

## **Effect modification of greenness on the association between heat and mortality: a multi-city multi-country study**

Hayon Michelle Choi

Advisor: Michelle L. Bell



*This work contains preliminary results; therefore, some results could change during future analysis.*

### **Introduction**

A substantial number of multi-city studies on the health impact of temperature-mortality have shown evidence for an increased risk of death from extreme temperatures (e.g., low and high ambient temperature).<sup>1-3</sup> The temperature-mortality relationship varies across countries, cities, and climatic regions due to various geographic and socioeconomic factors.<sup>4, 5</sup> Therefore, identifying risk factors that affect the temperature-mortality relationship in different environmental settings is critical to reducing health impacts.<sup>6</sup>

Currently, more than half of the world's population live in urban areas and this population is expected to increase.<sup>7</sup> Urbanization plays an important role in driving surface warming at the local scale.<sup>8</sup> The urban heat island effect, which indicates an increase in temperature in urban areas compared to rural underdeveloped areas, can lead to extreme heat events.<sup>9</sup> As the impervious surface increases in the urban and suburban areas, the buildings, concrete, and asphalt trap heat and contribute to the warming effect.<sup>10</sup> Evaluating the characteristics of the urban environment, which has benefits for human health (e.g., job opportunities), is important to understand the full spectrum of consequences for human health.<sup>11</sup> Among the built environments, urban vegetation is

recognized as a crucial factor for changing the micro- and meso- climate.<sup>12</sup> Vegetation lowers the temperature close to the surface through shading, evapotranspiration, and absorbing solar radiation through photosynthesis.<sup>13</sup>

Greenspace such as urban parks, and diversity of vegetation could increase the cooling effect and lessen the heat storage through evapotranspiration.<sup>14, 15</sup> The effectiveness of green infrastructure in reducing urban thermal islands has been demonstrated through measurements (e.g., field measurements, scale models, and thermal remote sensing), and computer simulation.<sup>16-18</sup> According to a review study,<sup>19</sup> green infrastructures (trees, parks, forests, and green roofs) have a higher level of thermal comfort than other urban spaces. Another study has shown that thermal comfort and the reduced urban heat island effect of urban greenspace (UGS) depend on its size and shape. That study showed that the cooling effect of a UGS is directly correlated with its vegetation cover and tree shade area.<sup>20</sup>

In addition to the impact of greenness on temperature, there is increasing evidence that greenness (e.g., urban parks) is associated with improved health.<sup>21-23</sup> Specifically, greenness can increase mental health and well-being, physical activity, and social cohesion. Urban greenspace could affect peoples' daily indoor/outdoor activity patterns, which in turn could impact how ambient environmental exposures such as temperature affect health. Urban greenness can modify the ambient temperature and atmospheric moisture, which may change the temperature-related health risks, with differences across cities and countries.<sup>24</sup> Therefore, research is needed to understand how greenspace in urban areas can modify the relationship between heat and health. To understand this issue, data from a large number of cities are needed to provide the heterogeneity of urban greenness. Therefore, we aimed to explore the effect of urban greenspace on heat-mortality association in a multi-city, multi-country dimension.

## Methods

### *Data Collection*

We used daily time-series data of the Multi-Country Multi-City (MCC) Collaborative Research Network (MCC) study, which has been described in previous publications.<sup>25-28</sup> We obtained daily time-series data of mortality (all-cause/ respiratory/ cardiovascular) and daily mean temperature for each of 512 cities in 34 countries. For each location, daily mortality counts were analyzed for all causes or non-external causes only (ICD-9 codes 0 to 799 and ICD-10 codes A0 to R99), and the two main causes of death: respiratory disease (ICD-10 codes J00 to J99) and cardiovascular disease (ICD-10 codes I00 to I99) were obtained. The availability of cause-specific mortality data varied by country. The study periods varied depending on country, ranging from 4 to 19 years. Details of the dataset (country name, the number of cities, and the study period for each country) are listed in Table 1.

