



Urban-rural disparity in heatwave effects on diabetes mortality in eastern China: A case-crossover analysis in 2016–2019

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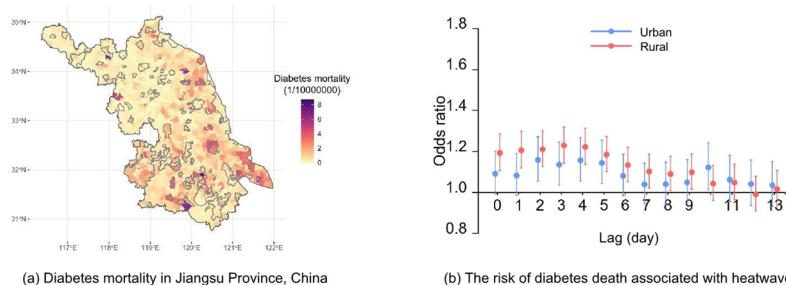
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HIGHLIGHTS

- The association between exposure to heatwave and diabetes mortality is stronger in rural areas than that in urban areas.
- The risk of diabetes deaths increases with the increase of heatwave intensity in rural areas.
- Rural females and those with less than 10 years of education are most vulnerable to heatwave-related diabetes deaths.

GRAPHICAL ABSTRACT

Geographical distribution of diabetes mortality and the effect of heatwave exposure on diabetes death in urban and rural areas



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ABSTRACT

Diabetics are sensitive to high ambient temperature due to impaired thermoregulation. However, available evidence on the impact of prolonged high temperature (i.e., heatwave) on diabetes deaths is limited and whether urban and rural areas differ in heatwave vulnerability remains unknown so far. A time-stratified case-crossover analysis was employed to estimate the association between heatwaves and diabetes deaths in 1486 districts (509 urban and 977 rural areas) of eastern China (Jiangsu Province), 2016–2019. For each decedent, residential heatwave exposure was measured by matching daily mean temperatures to the geocoded residential address. We adopted nine-tiered heatwave definitions incorporating intensity and duration. Stratified analyses by decedents' characteristics (gender, age, and education) were also conducted. During the study period, there were 18,685 deaths from diabetes (urban proportion: 36.95 %, p -value for urban-rural difference < 0.05). Heatwaves were associated with an increased risk of diabetes deaths, with greater and longer-lasting effects in rural areas than urban areas [e.g., rural odds ratio (OR): 1.19 (95 % confidence interval (CI): 1.14, 1.25) vs. urban OR: 1.09 (95 % CI: 1.05, 1.12)]. Risk of diabetes deaths increased

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² Dr. Jian Cheng and Dr. Zhiwei Xu have equal contributions to this study, including conceptualization, data curation, formal analysis, methodology, project administration, validation, and supervision. Thus, they should take responsibility for the integrity of the data and the accuracy of the data analysis.

with the intensity of heatwaves in rural areas (p -value for trend <0.01), but not in urban areas. Stratified analyses in rural areas suggested that females and less-educated people were more vulnerable to heatwave-related diabetes deaths. Our findings revealed the urban-rural disparity in the risk of diabetes deaths associated with heatwaves. Rural diabetics should be made aware of the increased death risk posed by heatwaves in the context of warming climate.

1. Introduction

Diabetes is a worldwide threat to public health, which could lead to a series of complications, such as diabetic foot ulcers (Grennan, 2019), cardiovascular diseases (International Hypoglycaemia Study, 2019), and even sudden deaths (Balkau et al., 1999; Tan et al., 2020). The World Health Organization has estimated that >420 million people live with diabetes globally (WHO, 2021), posing a substantial economic burden on patients, their families, and the wider society (GBD, 2020).

To prevent the serious outcomes of diabetes, many efforts in past years have been made to identify the underlying risk factors, such as individual and socioeconomic factors (Yang et al., 2016; Yang et al., 2010). Environmental factors such as ambient high temperature have increasingly been found to be a potential risk factor for diabetes deaths (Rojas-Rueda et al., 2021; Yang et al., 2016) and it has been documented that diabetics are vulnerable to high ambient temperature because of their impaired thermoregulation (Rutkove et al., 2009), autonomic neuropathy (Scott et al., 1988), and disrupted cardiovascular regulation (Kenny et al., 2016; Song et al., 2021). An earlier population-based meta-analysis reported an increase of 18 % in diabetes mortality associated with exposure to heatwaves (persistent days of high temperature) (Moon, 2021). With more frequent, more intense, and longer heatwaves through this century (IPCC, 2021), it is important to understand how heatwaves affect diabetics' health.

