



## Effects of Heat Exposure

# Associations of heat and cold with hospitalizations and post-discharge deaths due to acute myocardial infarction: what is the role of pre-existing diabetes?

Zhiwei Xu,<sup>1</sup> Shilu Tong,<sup>2,3,4</sup> Hung Chak Ho,<sup>5,6</sup> Hualiang Lin ,<sup>7</sup> Haifeng Pan<sup>8</sup> and Jian Cheng<sup>8,9\*</sup>

<sup>1</sup>School of Public Health, Faculty of Medicine, University of Queensland, Brisbane, Australia, <sup>2</sup>Department of Clinical Epidemiology and Biostatistics, Shanghai Children's Medical Center, Shanghai Jiaotong University School of Medicine, Shanghai, China, <sup>3</sup>School of Public Health and Social Work, Institute of Health and Biomedical Innovation, Queensland University of Technology, Brisbane, Australia, <sup>4</sup>School of Public Health, Institute of Environment and Population Health, Anhui Medical University, Hefei, China, <sup>5</sup>Department of Urban Planning and Design, The University of Hong Kong, Hong Kong, China, <sup>6</sup>School of Geography and Remote Sensing, Guangzhou University, Guangzhou, China, <sup>7</sup>Department of Epidemiology, School of Public Health, Sun Yat-sen University, Guangzhou, China, <sup>8</sup>Department of Epidemiology and Biostatistics, School of Public Health, Anhui Medical University, Hefei, China and <sup>9</sup>Anhui Province Key Laboratory of Major Autoimmune Disease, Hefei, China

\*Corresponding author. Department of Epidemiology and Biostatistics, School of Public Health, Anhui Medical University, 81 Meishan Road, Hefei, Anhui Province 230032, China. E-mail: jiancheng\_cchh@163.com

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## Abstract

**Background:** The existing evidence suggests that pre-existing diabetes may modify the association between heat and hospitalizations for acute myocardial infarction (AMI).

**Methods:** This study included patients who were hospitalized for AMI from 1 January 2005 to 31 December 2013 in Brisbane, Australia, and also included those who died within 2 months after discharge. A time-stratified case-crossover design with conditional logistic regression was used to quantify the associations of heat and cold with hospitalizations and post-discharge deaths due to AMI in patients with and without pre-existing diabetes. Stratified analyses were conducted to explore whether age, sex and suburb-level green space and suburb-level socio-economic status modified the temperature–AMI relationship. Heat and cold were defined as the temperature above/below which the odds of hospitalizations/deaths due to AMI started to increase significantly.

**Results:** There were 14 991 hospitalizations for AMI and 1811 died from AMI within 2 months after discharge during the study period. Significant association between heat and hospitalizations for AMI was observed only in those with pre-existing diabetes (odds ratio: 1.19, 95% confidence interval: 1.00–1.41) [heat (26.3°C) vs minimum morbidity temperature (22.2°C)]. Cold was associated with increased odds of hospitalizations for AMI in

both diabetes and non-diabetes groups. Significant association between cold and post-discharge deaths from AMI was observed in both diabetes and non-diabetes groups.

**Conclusions:** Individuals with diabetes are more susceptible to hospitalizations due to AMI caused by heat and cold.

**Key words:** Heat, cold, diabetes, acute myocardial infarction

#### Key Messages

- Significant association between heat and hospitalizations for acute myocardial infarction (AMI) was only observed in individuals with pre-existing diabetes.
- In both diabetes and non-diabetes groups, the magnitude of the association between cold and hospitalizations for AMI increased with decreasing levels of economic resources at the suburb level.
- A significant relationship between cold and post-discharge deaths from AMI was observed in both diabetes and non-diabetes groups.