### *Greenspace*

For each city, we estimated greenness using the Enhanced Vegetation Index (EVI) from the Moderate Resolution Imaging Spectroradiometer product MOD13Q1 (NASA, 2020). We also examined the Normalized Difference Vegetation Index (NDVI) for supplementary analysis. NDVI is calculated as the difference between the near-infrared and visible reflectance divided by the sum of those two (i.e.,  $NDVI = (NIR - RED) / (NIR + RED)$ ).<sup>29</sup> The NDVI ranges from -1 to +1 with higher values indicating denser vegetation and a value of 0 or below indicating non-vegetated areas (e.g., rock, barren, waterbody features).<sup>30</sup> The calculation of EVI is similar to NDVI but corrects for bias caused by the particles in the air, ground cover below the vegetation, and areas with large amount of chlorophyll.<sup>31</sup> The EVI is calculated as

$$EVI = G[(NIR - RED)/(NIR + C_1RED - C_2blue + L)]$$

, where  $G$  is a gain factor,  $blue$  is the reflectance in the blue band of MOD13Q1,  $L$  is the canopy background adjustment addressing differential and non-linear near-infrared and red radiant transfer through a canopy, and  $C_1$  and  $C_2$  are the coefficients of the aerosol resistance terms using the blue band for correcting for aerosol influences in the red band.<sup>32</sup> MOD13Q1 uses 1 for  $L$ , 6 for  $C_1$ , 7.5 for  $C_2$ , and 2.5 for  $G$ .<sup>32</sup>

MOD13Q1 is generated for every 16 days at 250-meter spatial resolution. The city-specific EVI and NDVI values were calculated for every 16 days during the period for which the MCC data (e.g., meteorological data, health data) were available. We estimated the average EVI for every city using the pixel values within and surrounding the city's boundary. The average of the calculated EVI values through the observation period was used as the representative greenness index of each city. Multiple data sources including the U.S. Census Bureau, Statistics Canada, and the Database of Global Administrative Areas provided the GIS shapefile data for the boundaries of cities. We conducted mosaicking and reprojecting of MOD13Q1 product tiles using Google Earth Engine and the calculation for the city-specific EVI calculation was performed by the R statistical program. Hereafter, we refer to EVI as "greenspace" or "greenness". Sensitivity analysis was conducted using similar calculations to estimate NDVI as an alternate metric for greenspace to facilitate comparison with earlier studies.

### *Data Analysis*

We conducted a two-stage seasonal analysis using time-series data from the 512 cities in the 34 countries. In the first stage, we applied a time series model separately for each city to estimate the city-specific heat-mortality relationship. These estimated relationships were then pooled in the

second stage to generate an overall estimate of the heat-mortality association, accounting for potential effect modification by greenness. This approach has been described previously.<sup>26,33</sup>

### **First-stage analysis (city-specific temperature-mortality associations)**

We applied quasi-Poisson regression separately in each city to derive estimates of the city-specific heat-mortality association during the summer months. In this first-stage analysis, seasonality was controlled using a natural cubic B-spline of day of the year with equally spaced knots and 4-degree of freedom (df). A linear interaction between this spline functions and year was used. Long-term trend was controlled using a natural cubic B-spline with 1 degree of freedom per ten years, and an indicator for day of the week was also added in the model. A distributed lag non-linear model (DLNM) was applied to describe the non-linear exposure-response relationship and non-linear lag-response relationship. Specifically, we selected cross-basis for exposure with a quadratic B-spline for the exposure-response with two internal knots placed at the 50<sup>th</sup> and 90<sup>th</sup> percentiles of city-specific summer temperature distributions, and a natural cubic B-spline for the lag-response with an intercept, and two internal knots placed at equally spaced values in the log scale. A lag period of 10 days was selected to capture the delay in the effects of extreme heat. Choices of modelling assumptions and lag days are based on a previous multi-country scale studies.<sup>28,34</sup> The first-stage analysis was performed with the R packages *dlnm*.<sup>35</sup>