Prior studies looking at the association between heat or heatwave exposure and risk of diabetes deaths mainly focused on urban areas, probably due to urban regions having higher population density and being warmer than rural areas (i.e., urban heat island effect) (Founda and Santamouris, 2017; Xu et al., 2019). However, heatwave vulnerability is not only related to heat exposure but also associated with heat sensitivity and adaptation (Chen et al., 2016; Hondula et al., 2015). People living in rural areas have less access to medical resources and indoor cooling space, restricting their capacity to respond to heatwaves (Chen et al., 2018; Li et al., 2017). Aside from the differences in heatwave exposure and vulnerability, the risk of diabetes death also varied in urban and rural areas. For example, an earlier nationwide study in China found that diabetics in rural areas had a higher death risk than that in urban areas (Bragg et al., 2017). Converging evidence indicated a probably faster-growing urban-rural gap in the risk of diabetes deaths related to heatwaves in the context of urbanization and climate warming (Li et al., 2017). However, to the best of our knowledge, no study has examined whether there is an urban-rural disparity in the risk of diabetes deaths associated with heatwave exposure and the vulnerable populations remain unknown so far.

In the present study, a case-crossover analysis was performed to associate diabetes deaths with residential exposure to heatwaves at individual level in 1486 districts of Jiangsu Province, China. The aims of this study were to: (1) examine whether the association between short-term residential exposure to heatwaves and risk of diabetes deaths differed between urban areas and rural areas; and (2) investigate if the association between heatwave exposure and risk of diabetes deaths was modified by heatwave characteristics (i.e., duration and intensity) and decedents' characteristics (i.e., gender, age, years of education).

2. Methods

2.1. Data collection

This study was conducted in Jiangsu Province, consisting of 509 urban districts and 977 rural districts in eastern China (Fig. 1A–B). Jiangsu

Province had 78.6 million residents (urban proportion: 48.7 %) living in an area of 107,200 km² in 2019 (Jiangsu statistical yearbook-2020).

Daily records of diabetes death data from 1 January 2016 to 31 December 2019 were collected from the Death Surveillance System in Jiangsu Provincial Center for Disease Prevention and Control, including each individual's gender, age, education, death date, and the longitude and latitude of their residential address. Diabetes deaths were the primary cause of death and extracted based on the International Statistical Classification of Diseases and Related Health Problems, 10th Revision (ICD-10, codes E10–E14).

Daily mean temperature data covering the same study period in Jiangsu Province were obtained from the ERA5-Land dataset with a spatial resolution of 9×9 km². The ERA5-Land is a publicly available reanalysis dataset providing global-scale, hourly atmospheric land and oceanic climate variables, which has been applied in water resource, land, and environmental management research (Munoz-Sabater et al., 2021; Nepal et al., 2021). Daily ambient temperature data was matched with each decedent's address and was then used to estimate residential heatwave exposure.

Daily relative humidity and air pressure data were obtained from the Meteorological Bureau of Jiangsu Province. The daily mean concentrations of particulate matter with a diameter ≤ 2.5 μ m (PM_{2.5}), particulate matter with a diameter ≤ 10 μ m (PM₁₀), ozone (O₃), sulfur dioxide (SO₂), and nitrogen dioxide (NO₂) data were obtained from China National Environmental Monitoring Centre (<http://www.cnemc.cn/>). City-level daily relative humidity, air pressure, and air pollutants (matched with each decedent's city) were included in the model as covariates (Yin et al., 2018).

2.2. Heatwave definition

Following previous studies (Cheng et al., 2019; Tao et al., 2022), the intensity and duration of high temperatures were incorporated to define a heatwave. Specifically, we applied three intensities (≥ 95 th or 97.5th or 99th percentile of the distribution of daily mean temperature) and three durations (≥ 2 or 3 or 4 consecutive days) in this study. Details of the nine heatwave definitions are shown in Supplementary Table S1. To estimate heatwave effects, we limited the study period to the five warmer months (May–September) from 2016 to 2019 (Chen et al., 2016; Yin et al., 2018).

2.3. Data analysis

A time-stratified case-crossover design with a conditional logistic regression was used to examine the association between residential heatwave exposure and odds of diabetes deaths. In this design, each case serves as its own control, and the matched case-control pair is regarded as a stratum. In this study, the death date of a diabetic was defined as the case day. The same days in other weeks within the same month were chosen as the control days. For example, if a case occurred on the 8th of January 2019 (Tuesday), other Tuesdays within the same month (including the 1st, 15th, 22nd, and 29th of January 2019) would be the control days (Cheng et al., 2021). Case-crossover design has the advantage of adjusting for seasonal and long-term trends as well as individual characteristics that do not change in a short time period, such as age and gender.