## Introduction

Diabetes is one of the leading causes of both years of life lost and years lived with disability (YLDs) globally and it resulted in 1.37 [95% uncertainty interval (UI): 1.34–1.40] million deaths in 2017.<sup>1,2</sup> From 2007 to 2017, the number of YLDs for diabetes increased by 30.1% globally and diabetes became increasingly prevalent in both developed and developing regions, particularly in low-income countries.<sup>3</sup> Apart from the widely recognized lifestyle-related risk factors (e.g. obesity), the association between environmental risk factors (e.g. heat and cold) and diabetes has been increasingly reported.<sup>4,5</sup> Our prior work has observed that heatwaves increased the risks of hospitalizations and post-discharge deaths due to diabetes in Brisbane, Australia.<sup>6</sup>

Exposures to heat and cold are not just associated with hospitalizations for diabetes, but also linked to the complications of diabetes [e.g. stroke<sup>7</sup> and acute myocardial infarction (AMI)].<sup>8</sup> AMI is one of the most common complications of diabetes as well as one of the leading causes of death among diabetics.<sup>9,10</sup> Lam *et al.* have found that in Hong Kong, China, the association between heat and hospitalizations for AMI only existed in those patients with pre-existing diabetes,<sup>11</sup> indicating that diabetes may play a role in the association between heat and AMI. However, so far, no studies have explored whether pre-existing diabetes plays a role in the association between heat and AMI in other regions.

Although heat and cold pose a threat to all individuals, existing evidence has suggested that people with good socio-economic status (e.g. high income)<sup>12</sup> and individuals

living in suburbs with abundant green space<sup>13</sup> tend to adapt to heat well, motivating us to explore whether individual- or suburb-level characteristics modified the temperature–AMI association. In addition, prior studies quantifying the associations of heat and cold with AMI tended to use province- or city-wide temperature data to represent the exposure of all participants in one province/city,<sup>14,15</sup> which might cause potential exposure-measurement bias as the metropolitan area of a city is generally warmer than its surrounding areas.<sup>16,17</sup> This exposure-measurement bias could have been largely reduced if suburb-level temperature data were used.

To date, no studies have examined the associations of heat and cold with hospitalizations and post-discharge deaths due to AMI. Our study used suburb-level temperature data to assess the associations of heat and cold with hospitalizations and post-discharge deaths due to AMI among those with pre-existing diabetes (hereafter called the diabetes group) and those without pre-existing diabetes (hereafter called the non-diabetes group), and to further examine whether age, sex, suburb-level vegetation coverage and suburb-level socio-economic status modified the temperature–AMI association in both the diabetes and the non-diabetes groups in Brisbane, Australia.

## Methods

### Data collection

Our study included individuals who were admitted to the five biggest hospitals in Brisbane from 1 January 2005 to

31 December 2013. More information about the study has been provided elsewhere.<sup>6</sup> The detailed information collected on participants included a reference number, age, sex, primary diagnosis and other diagnoses at each admission recorded as ICD-code 10 (International Classification of Diseases, 10th revision) and the postcode of each patient's residential suburb. Participants were considered to have pre-existing diabetes if diabetes was recorded as a diagnosis at prior hospitalizations. Those individuals who died within 2 months after they were discharged were included in this cohort. We collected information obtained from Registrar General Death Database on mortality within 2 months of discharge.

Data on the suburb-level normalized difference vegetation index (NDVI) covering the study period were obtained from the Australian Bureau of Meteorology. Data on a commonly used indicator of suburb-level socio-economic status, the Socio-economic Indexes for Areas (SEIFA), were collected from the Australian Bureau of Statistics. SEIFA has four different sub-indexes and this study used three sub-indexes, namely the Index of Relative Socio-economic Advantage and Disadvantage (indicator of the suburb-level socio-economic advantage level), the Index of Economic Resources (indicator of the level of economic resources at the suburb level) and the Index of Education and Occupation (indicator of suburb-level education and the occupation level). Daily raster data on maximum and minimum temperatures for every postcode of Brisbane from 1 January 2005 to 28 February 2014 were sourced from the website of the Australian Bureau of Meteorology online archive (<http://www.bom.gov.au/jsp/awap/temp/archive.jsp?colour=colour&map=maxave&year=2004&month=3&period=daily&area=nat>). The daily mean temperature in each postcode was calculated by averaging the daily maximum temperature and daily minimum temperature,<sup>18</sup> and was used in this study as the temperature indicator. We selected the mean temperature in the data analysis as our prior work suggested that the mean temperature seemed to be an optimal temperature indicator in assessing health impacts of temperature in Brisbane.<sup>18,19</sup> Daily data on relative humidity that were originally collected from two monitoring stations (Brisbane station and Brisbane Aero station) were provided by the Australian Bureau of Meteorology. Daily data on nitrogen dioxide (NO<sub>2</sub>) (µg/m<sup>3</sup>) and particulate matter ≤10 µg/m<sup>3</sup> (PM<sub>10</sub>) that were originally collected from two monitoring stations (Brisbane Central Business District station and Brisbane Rocklea station) were obtained from the Queensland Department of Environment and Heritage Protection. As influenza may also be a potential confounder, we also collected daily data on influenza counts covering the study period from Queensland Health.