### **Second-stage pooled analysis (effect modification by greenspace)**

In the second stage analysis, we pooled the overall cumulative city-specific estimates of first-stage using R package *mvmeta*.<sup>36</sup> To estimate the modifying effects of greenspace, we considered greenspace as a continuous variable while adjusting for city-specific average temperature, city-specific temperature range, and an indicator for country as meta-predictors in a multivariate meta-

regression. We derived the best linear unbiased prediction (BLUP) for the exposure-response associations. The minimum mortality temperature (MMT) for each city, which corresponds to the temperature with the minimum risk of mortality, was derived from the BLUP of time-varying overall cumulative exposure-response relationships in each city. We used these MMTs as reference values to calculate the relative heat risk, using re-centered quadratic B-spline basis for modelling exposure-response.

The heat-mortality associations were expressed as the percent change [95% confidence interval (CI)] in relative risk (comparing the 99<sup>th</sup> temperature percentile to the MMT) associated with an interquartile range (IQR, for each city) increase in greenspace as measured by EVI. Analysis was also conducted separately for all-cause, respiratory, and cardiovascular mortality.

### **Heat-mortality relative risk by greenspace**

We examined the overall heat-mortality risk by country for countries with more than 10 cities (12 countries in total). The heat-mortality effect estimates were assessed as the first-stage analysis for each city, generating the relative heat risk comparing risk of mortality at the 99<sup>th</sup> percentile of temperature to the MMT for each city. Then effect estimates were pooled for each country, considering city-specific average temperature and city-specific temperature range as meta-predictors, to generate an overall heat-mortality association for each country. We plotted the pooled heat relative risk in each country and green space in each country.

For sensitivity analysis we presented the heat risk in various ways, comparing risks of mortality: 1) at the 99<sup>th</sup> temperature percentile compared to the 75<sup>th</sup> temperature percentile for each city, and 2) at 28.66 C° (the 99<sup>th</sup> temperature percentile averaged across all cities) compared to 24.84 C° (the 75<sup>th</sup> temperature percentile averaged across all cities). The first of these approaches considers

relative heat comparisons, considering temperature values specific to the distribution of temperature within each city, whereas the second considers absolute heat comparisons. These risks have different interpretations for adaptation.<sup>38</sup> Also, we assessed NDVI as an effect modification for heat-mortality relationship as another indicator of greenspace.

This study was approved by the Behavioural & Social Sciences Ethical Review Committee, University of Queensland.

## Results

This study included 512 cities and covered the period from 2000 to 2018 during the warm seasons (four warmest months for each city), with different years for different regions based on data availability (Table 1). The mean temperature was highest for Thailand at 28.81°C and lowest for Estonia at 15.37°C. Based on the cities included, Greece had the highest daily death counts for all-cause and cardiovascular mortality for a single city (74.5 and 34.5 deaths/day, respectively), and Japan had the highest daily mean respiratory mortality counts when averaging across 47 cities (8.2 deaths/day).

**Table 1. Summary of the study periods, number of deaths/day, and mean temperatures in the 34 countries/regions.**

Country/ region	Number of cities	Study Years	Temperature °C		Deaths/day [mean across cities]		
			Mean (s.d.)	Minimum, Maximum	all-cause	cardiovascular	respiratory
Argentina	2	2005-2015	23.63 (0.21)	23.62, 23.65	63.3	-	-
Australia	3	2000-2009	22.39 (1.88)	20.48, 24.23	44.5	-	-
Brazil	18	2000-2011	26.04 (2.39)	20.81, 29.06	34.9	-	-
Canada	24	2000-2015	17.29 (1.99)	14.51, 21.22	12.5	4.0	1.0
Chile	4	2000-2014	19.24 (2.49)	17.48, 21.01	51.4	-	-
China	12	2000-2015	24.77 (3.37)	17.64, 28.20	27.6	10.4	2.8
Colombia	5	2000-2013	23.86 (5.92)	14.07, 28.71	33.2	9.2	3.6
Costa Rica	1	2000-2017	23.33 (-)	-	4.7	1.4	0.4
Czech Republic	4	2000-2015	17.56 (0.90)	16.62, 18.73	20.5	9.8	1.1