After exposure to heatwaves, the risk of mortality can increase on the same day of exposure or/and several days after exposure (Xu et al., 2018). In the phase of data exploration, we used 0–30 days as the lag period and observed a significant association between heatwave exposure and odds of diabetes deaths over two weeks (lag 0 to lag 13), which was consistent with a prior study on heatwaves and mortality in 272 Chinese cities

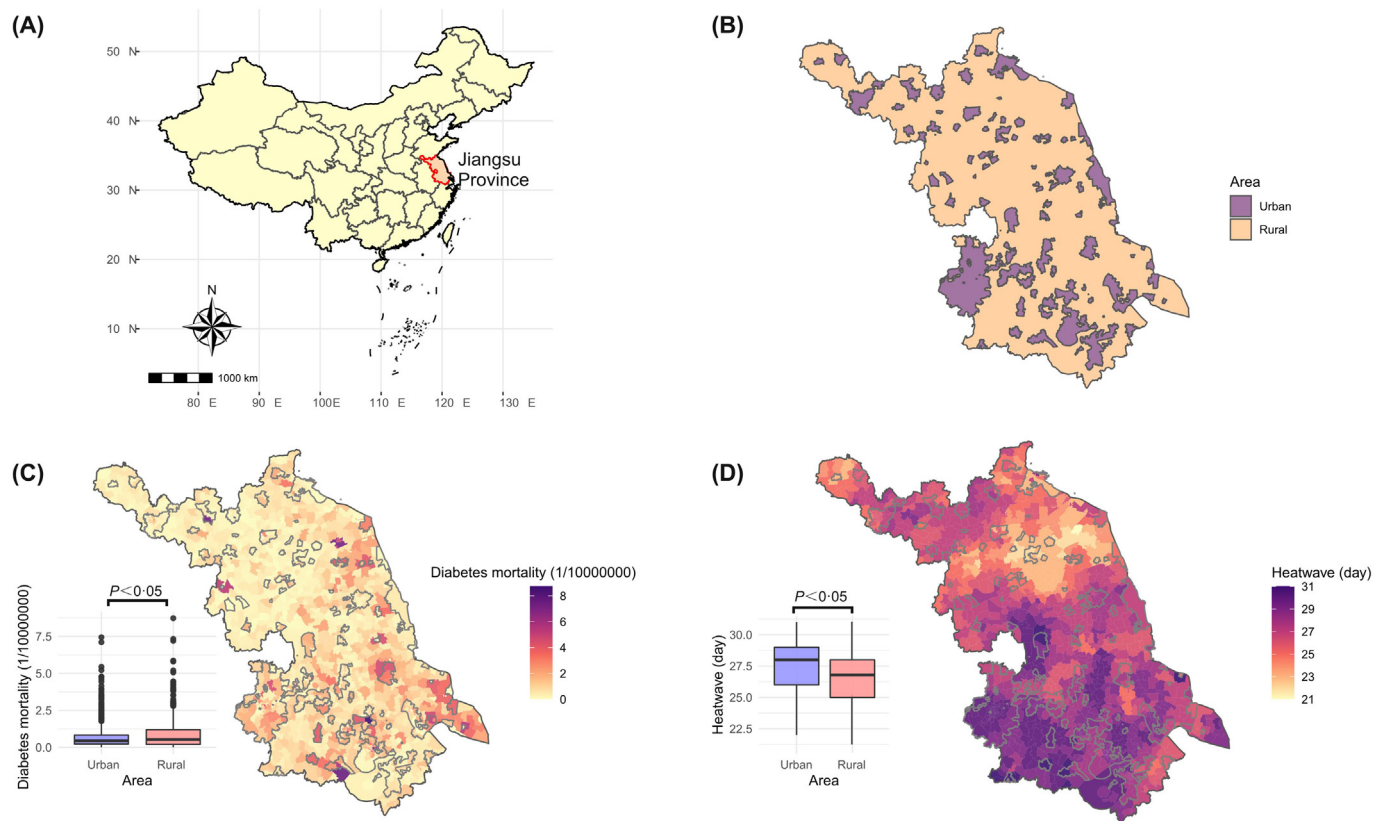


Fig. 1. Geographical distribution of diabetes mortality and heat exposure features across urban and rural areas in Jiangsu Province, China (May–September 2016–2019). (A) Geographical location of Jiangsu Province, China; (B) urban and rural areas in Jiangsu Province; (C) Diabetes mortality; (D) total heatwave days (the heatwave intensity is defined as ≥ 95 th percentile of the distribution of daily mean temperature, and the duration is ≥ 2 days).