## Data analysis

A time-stratified case-crossover design with conditional logistic regression was used to quantify the associations of heat and cold with hospitalizations and post-discharge deaths due to AMI in the diabetes group and the non-diabetes group.<sup>20</sup> For each AMI patient, the exposure on the day of the AMI was compared with exposures on the same day of other weeks in the same month. AMI cases from all postcodes were included in the same data and each stratum was coded continuously.<sup>21</sup> There were no duplicates in strata between postcodes. A natural cubic spline with three degrees of freedom (*dfs*) for temperature was used to capture the possible non-linear relationship between temperature and AMI. The temperature corresponding to the minimum odds of hospitalizations for AMI [also called the minimum morbidity temperature (MMT)] was used as the reference temperature to calculate the associations of heat and cold with hospitalizations for AMI. The MMT for the entire study area was calculated according to the methods described in prior literature.<sup>22</sup> We identified the temperature above/below which the odds of hospitalizations/deaths due to AMI started to increase significantly<sup>23</sup> and used these temperature values to define heat and cold. The moving average temperature of 1–21 days was used to assess the possible lag effect in the initial data mining.<sup>22</sup> The proper lag period for assessing the health impacts of heat and cold may vary across different disease types<sup>24</sup> and hence we checked the lag plots and chose the moving average of 0–1 days' temperature as the lag period for heat and the moving average of 0–10 days' temperature as the lag period for cold. Relative humidity, PM<sub>10</sub>, NO<sub>2</sub> and influenza were adjusted in the model as potential confounders. The 1st and 3rd quartiles of SEIFA domains and NDVI were used to convert these variables into categorical variables and the case-crossover analysis was conducted in each category of SEIFA and NDVI. The 1st, 2nd and 3rd quartiles of SEIFA domains and NDVI are reported as 'low', 'middle' and 'high' levels, respectively, in the 'Results' section. Statistical testing of the difference in estimates between subgroups (e.g. age, sex, NDVI and SEIFA) was conducted to understand whether the difference was statistically significant.<sup>25</sup>

To make sure that the results were robust to the lag period used, we performed sensitivity analyses by changing the lag period for the association between cold and hospitalizations for AMI from 8 to 14 days. All data analyses were conducted in R package (version 3.5.3) using 'dlnm', 'dplyr', 'tsModel' and 'survival' packages.

## Results

The descriptive statistics of hospitalizations and post-discharge deaths due to AMI in the diabetes group and the

**Table 1** Descriptive statistics of hospitalizations and post-discharge deaths due to acute myocardial infarction in Brisbane from 2005 to 2013

		Hospitalizations (%)			Post-discharge deaths (%)		
		Diabetes	Non-diabetes	<i>P</i> -value	Diabetes	Non-diabetes	<i>P</i> -value
Sex	Male	2013 (61.9)	7463 (63.6)	0.080	236 (54.6)	646 (46.8)	0.005
	Female	1239 (38.1)	4276 (36.4)		196 (45.4)	733 (53.2)	
Age	<65	1079 (33.2)	4808 (41.0)	<0.001	49 (11.3)	92 (6.7)	0.002
	≥65	2173 (66.8)	6931 (59.0)		383 (88.7)	1287 (93.3)	
NDVI	Low	404 (12.9)	1608 (14.3)	0.023	61 (14.7)	212 (16.4)	0.302
	Middle	2149 (68.8)	7459 (66.2)		266 (64.1)	850 (65.6)	
	High	571 (18.3)	2200 (19.5)		88 (21.2)	233 (18.0)	
Suburb socio-economic advantage level <sup>a</sup>	Low	1157 (37.0)	3527 (31.3)	<0.001	146 (35.2)	367 (28.3)	0.022
	Middle	1649 (52.8)	6116 (54.2)		216 (52.0)	723 (55.8)	
	High	318 (10.2)	1643 (14.6)		53 (12.8)	205 (15.8)	
Suburb economic resources <sup>b</sup>	Low	770 (24.6)	2225 (19.7)	<0.001	106 (25.5)	259 (20.0)	0.034
	Middle	2070 (66.3)	7729 (68.5)		270 (65.1)	881 (68.0)	
	High	284 (9.1)	1332 (11.8)		39 (9.4)	155 (12.0)	
Suburb education and occupation <sup>c</sup>	Low	1100 (35.2)	3185 (28.2)	<0.001	127 (30.6)	297 (22.9)	0.005
	Middle	1627 (52.1)	6220 (55.1)		221 (53.3)	739 (57.1)	
	High	397 (12.7)	1881 (16.7)		67 (16.1)	259 (20.0)	