Ecuador	2	2014-2018	21.49 (8.21)	15.69, 27.29	31.2	9.1	3.8
Estonia	3	2000-2018	15.37 (0.33)	15.02, 15.68	5.5	2.7	0.1
Finland	1	2000-2014	15.93 (-)	-	19.3	6.8	0.9
France	18	2000-2014	19.32 (2.03)	16.69, 23.21	15.6	3.8	0.8
Germany	1	2000-2015	17.51 (-)	-	14.3	-	-
Greece	1	2001-2010	27.15 (-)	-	74.5	34.5	7.1
Guatemala	1	2000-2016	20.47 (-)	-	21.4	-	-
Iran	1	2002-2015	25.88 (-)	-	33.5	10.7	1.6
Italy	12	2006-2015	24.07 (0.75)	22.95, 25.37	12.5	-	-
Japan	47	2000-2015	24.99 (1.58)	19.89, 28.22	56.9	15.6	8.2
Korea	35	2000-2018	23.33 (1.14)	19.46, 25.05	10.8	2.3	0.7
Mexico	4	2000-2014	23.17 (5.94)	15.74, 28.71	23.3	6.2	1.8
Paraguay	1	2013-2016	28.62 (-)	-	7.7	2.6	0.6
Philippines	3	2006-2010	28.67 (1.27)	27.31, 29.83	27.4	8.1	3.1
Portugal	4	2000-2018	23.54 (3.95)	19.93, 29.12	29.8	9.7	3.1
Puerto Rico	1	2000-2016	19.23 (-)	-	34.9	9.3	3.6
Romania	6	2000-2016	22.03 (3.44)	17.62, 28.16	7.3	-	-
South Africa	49	2000-2013	22.06 (2.34)	15.04, 26.70	27.7	4.0	3.2
Spain	37	2000-2014	23.17 (2.44)	18.29, 27.17	6.5	2.1	0.7
Switzerland	3	2000-2013	19.39 (2.39)	17.11, 24.10	5.0	1.6	0.4
Sweden	7	2000-2016	16.33 (0.31)	15.96, 16.53	10.8	4.3	0.7
Thailand	60	2000-2008	28.81 (1.75)	16.41, 30.18	7.8	1.5	0.9
Taiwan	3	2000-2014	28.54 (0.39)	28.10, 28.82	43.2	8.9	4.4
UK	52	2000-2016	16.34 (1.87)	14.39, 28.29	8.6	2.7	1.1
USA	95	2000-2006	23.49 (3.29)	15.87, 29.69	19.1	5.7	1.7

*\*Note: “-“ indicates there were no available dataset for the specific country/city. Not all countries have cause-specific data. s.d. for standard deviation.*