(Yin et al., 2018). Thus, in this study, we adopted a lag of up to 13 days to examine the association between heatwave and diabetes deaths. To avoid collinearity issues, covariates were included when the Spearman correlation coefficients were < 0.6 (Mela and Kopalle, 2002). Natural cubic splines were used for relative humidity, air pressure, $PM_{2.5}$, and O_3 to capture potential non-linear relationship between these covariates and the odds of diabetes deaths. The optimal model was determined by the lowest Akaike Information Criterion value (Tables S2).

To estimate the average effect of heatwave exposure over a period, we pooled the odds ratio (OR) estimates from lag 0 to lag 13 days via the meta-analysis (Schwarzer et al., 2015). Additionally, we utilized the meta-regression technique to check whether there was a trend in odds of diabetes deaths with a change in heatwave intensity or duration (Saint-Maurice et al., 2020).

Subgroup analyses were conducted to evaluate whether age, gender, and years of education modified the association between heatwave exposure and odds of diabetes deaths in urban and rural areas. Age was categorized into three groups (< 65 years, 65–74 years, and ≥ 75 years). Years of education were dichotomized into “ < 10 years” (low education level) or “ ≥ 10 years” (high education level) (Zhou et al., 2017). Z test and meta-regression were adopted to compare differences in effect estimates across these subgroups.

2.4. Sensitivity analysis

A series of sensitivity analyses were performed to check the robustness of our findings. We firstly altered the smoothing degrees in the natural cubic spline function for each environmental variable (Table S2). In addition to relative humidity and air pressure, the daily mean concentrations of PM_{10} , SO_2 , and NO_2 were also adjusted for in the regression model (Li et al., 2014; Xu et al., 2019) (Figs. S4–5). All data analyses were performed

in R software (version: 4.1.0). A two-sided p -value < 0.05 was considered statistically significant.

3. Results

3.1. Descriptive analysis

Table 1 showed daily statistics of diabetes deaths and mean temperature in urban and rural areas in Jiangsu Province, China. During the study period, there were a total of 18,685 deaths from diabetes in Jiangsu Province, China (63.05 % in rural areas, and 36.95 % in urban areas). The average age at death was 77 years in urban areas and 75 years in rural areas. Diabetes mortality was higher in rural areas (0.064 %) than in urban areas (0.045 %) (p -value < 0.05 , Fig. 1C). Total heatwave days (defined as ≥ 95 th percentile & ≥ 2 days) in urban areas outnumbered those in rural areas (p -value < 0.05 , Fig. 1D), and this finding was also robust to other heatwave definitions (Supplementary Table S1).

Spearman correlation analysis showed that correlation coefficients between temperature, relative humidity, air pressure, $PM_{2.5}$, and O_3 were all lower than 0.6 (Fig. S1). For example, relative humidity ($\rho = 0.01$) and O_3 ($\rho = 0.01$) were positively correlated with temperature, while air pressure ($\rho = -0.59$) and $PM_{2.5}$ ($\rho = -0.11$) were negatively correlated with temperature.

3.2. Association between short-term residential exposure to heatwaves and odds of diabetes deaths

Fig. 2 showed that the association between intense heatwaves (≥ 97.5 th or ≥ 99 th percentile) and diabetes deaths was stronger in rural areas than that in urban areas (p -value < 0.05) (specific effect estimates shown in Table S4). The ORs were generally higher during lag 0 to lag 7 days in

Table 1

Descriptive daily statistics of diabetes deaths and mean temperature in urban and rural areas in Jiangsu Province, China, 2016–2019.