<sup>a</sup>Index of Relative Socio-economic Advantage and Disadvantage.

<sup>b</sup>Index of Economic Resources.

<sup>c</sup>Index of Education and Occupation.

non-diabetes group are shown in Table 1. During 1 January 2005 to 31 December 2013 in Brisbane, there were 14 991 hospitalizations for AMI and 1811 died within 2 months after discharge. In the patients who were hospitalized for AMI, the proportion having pre-existing diabetes was higher in individuals aged ≥65 years than in those aged <65 years. Conversely, among deaths from AMI, the proportion having diabetes was higher in individuals aged <65 years than in those aged ≥65 years. In both hospitalizations and post-discharge deaths due to AMI, the proportion having pre-existing diabetes was higher in those with a low socio-economic level than in the other two groups (i.e. the middle- and high-level groups). Among the deaths from AMI, males had a higher proportion of pre-existing diabetes than females. The descriptive statistics of the mean temperature and relative humidity are presented in Supplementary Table S1 (available as Supplementary data at *IJE* online).

Figure 1 illustrates the exposure–response relationship between ambient temperature and hospitalizations for AMI, revealing that a significant relationship between heat and hospitalizations for AMI was only observed in the diabetes group. Figure 2 presents the exposure–response relationship between ambient temperature and post-discharge deaths from AMI in the diabetes group and the non-diabetes group.

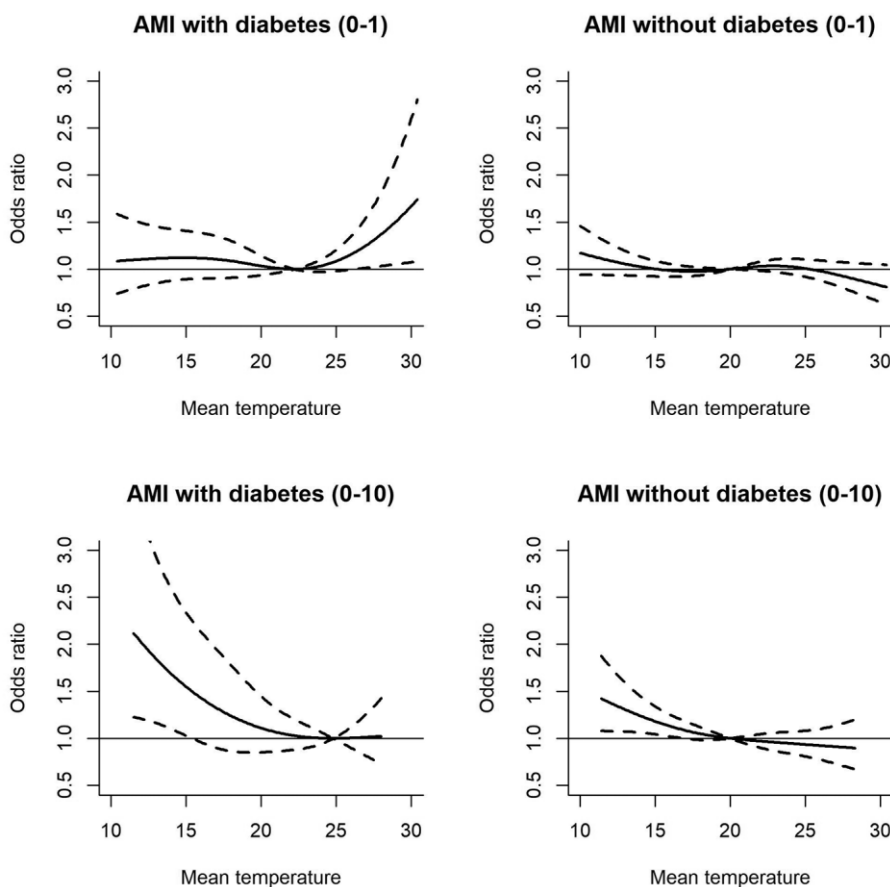
Table 2 shows the relationship between heat and hospitalizations for AMI in the diabetes group stratified by age,

sex, NDVI and SEIFA, suggesting that females, elderly people and those who lived in suburbs with a low socio-economic level or low economic-resources level appeared to have higher odds of heat-related AMI hospitalizations, although the differences were not statistically significant.