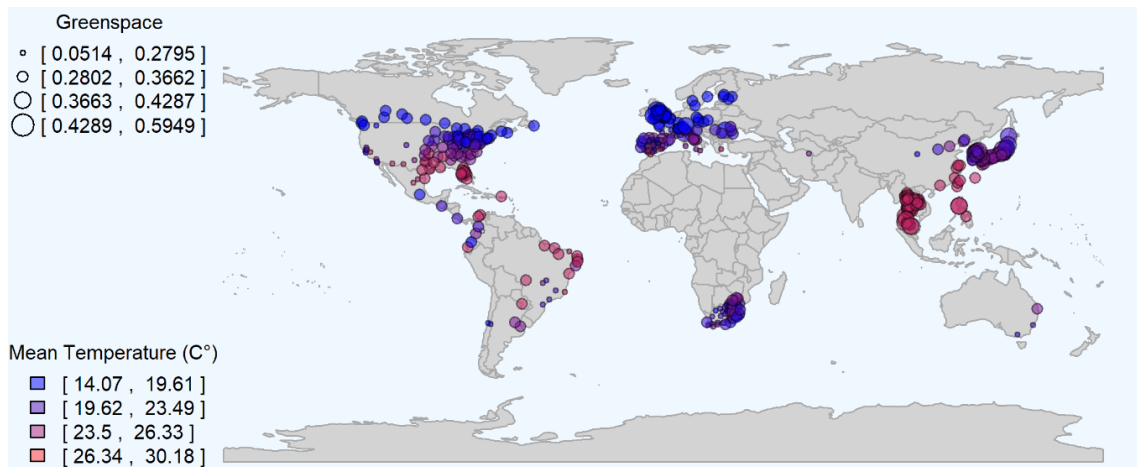
For the study cities, Philippines had the highest greenspace mean value (EVI of 0.516), whereas Iran had the lowest greenspace value with 0.094 (Table 2). For NDVI, Japan had the highest mean value of 0.696, and Iran lowest at 0.131 (Table S1). UK had the highest variation of greenspace variation among cities with EVI of 0.461 (Minimum: 0.051, Maximum: 0.512), and Ecuador had the lowest variation with 0.027 (Minimum: 0.35, Maximum: 0.377 in Ecuador). Italy had the highest NDVI variation among cities with 0.593 (Minimum: 0.201, Maximum: 0.794), while Argentina had the lowest variation with 0.002 (Minimum: 0.558, Maximum: 0.56) (Table S2).

**Table 2. Summary of the greenspace in the 34 countries/regions.**



Country/Region	Greenspace	
	Mean (s.d.)	Minimum, Maximum
Argentina	0.380 (0.021)	0.365, 0.394
Australia	0.221 (0.104)	0.151, 0.341
Brazil	0.286 (0.076)	0.164, 0.404
Canada	0.326 (0.044)	0.250, 0.388
Chile	0.194 (0.053)	0.157, 0.231
China	0.349 (0.076)	0.192, 0.452
Colombia	0.325 (0.086)	0.199, 0.439
Costa Rica	0.451 (-)	-
Czech Republic	0.385 (0.044)	0.327, 0.433
Ecuador	0.364 (0.019)	0.350, 0.377
Estonia	0.364 (0.081)	0.295, 0.454
Finland	0.366 (-)	-
France	0.235 (0.032)	0.179, 0.300
Germany	0.314 (-)	-
Greece	0.119 (-)	-
Guatemala	0.454 (-)	-
Iran	0.094 (-)	-
Italy	0.316 (0.117)	0.116, 0.516
Japan	0.444 (0.055)	0.256, 0.542
Korea	0.421 (0.080)	0.207, 0.504
Mexico	0.213 (0.058)	0.129, 0.267
Paraguay	0.279 (-)	-
Philippines	0.516 (0.112)	0.437, 0.595
Portugal	0.283 (0.071)	0.189, 0.344
Puerto Rico	0.322 (-)	-
Romania	0.369 (0.088)	0.271, 0.509
South Africa	0.264 (0.095)	0.082, 0.454
Spain	0.231 (0.051)	0.170, 0.379
Switzerland	0.391 (0.105)	0.239, 0.547
Sweden	0.353 (0.022)	0.329, 0.373
Thailand	0.411 (0.059)	0.242, 0.555
Taiwan	0.391 (0.044)	0.342, 0.429
UK	0.355 (0.071)	0.051, 0.512
USA	0.371 (0.082)	0.142, 0.488