	Total (mean \pm SD, count)	Urban (mean \pm SD, count)	Rural (mean \pm SD, count)
Daily diabetes death	31.00 \pm 7.00	11.00 \pm 3.00	19.00 \pm 5.00
Gender			
Male	13.00 \pm 4.00	5.00 \pm 2.00	8.00 \pm 3.00
Female	18.00 \pm 5.00	6.00 \pm 2.00	11.00 \pm 4.00
Age			
<65 years	5.00 \pm 2.00	2.00 \pm 1.00	3.00 \pm 2.00
65–74 years	8.00 \pm 3.00	3.00 \pm 2.00	5.00 \pm 2.00
≥ 75 years	18.00 \pm 5.00	7.00 \pm 2.00	11.00 \pm 4.00
Years of education			
<10 years	29.00 \pm 6.00	10.00 \pm 3.00	19.00 \pm 5.00
≥ 10 years	2.00 \pm 1.00	1.00 \pm 1.00	1.00 \pm 1.00
Daily mean temperature	Total (mean \pm SD, °C)	Urban (mean \pm SD, °C)	Rural (mean \pm SD, °C)
Mean	24.90 \pm 0.36	25.00 \pm 0.33	24.85 \pm 0.36
95th percentile	30.53 \pm 0.55	30.69 \pm 0.56	30.45 \pm 0.53
97.5th percentile	31.25 \pm 0.62	31.44 \pm 0.61	31.15 \pm 0.60
99th percentile	31.98 \pm 0.58	32.15 \pm 0.58	31.90 \pm 0.56

Note: SD represents the standard deviation.

rural areas, whereas the ORs were relatively lower in urban areas and not statistically significant after lag 3 days among most heatwave definitions. Notably, more intense heatwaves were associated with greater ORs in rural areas (p -value for trend <0.01, Table 2), whereas we did not observe such a trend in urban areas. Additionally, we did not find a modification effect of heatwave duration on the association between short-term heatwave exposure and odds of diabetes deaths in either urban or rural areas (Table 2).

3.3. Subgroup analysis

Fig. 3 showed the association between short-term heatwave exposure and odds of diabetes deaths in different subgroups in rural areas (specific effect estimates presented in Table S5), suggesting that the association between heatwaves and odds of diabetes deaths was stronger in females than that in males (Fig. 3A). Compared with elderly diabetics (≥ 75 years), younger diabetics (<65 years) had a higher risk of death