The association between cold and hospitalizations for AMI in the diabetes group and the non-diabetes group is presented in Table 3. The range from the MMT to the temperature value below which the odds of AMI hospitalizations started to increase significantly in the diabetes group (15.3°C to 24.8°C) was narrower than for the non-diabetes group (13.8°C to 28.3°C). Interestingly, in both the diabetes and non-diabetes groups, the magnitude of the association between cold and hospitalizations for AMI increased with the decrease in the level of economic resources at the suburb level.

As Figure 2 suggests that the odds of post-discharge deaths from AMI decreased with the increase of ambient temperature, we present only the association between cold and post-discharge deaths from AMI here. Table 4 shows the association between cold and post-discharge deaths from AMI in the diabetes group and the non-diabetes group, suggesting that the odds of post-discharge deaths in the diabetes group started to increase significantly as soon as the temperature started to drop from the minimum mortality temperature (from 28.2°C to 28.1°C).

The sensitivity analysis results are presented in Supplementary Figures S1 and S2 (available as



**Figure 1** The association between ambient mean temperature and hospitalizations for acute myocardial infarction (AMI) in patients with or without pre-existing diabetes. The numbers in parentheses are the numbers of lag days (0–1: moving average of 0–1 days' mean temperature; 0–10: moving average of 0–10 days' mean temperature)

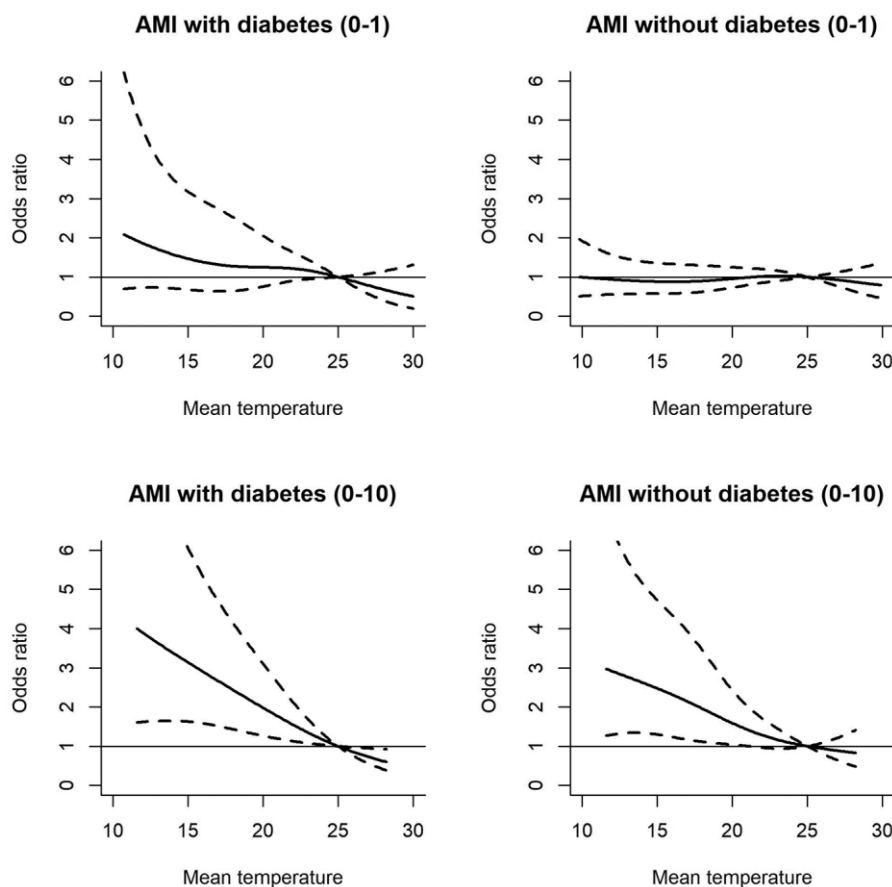
Supplementary data at *IJE* online), suggesting that the main results were robust to the lag period used.