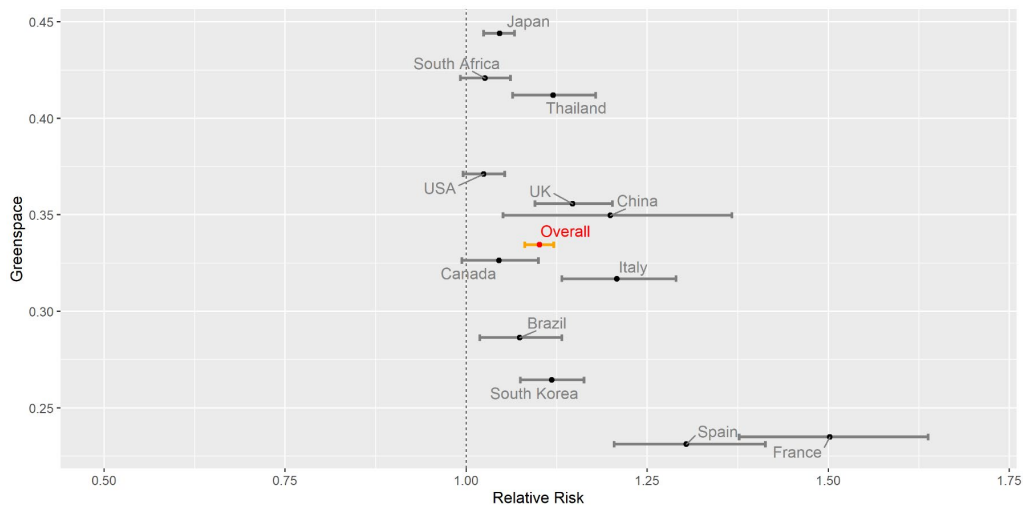
*\*Note: “-“ indicates there was only one city for the specific country. s.d. for standard deviation. Mean values refer to the average of city-specific values for cities within each country/region. Minimum and maximum refer to the lowest and highest city-specific values for cities within that country/region.*



**Figure 1. Map of the 512 cities/location included in the analysis**

*Note: The locations represent metropolitan areas, provinces, or larger areas from 34 countries. The colors represent different ranges of average daily mean temperature shown in Table 1; the size of the circles indicate the average greenspace value (EVI) shown in Table 2.*

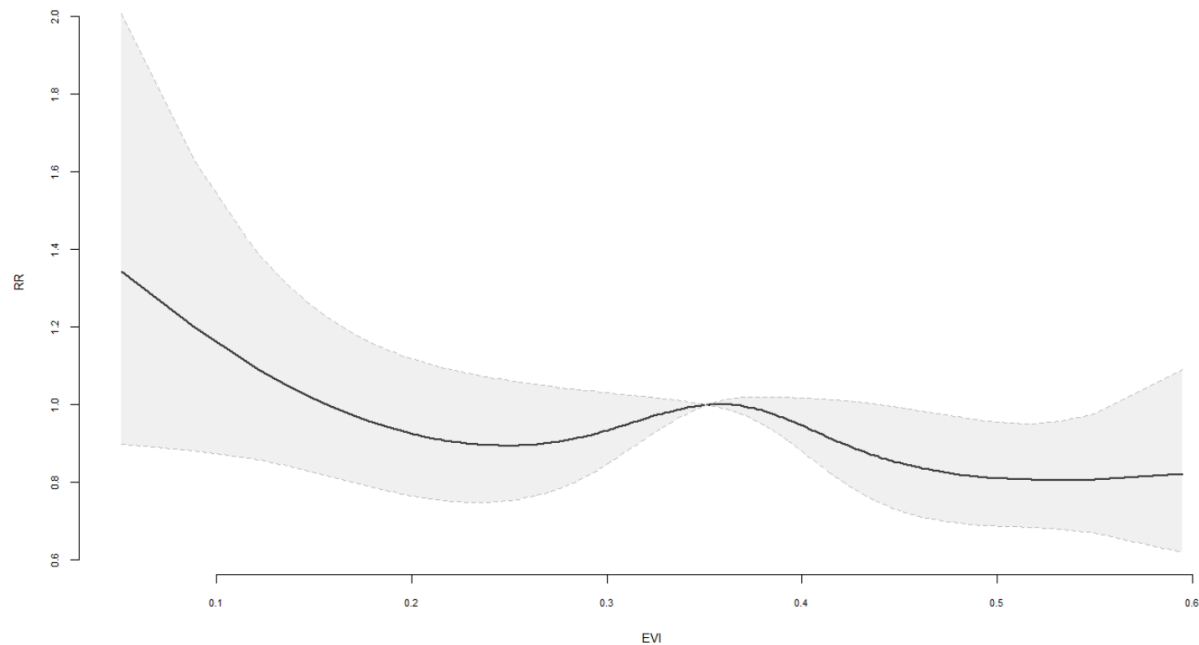
The geographical distribution, average mean temperature, and mean greenspace values (EVI) of the 512 locations represent the various regions included in this study, which include different climatic conditions from Northern Europe to Southeast Asia (Figure 1). Greenspace levels differed by location. The mean NDVI values for each location are displayed in Figure S1.