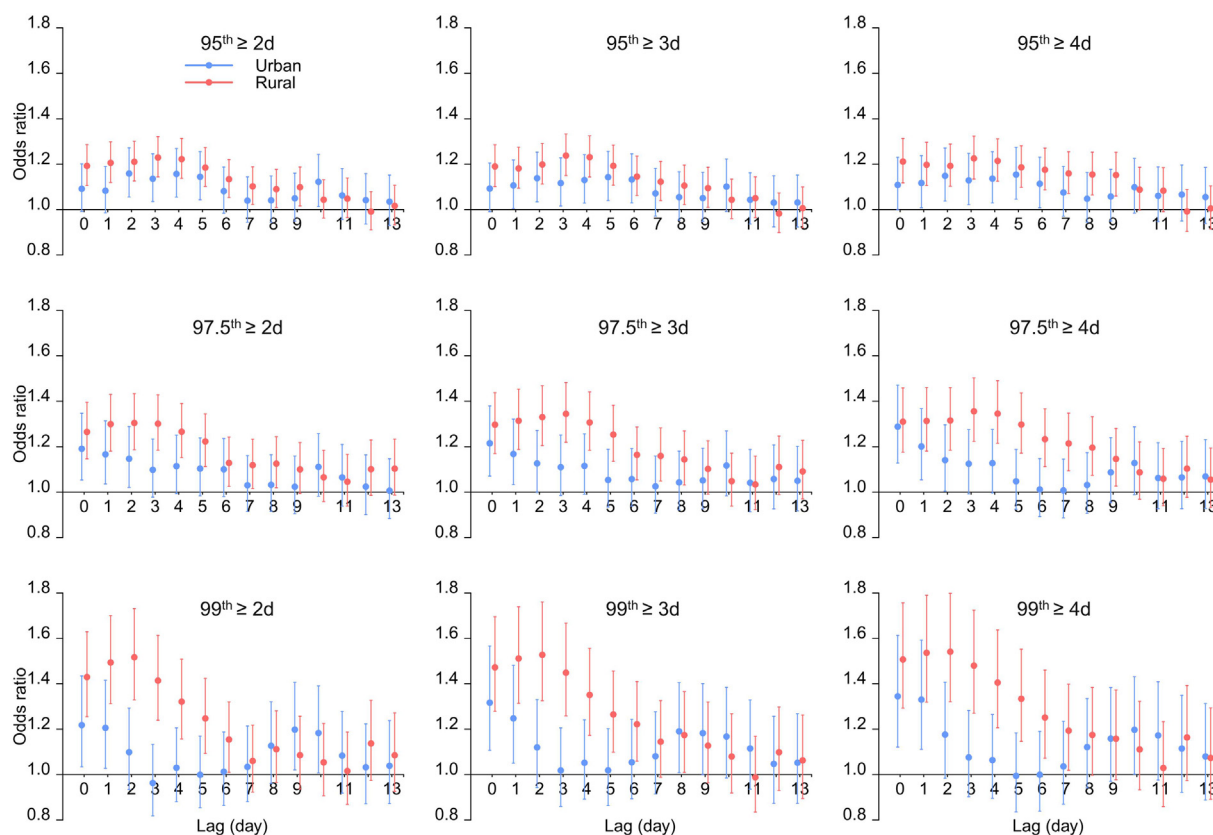


Fig. 2. Estimated lag-response associations between heatwave exposures and diabetes deaths for nine heatwave definitions over various lag days in urban and rural areas in Jiangsu Province, China.

Table 2

The pooled odds ratios and 95 % confidence intervals of associations between heatwave exposures and diabetes deaths over lag 0–13 days in the total, urban, and rural areas in Jiangsu Province, China.

Heatwave definition		Total area	Urban area	Rural area
Intensity	Duration			
≥ 95th	≥ 2 days	1.11 (1.08,1.14)	1.09 (1.06,1.12)	1.13 (1.08,1.17)
	≥ 3 days	1.11 (1.08,1.15)	1.09 (1.06,1.12)	1.13 (1.09,1.17)
	≥ 4 days	1.13 (1.10,1.16)	1.10 (1.07,1.13)	1.15 (1.11,1.19)
≥ 97.5th	≥ 2 days	1.14 (1.10,1.18)	1.09 (1.05,1.12)	1.17 (1.13,1.23)
	≥ 3 days	1.15 (1.10,1.19)	1.09 (1.05,1.12)	1.19 (1.14,1.25)
	≥ 4 days	1.16 (1.12,1.21)	1.10 (1.06,1.14)	1.22 (1.16,1.27)
≥ 99th	≥ 2 days	1.16 (1.10,1.22)	1.08 (1.04,1.13)	1.22 (1.13,1.31)
	≥ 3 days	1.19 (1.13,1.25)	1.12 (1.07,1.17)	1.24 (1.15,1.34)
	≥ 4 days	1.21 (1.15,1.27)	1.13 (1.07,1.18)	1.28 (1.19,1.38)
<i>p</i> -Value for trend in intensity		<0.01	0.57	<0.01
<i>p</i> -Value for trend in duration		0.30	0.34	0.37

Note: *p*-values for trend were derived by the meta-regression technique.

associated with heatwaves (Fig. 3B). In addition, diabetics with <10 years of education were more susceptible to heatwaves than diabetics with ≥ 10 years of education (Fig. 3C). Results of subgroup analyses for urban areas were shown in Table S5 and Fig. S3.

3.4. Sensitivity analysis

Sensitivity analysis results were presented in Table S2 and Figs. S4–5. Altering smoothing degrees in nature cubic splines of covariates returned similar results to our main analyses, indicating the robustness of our findings. Meanwhile, the pattern of heatwave-related diabetes deaths association remained after adjusting for other air pollutants.

4. Discussion

This is the first large-scale study to investigate the urban-rural disparity in the association between short-term residential exposure to heatwaves and risk of diabetes deaths. We found an increased risk of diabetes deaths associated with heatwave exposure, with greater and longer-lasting effects in rural areas than urban areas. The risk of diabetes deaths increased with the increase of heatwave intensity in rural areas only. Females and less-educated people (<10 years of education) in rural areas were more vulnerable to heatwave-related diabetes deaths.

In line with previous investigations (Moon, 2021; Xu et al., 2019), we found a significant association between short-term exposure to heatwaves and increased risk of diabetes deaths. It was reported that heatwave exposure could trigger dehydration in diabetics, which might lead to diabetic ketoacidosis (Manz, 2007) and hyperosmolar hyperglycemic state (Stoner, 2017). After exposure to high temperatures, diabetics could suffer damage to autonomic neuropathy, disrupting blood sugar control and cardiovascular regulation (Kenny et al., 2016; Song et al., 2021). Moreover, the increased heat stress during heatwave days may also aggravate the problems caused by complications of diabetes, especially for cardiovascular disease, stroke, and peripheral artery disease (Moon, 2021; Peterson et al., 2012).