## Discussion

Our study has yielded several intriguing findings. First, the significant association between heat and hospitalizations for AMI was observed only in the diabetes group. The association between heat and hospitalizations did not attenuate when suburb green space increased from the low level to the middle level. Second, during cold days, in the diabetes group, the range from the MMT to the temperature value below which the odds of AMI hospitalizations started to increase significantly was narrower than that in the non-diabetes group. Third, the magnitude of the association between cold and hospitalizations for AMI appeared to increase with the decrease in the level of economic resources at the suburb level.

Although the exact biological mechanisms underlying the association between heat and AMI remain to be explored, it has been documented that exposure to heat may affect surface blood circulation and lead to sweating,

thereby increasing cardiac strain, blood viscosity, platelet and red cell counts and plasma cholesterol.<sup>26,27</sup> These biological changes contribute to the occurrence of AMI. Our finding that the significant association between heat and hospitalizations for AMI occurred in the diabetes group is consistent with a previous Hong Kong study.<sup>11</sup> Diabetics have reduced endothelial function, which can impair thermoregulation and impact hemostasis, and consequently increase cardiac stress and the risk of myocardial infarction.<sup>28</sup> It has been reported that individuals with type 2 diabetes have impairments in heart-rate variability, which may also be associated with their higher risk of myocardial infarction during hot days.<sup>29–31</sup> Brisbane and Hong Kong both have a subtropical climate (although they are located in different hemispheres) and the similar finding in these two cities calls for future studies exploring whether individuals with diabetes are more susceptible to heat-related hospitalizations for AMI in cities with other climates. If this finding was confirmed in future studies, it would likely suggest that diabetes may play a role in the relationship between heat and AMI.



**Figure 2** The association between ambient mean temperature and post-discharge deaths from acute myocardial infarction (AMI) in individuals with or without pre-existing diabetes. The numbers in parentheses are the numbers of lag days (0–1: moving average of 0–1 days' mean temperature; 0–10: moving average of 0–10 days' mean temperature)

Our study suggests that during cold days, in the diabetes group, the range from the MMT to the temperature value below which the odds of AMI hospitalizations started to increase significantly was narrower than that in the non-diabetes group. It has been documented that AMI events can be triggered by the direct and indirect effects of cold exposure.<sup>32</sup> The direct effect of cold exposure involves an increase in heart rate and blood pressure, diuresis and blood viscosity but a decrease in plasma volume and haemoconcentration.<sup>32–34</sup> The indirect effect of cold exposure may arise from the exacerbation of pre-existing pulmonary conditions.<sup>32</sup> People with type 2 diabetes are less able to prevent decreases in core temperature associated with cold exposure and this may amplify the adverse effect of cold exposure on AMI in this group.<sup>29</sup> Hence, diabetics and their caregivers need to take pre-emptive action before the cold season arrives.

The elderly are generally more vulnerable to the health impacts of heat and cold than are young people.<sup>35,36</sup> However, in prior studies assessing whether the associations of heat and cold with AMI differed across different age groups, results have been inconsistent.<sup>15,37,38</sup> In our

study, we observed that in both the diabetes and non-diabetes groups, the associations of heat and cold with hospitalizations due to AMI in the patients aged  $\geq 65$  years appeared to be stronger than in those aged  $< 65$  years (although the differences were not statistically significant), indicating that elderly people need extra protection on hot or cold days. In Australia, the health impact of heat on the elderly results in substantial economic loss,<sup>39</sup> calling for proper adaptation strategies to be developed.