**Figure 2. Relative risk of mortality comparing the 95<sup>th</sup> percentile of temperature to the MMT, by greenspace value (EVI) for 12 countries and overall.**

*Note:* Each country-specific value represents the overall estimate across all study cities in that country. The Overall value represents the estimate across all countries. Horizontal lines reflect 95% confidence intervals.

The relative risk for heat was generally higher among countries with low greenspace values (Figure 2). Japan with a high greenspace value showed low heat risk (Greenspace EVI: 0.44, Heat Risk (CI): 1.046 (1.024, 1.067)), whereas Spain and France with low greenspace values represented high heat relative risk (EVI: 0.23, Heat Risk (CI): 1.301 (1.198, 1.413) in Spain, EVI: 0.23, Heat Risk (CI): 1.502 (1.377, 1.638) in France). The same pattern was observed for NDVI and heat relative risk (NDVI: 0.69 for Japan, NDVI: 0.38 for Spain, and NDVI: 0.39 for France) (Figure S3).



**Figure 3. Pooled mortality relative risk for different level of greenspace**

*Note:* The pooled relative risk curve is centered by the greenspace median value (0.35). Shaded grey shape reflects the 95% confidence intervals.

The pooled relative risk for different level of greenspace is represented in Figure 3. Increasing EVI from 0.35 (mean value) to 0.49 (IQR= 0.14) is associated in decreasing the heat-related RR (99th

temperature percentile vs minimum mortality temperature) from 1.001 (95%CI: 1, 1.002) to 0.810 (95%CI: 0.687, 0.955). Also, increasing NDVI from 0.54 (mean value) to 0.73 (IQR= 0.19) is associated with a decrease in the heat-related RR (99th temperature percentile vs minimum mortality temperature) from 1.001 (95%CI: 1, 1.004) to 0.804 (95%CI: 0.677, 0.954).

Table 3 presents the effect modification by greenspace on the heat-mortality relationship expressed as the percent decrease in heat relative risk (comparing mortality risk at the 99th temperature percentile to the MMT, using city-specific values) for an IQR increase in greenspace (IQR for EVI: 0.148). There was a statistically significant effect modification for greenspace on heat-related mortality for all cause and cardiovascular mortality. One IQR increase in greenspace was associated with an 8.7% (95% CI: 1.6, 15.3; p-value 0.017) decrease in the heat-mortality relative risk comparing risk at the 99th temperature percentile to the MMT, and a 16.8% (95% CI: 3.1, 28.5; p-value 0.018) decrease in the heat-related relative risk for respiratory mortality.

**Table 3. The overall effect modification of greenspace (EVI) on heat-mortality relationship**

*Notes:* Results indicate % risk decrease in the relative risk comparing mortality risk at the 99th temperature percentile to the MMT, using city-specific values for an IQR increase in greenspace (IQR EVI: 0.148).