We found that the association between heatwave exposure and risk of diabetes deaths in rural areas was stronger than that in urban areas. This finding is novel and could partially be explained by two reasons. First, although urban areas generally have a higher ambient temperature, they might have more access to air conditioning and public cooling buildings (e.g., shopping malls) than rural areas. Second, the educational difference between urban and rural areas may also play an important role, and this was reflected in our finding that less-educated diabetics in rural areas were more vulnerable to heatwaves. It has been reported that low educational attainment was related to low levels of health awareness (Li et al., 2017; Su et al., 2021),

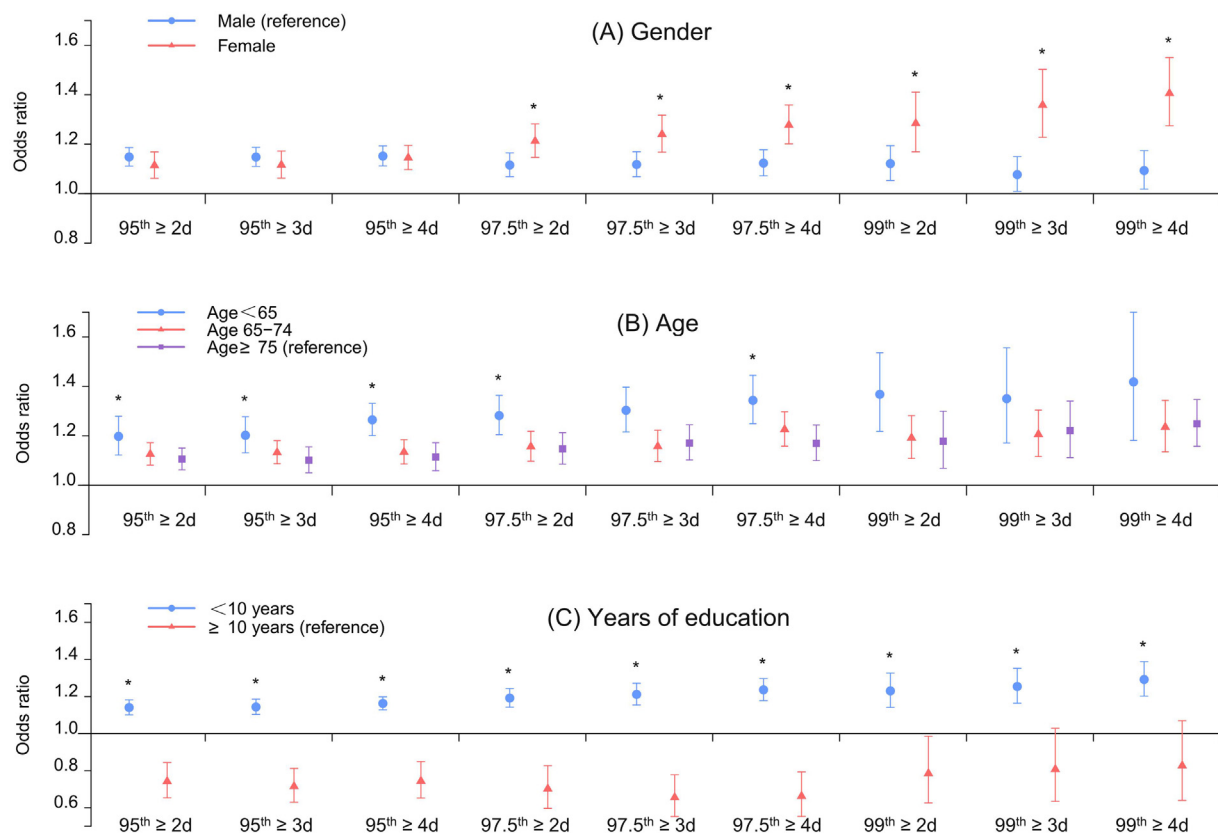


Fig. 3. Estimated odds ratios of diabetes deaths associated with heatwaves for nine heatwave definitions in different subgroups in rural areas of Jiangsu Province, China. Asterisk (*) indicated the difference was statistically significant. *p*-Values for multiple comparisons were adjusted by Bonferroni correction.

which may be associated with worse diabetes management and a higher risk of deaths.

This study measured heatwave exposure at residential level instead of city level (Vered et al., 2020; Yin et al., 2018). Prior investigations revealed that using temperature data from a limited number of ground monitoring stations could be subject to measurement bias and may underestimate the health risk associated with ambient temperature exposure (Chen et al., 2019; Hondula et al., 2015). In this study, we observed that daily mean temperatures varied spatially in Jiangsu Province, and hence using residential heatwave exposure could improve the accuracy of exposure measurement and precision of risk estimation (Basagana et al., 2021).