In a prior study, we did not find any modification effect of urban green space on the effects of heatwaves on hospitalizations or post-discharge deaths due to diabetes,<sup>6</sup> but we previously noticed that people living in suburbs with high-level green space were less vulnerable to the effect of heatwaves on Alzheimer's disease compared with those living in suburbs with low-level green space.<sup>13</sup> In the current study, we found that the lowest association between heat and hospitalizations for AMI was seen in suburbs with high-level green space (Table 2), suggesting that green space may protect people from heat-related AMI. However, we did not observe higher odds of having heat-related hospitalizations for AMI in low-level green space

**Table 2** The relationship between heat (26.3°C vs 22.2°C) and hospitalizations for acute myocardial infarction in patients with pre-existing diabetes stratified by age, sex and suburb characteristics

Individual and suburb characteristics		Heat (26.3°C vs 22.2°C)		
		Odds ratio (OR)	95% confidence interval	P-value
Total		1.19	1.00–1.41	
Sex	Males	1.08	0.87–1.35	0.17
	Females	1.38	1.05–1.81	Reference
Age	<65	1.11	0.83–1.49	0.52
	≥65	1.25	1.01–1.54	Reference
Suburb NDVI	Low	1.16	0.71–1.90	0.33
	Middle	1.25	1.02–1.54	0.09
	High	0.84	0.55–1.27	Reference
Suburb socio-economic advantage level	Low	1.33	0.74–2.40	0.62
	Middle	1.14	0.89–1.46	0.96
	High	1.13	0.86–1.47	Reference
Suburb economic resources	Low	1.18	0.85–1.65	0.86
	Middle	1.15	0.93–1.43	0.91
	High	1.11	0.61–2.02	Reference
Suburb education and occupation	Low	1.10	0.83–1.47	0.93
	Middle	1.24	0.97–1.58	0.62
	High	1.07	0.63–1.82	Reference

**Table 3** The relationship between cold and hospitalizations for acute myocardial infarction in patients with or without pre-existing diabetes stratified by age, sex and suburb characteristics

Individual and suburb characteristics		Diabetes (15.3°C vs 24.8°C)			Non-diabetes (13.8°C vs 28.3°C)		
		Odds ratio (OR)	95% confidence interval	P-value	Odds ratio (OR)	95% confidence interval	P-value
Total		1.51	1.01–2.27		1.40	1.00–1.95	
Sex	Males	1.24	0.91–1.68	0.44	1.09	0.63–1.89	0.27
	Females	1.62	0.88–2.95	Reference	1.61	1.06–2.45	Reference
Age	<65	1.17	0.56–2.44	0.44	1.30	0.77–2.19	0.72
	≥65	1.66	1.02–2.71	Reference	1.47	0.95–2.28	Reference
Suburb socio-economic advantage level	Low	2.06	1.02–4.13	0.14	1.58	0.99–2.52	0.37
	Middle	1.57	0.89–2.79	0.25	1.42	0.58–3.47	0.66
	High	0.70	0.20–2.44	Reference	1.12	0.62–2.03	Reference
Suburb economic resources	Low	5.17	2.14–12.50	0.02	1.66	1.09–2.52	0.11
	Middle	1.18	0.71–1.96	0.56	1.33	0.50–3.51	0.45
	High	0.77	0.20–2.95	Reference	0.83	0.40–1.73	Reference
Suburb education and occupation	Low	1.59	0.77–3.26	0.68	0.67	0.36–1.25	0.60
	Middle	1.41	0.79–2.50	0.53	2.45	1.53–3.91	0.03
	High	2.11	0.68–6.56	Reference	0.88	0.39–2.00	Reference

than in middle-level green space. The findings from the current study and our prior studies imply that the modification effect of urban green space on the health impacts of heat may vary across different diseases.

In the present study, we also found that the association between cold and hospitalizations due to AMI appeared to be stronger in people living in suburbs with low-level economic resources. Given the fact that the highest prevalence

of diabetes in Australia was generally in the lowest socio-economic groups,<sup>40</sup> adaptation strategies targeting those lowest socio-economic groups (particularly those with diabetes) may ease the burden of AMI attributable to extreme temperatures. Although ozone and traffic noise were not analysed in this study, it can be expected that air pollution and traffic noise may interact with heat and cold,<sup>41–44</sup> and hence diabetics living in suburbs with higher levels of air

**Table 4** The relationship between cold and deaths from acute myocardial infarction in patients with or without pre-existing diabetes stratified by age and sex

Individual characteristics		Diabetes (28.1°C vs 28.2°C)			Non-diabetes (18.0°C vs 28.2°C)		
		Odds ratio (OR)	95% confidence interval	P-value	Odds ratio (OR)	95% confidence interval	P-value
Total		1.02	1.00–1.03		2.36	1.01–5.55	
Sex	Males	1.03	1.01–1.05	0.17	5.74	1.56–21.10	0.07
	Females	1.01	0.99–1.03	Reference	1.15	0.36–3.62	Reference
Age	<65	1.01	0.98–1.04	0.56	2.16	0.89–5.20	0.60
	≥65	1.02	1.00–1.03	Reference	3.05	0.89–6.08	Reference

pollution and traffic noise may be at greater risk of temperature-related AMI.

