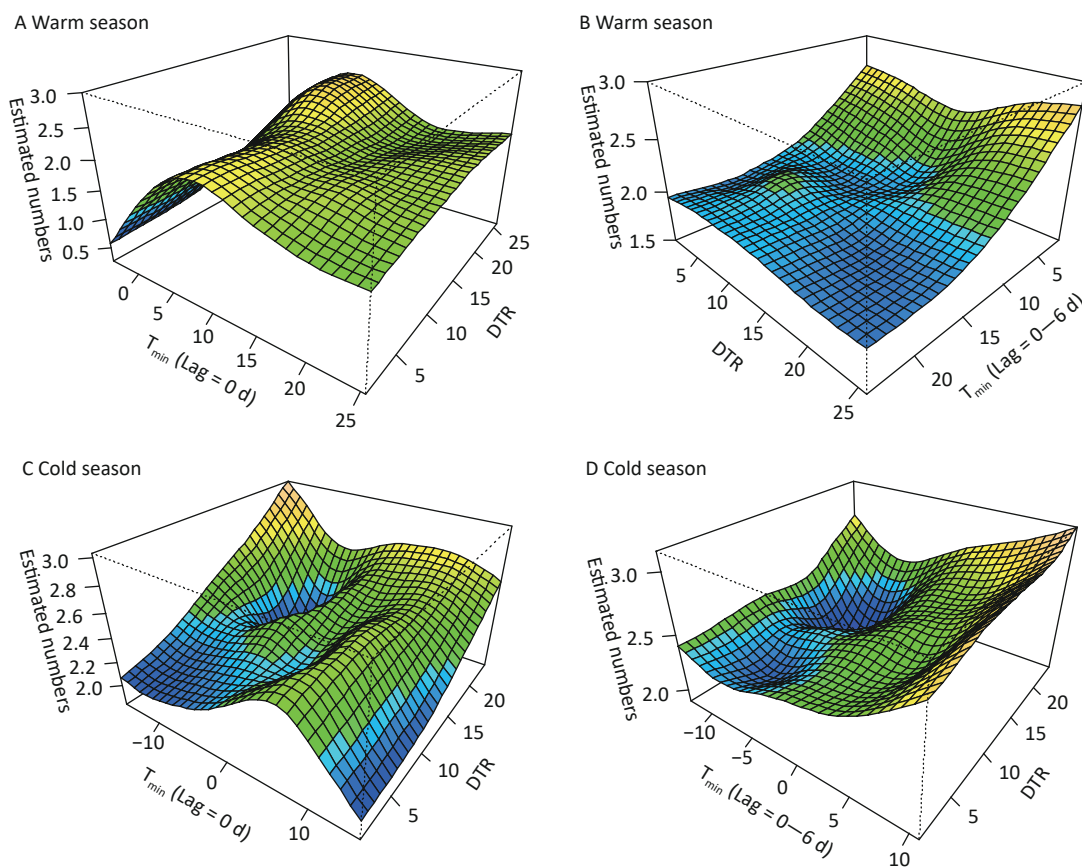


Figure 3. The synergistic effects of the daily minimum temperature (T_{\min}) and diurnal temperature range (DTR) on digestive risk. (A) and (C) indicate the immediate effects, (B) and (D) refer to the lag (0–6 d) effects of T_{\min} .

confined to one hospital and the population coverage was relatively limited, therefore, the impacts of temperature on morbidity might be biased. Larger sample sizes and further investigations are required to ascertain how generalizable these results are to other regions. Second, the current study specifically explored the influence of daily T_{min} and DTR on digestive admissions, but the effect of temperature fluctuations between days was not analysed, which is worthy for further study. Future studies could also examine the effects of temperature on the infection and virulence of *Helicobacter pylori*, levels of inflammatory factors, hormone secretion, etc. Finally, there might be some deviations between the temperature exposure of individuals and the meteorological data observed at fixed locations.

Conflict of interests The authors declare no competing interests in connection with the work submitted.

Author Contribution Pan Ma: Conceptualization, methodology, formal analysis, writing- original draft, visualization, and funding acquisition. Yang Yang: Methodology, data curation, and writing- review & editing. Ning Zhou: Datacuration, writing- review & editing, and funding acquisition. Xinzi Wang: Investigation, data curation, and visualization. Yulu Wang and Wenjuan Feng: Investigation, methodology, and data curation. Zhaoqin Bai: Investigation, resources, and supervision. Shigong Wang: Conceptualization, resources, and project administration.

[#]Correspondence should be addressed to Ning Zhou, Tel: 86-15117162616, E-mail: zhouning198278@163.com
Biographical note of the first author: Pan Ma, female,

born in 1990, associate professor, majoring in weather and climate effects on human health.

Received: November 23, 2023;

Accepted: July 11, 2024

REFERENCES

1. Kamangar F, Nasrollahzadeh D, Safiri S, et al. The global, regional, and national burden of oesophageal cancer and its attributable risk factors in 195 countries and territories, 1990-2017: a systematic analysis for the global burden of disease study 2017. *Lancet Gastroenterol Hepatol*, 2020; 5, 582-97.
2. Wang YC, Huang YT, Chase RC, et al. Global burden of digestive diseases: a systematic analysis of the global burden of diseases study, 1990 to 2019. *Gastroenterology*, 2023; 165, 773-83. e15.
3. Liu DY, Gao AN, Tang GD, et al. Relationship between onset of peptic ulcer and meteorological factors. *World J Gastroenterol*, 2006; 12, 1463-7.
4. Boulay F, Berthier F, Dahan C, et al. Seasonal variations in variceal bleeding mortality and hospitalization in France. *Am J Gastroenterol*, 2001; 96, 1881-7.
5. Cheng J, Xu ZW, Zhu R, et al. Impact of diurnal temperature range on human health: a systematic review. *Int J Biometeorol*, 2014; 58, 2011-24.
6. Gasparrini A. Distributed lag linear and non-linear models in R: the package dlnm. *J Stat Softw*, 2011; 43, 1-20.
7. Ma P, Wang SG, Shang KZ, et al. The impact of meteorological comfort conditions on respiratory disease. *China Environ Sci*, 2018; 38, 374-82. (In Chinese)
8. Zhao Q, Li SS, Coelho MSZS, et al. High ambient temperature and risk of hospitalization for gastrointestinal infection in Brazil: a nationwide case-crossover study during 2000-2015. *Sci Total Environ*, 2022; 849, 157836.
9. Ma P, Li RL, Yue M, et al. Impacts of meteorological factors and environmental pollutants on digestive diseases in Beijing. *China Environ Sci*, 2016; 36, 1589-600. (In Chinese)
10. Wang MZ, Zheng S, He SL, et al. The association between diurnal temperature range and emergency room admissions for cardiovascular, respiratory, digestive and genitourinary disease among the elderly: a time series study. *Sci Total Environ*, 2013; 456-457, 370-5.