We observed that risk of diabetes deaths increased with the increase of heatwave intensity in rural areas, but not in urban areas. Similarly, previous studies in Brisbane (Australia) and 272 Chinese cities found that risk of health events increased with the increase in heatwave intensity (Xu et al., 2018; Yin et al., 2018). We speculated that work activities, heat adaptation, and socioeconomic disparities between urban and rural areas may contribute to the trend association (Anderson and Bell, 2011; Hondula et al., 2015). For instance, many rural residents are farmers or laborers and do outdoor work. Thus, they are more likely to be exposed to intense heatwaves. Furthermore, limited access to medical resources in rural areas might have an impact on diabetes deaths (Global Burden of Metabolic Risk Factors for Chronic Diseases, 2014). Our findings suggest that government could enhance heatwave warning services in rural areas during intense heatwave days.

Our subgroup analyses in urban areas found that heatwave effects were higher among elderly diabetics (≥ 75 years, Fig. S3), echoing previous multi-city studies in China (Yang et al., 2016) and England (Hajat et al., 2017). However, in rural areas, we observed that the death risk associated with heatwaves was higher among younger diabetics (<65 years) than their elderly counterparts. Although an earlier study in Brisbane (Australia) also found that younger diabetics were more vulnerable to heatwaves, the reasons behind that remain unclear. Therefore, future research is needed to investigate the effect of heatwaves on young diabetics in rural areas. We supposed that it may be related to urban-rural differences in working and living styles among age groups (Bragg et al., 2017). The outdoor work stress, exposure to heatwaves, and poor living standards might be associated with a higher risk of death in younger rural diabetics (Li et al., 2019; Yang et al., 2016).

We found that, in rural areas, females and less-educated people were more vulnerable to heatwave-related diabetes deaths. Several hypotheses in hormone and pathophysiology might account for gender differences in diabetes death (Kautzky-Willer et al., 2016; Rossouw et al., 2002). Besides, in some developing countries (such as China and India), there is a gender inequity in education, especially in rural areas (Li et al., 2017; Su et al., 2021). Because this was an ecological study, it should be acknowledged that there were other unmeasured confounders (e.g., socioeconomic factors), which might limit females and less-educated people to prevent the health risk from heatwaves in rural areas.

The main strength of this study lies in its large sample size and relatively precise measure of heatwave exposure. Our key findings on subgroups vulnerable to heatwaves (less-educated females in rural areas) could provide information for targeted prevention of heatwave-related diabetes deaths. However, several limitations of this study should be acknowledged. First, except for temperature data, other environmental data were collected from the ground monitoring stations, which were subject to a measurement bias (Chen et al., 2019). Second, despite the merits of case-crossover design, the observational nature of this study restricted us to draw an affirmative conclusion on a causal relation between heatwave exposure and risk of diabetes deaths.

5. Conclusion

This study revealed the urban-rural disparity in the association between short-term residential exposure to heatwaves and risk of diabetes deaths. People in rural areas of Jiangsu Province are more vulnerable to

heatwave-related diabetes deaths than those in urban areas, highlighting that education on heatwave prevention is urgently needed to raise health awareness among rural diabetics, especially for females and less educated people.

CRedit authorship contribution statement

Junwen Tao: Data curation, Formal analysis, Methodology, Software, Visualization, Writing – original draft. **Hao Zheng:** Data curation, Investigation, Resources, Writing – review & editing. **Hung Chak Ho:** Investigation, Resources, Writing – review & editing. **Xiling Wang:** Formal analysis, Investigation, Methodology, Writing – review & editing. **Mohammad Zahid Hossain:** Formal analysis, Methodology. **Zhongliang Bai:** Formal analysis, Methodology. **Ning Wang:** Formal analysis, Investigation, Methodology, Writing – review & editing. **Hong Su:** Formal analysis, Investigation, Resources, Supervision. **Zhiwei Xu:** Conceptualization, Data curation, Formal analysis, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – review & editing. **Jian Cheng:** Conceptualization, Data curation, Formal analysis, Funding acquisition, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – review & editing.

Data availability

Data on diabetes deaths were collected from the National Death Surveillance System in Jiangsu Provincial Center for Disease Prevention and Control. Daily mean temperature data covering the same study period were obtained from the ERA5-Land dataset (<https://cds.climate.copernicus.eu/>). Daily relative humidity and air pressure data were obtained from the Meteorological Bureau of Jiangsu Province. Raw diabetes deaths data, daily relative humidity, air pressure, and air pollution data will not be shared because authors are not authorized to distribute the data. Researchers who need the daily mean temperature data can visit the ERA5-Land dataset website.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.scitotenv.2022.160026>.

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