This study has several strengths. First, to the best of our knowledge, this is one of the few efforts so far assessing the association between temperature and hospitalizations for AMI in individuals with and without diabetes.<sup>45</sup> Second, the use of the suburb-level temperature data allowed us to minimize possible exposure-measurement bias. Finally, the higher vulnerability to heat-related hospitalizations for AMI among diabetics that we observed may assist in understanding the mechanisms behind the association between heat and AMI.

Several limitations of this study should also be acknowledged. First, due to ethical issues, we were unable to access data on the residential addresses of the participants and thus were unable to collect data on individual temperature exposure. Second, as this was a study conducted in a subtropical city, caution should be exercised in generalizing our findings to cities with other climates (e.g. temperate climate). Third, as the suburb-level mean-temperature data were not available, we were only able to calculate the mean temperature by averaging the maximum temperature and the minimum temperature in this study, although our prior work suggested that the mean temperature calculated in this way seemed appropriate in assessing the health effects of extreme heat in Brisbane.<sup>18</sup> Fourth, due to the primary design of this cohort study, only those deaths occurring within 2 months after hospital discharge were included as data on deaths within a longer period after discharge were unavailable. Fifth, only a limited number of confounders (e.g. relative humidity, PM<sub>10</sub>, NO<sub>2</sub> and influenza) were included in the model. Other factors associated with AMI (e.g. traffic noise) were not controlled for in the analyses,<sup>46</sup> although heat and cold have been increasingly reported to be associated with increased risk of myocardial infarction in many regions of the world with distinct traffic backgrounds.<sup>8</sup> Future studies examining the roles of other environmental hazards (particularly traffic noise) in the

associations of heat and cold with AMI are warranted. Specifically, accurate methods to estimate spatiotemporal changes in traffic noise should be pre-investigated, as noise itself is highly varied due to locations (e.g. near major road, hillside) and time (e.g. daytime, midnight). Thus, using a simple measurement of traffic noise (e.g. city-wide daily count) could only introduce bias but not increase the accuracy of the case-crossover design. Sixth, the NDVI data used in this study were available only at the monthly level, which might not be adequate to capture the within-month changes in NDVI and this may have prevented us from detecting the modification effect of green space over smaller time periods in this case-crossover study. Seventh, ozone is one of the gaseous air pollutants associated with AMI,<sup>47</sup> but we were unable to control for ozone in the regression analyses of heat and cold due to data unavailability. Eighth, we calculated the MMT for the entire study area rather than for each suburb because of the limited number of AMI cases/deaths in many suburbs, although we believed that the city-level MMT would be enough for developing adaptation strategies to prevent heat- or cold-related AMI. Ninth, we noticed that the number of post-discharge deaths from AMI in some subgroups (e.g. individuals living in the suburbs with high-level economic resources) was small, possibly restricting us from adequately detecting statistically significant results in these subgroups. However, one of the reasons that statistically significant results were not found in some subgroups was because we did not use extremely high or low percentiles (e.g. 99th and 1st) to define heat and cold. Because of the small sample size in some subgroups and the heat and cold definitions that we used, the wide confidence intervals of the effect estimates in subgroups overlapped with each other, possibly hindering us from detecting differences in heat/cold vulnerability across different subgroups. Tenth, the present study relied on a hospital diagnosis of diabetes and hence may not be immune to potential bias due to the under-diagnosis of diabetes.<sup>48</sup>



In conclusion, our study provides evidence that individuals with diabetes are more susceptible to hospitalizations due to AMI caused by heat and cold. Cold exposure is associated with increased odds of hospitalizations and post-discharge deaths of AMI patients. Diabetics, particularly those living in suburbs with low-level economic resources, may need extra protection to save them from cold-related AMI hospitalizations and deaths.

## Supplementary data

Supplementary data are available at *IJE* online.

## Ethics approval

This study was granted by the Queensland University of Technology Human Research Ethics Committee (approval number: 1500000369).

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## Data availability

The data that support the findings of this study are available on request from the corresponding author.

## Conflict of interest

None declared.

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