Cause specific mortality	Effect modification by greenspace [% relative risk decrease (CI), p-value]
All	8.7 (1.6, 15.3), 0.017
Respiratory	16.8 (3.1, 28.5), 0.018
Cardiovascular	6.2 (-6, 17), 0.301

We conducted sensitivity analysis using NDVI, an alternative metric of greenness. The overall correlation between EVI and NDVI was 0.95. These greenness metrics were highly correlated at different temperature strata (high and low) as shown in Figure S2. Results for effect modification were similar using NDVI (Table S2). Also, the main results did not change significantly when using different temperature comparisons (relative temperature comparison of 99<sup>th</sup> and 75<sup>th</sup>

percentiles and absolute temperature comparison of 28.66°C to 24.84°C) (Table S3). The results of sensitivity analysis were consistent in showing statistically significant effect modification by greenspace for all-cause and respiratory mortality.

## **Discussion**

This study quantified the effect modification of greenspace on the heat-mortality relationship in various locations on a global scale. To our knowledge, this study is the largest epidemiological study investigating greenspace as an effect modifier of heat-related mortality. We found a statistically significant effect modification of greenspace on heat-related mortality for all-cause and respiratory mortality. Higher greenspace was associated with protective effects on heat-mortality relationship for all-cause and respiratory mortality. Also, we compared various locations with different temperature levels and greenspace values. Overall, the total heat risk decreased as the greenspace values increased.

Our results are similar to previous studies on the effect modification of greenspace on the temperature-mortality association. A study in Ho Chi Minh City, Vietnam estimated that every 1-square-kilometer increase in greenspace per 1,000 people could prevent 7.4 heat-related deaths.<sup>39</sup> In 17 Chinese cities, the heat-mortality effects were higher in cities with a low proportion of greenspace.<sup>40</sup> Urban greenspace was found to have a mitigating effect on heat-related mortality in the elderly population in Lisbon, Portugal.<sup>41</sup> However, few studies were conducted on a multi-country scale and also the existing literature is largely on total mortality rather than cause-specific mortality. A multi-country analysis has shown low heat mortality effects in cities with higher green area (square meters per million persons).<sup>42</sup> This result is consistent with our finding of effect modification on heat-related all-cause mortality. This study assessed green area in year 2000 for only the metropolitan area for 340 cities in 22 countries. We calculated on a larger scale (512 cities

in 34 countries) and used sophisticated green space values for each city during the study period. A study in Greater Athens Area, Greece, observed no effect modification of greenspace on temperature-mortality relationship for respiratory and cardiovascular mortality.<sup>43</sup>

Many studies have shown that greenspace is associated with all-cause, respiratory, cardiovascular, heat-related mortality.<sup>44-46</sup> A national cohort in Canada showed a decreased all-cause mortality risk of 8-12% per IQR in exposure to greenspace (NDVI).<sup>44</sup> Also, the risk for respiratory and cardiovascular mortality decreased with increasing greenness with adjustment of socioeconomic and air pollution variables. Villeneuve et al. showed that higher greenspace exposure (NDVI within 500 m of residence) was associated with reduced non-accidental mortality, and the strongest association was found for respiratory disease mortality, while controlling for ambient air pollution in Ontario, Canada.<sup>45</sup> A cohort study in the USA found that greenness was associated with reduced overall, cancer, respiratory and kidney disease mortality, and no association with other causes including cardiovascular disease.<sup>46</sup> Studies found that higher exposure to greenspace was associated with decreased levels of depression, anxiety, and stress.<sup>47-49</sup> Moreover, higher greenspace is associated with higher levels of social engagement; reduces air pollution such as particulate matter, sulfur dioxide (SO<sub>2</sub>), and carbon monoxide; and alleviates thermal discomfort during heat stress.<sup>50-52</sup> These mechanisms could relate to our study results, where we found effect modification of the greenspace-heat association in all-cause and respiratory mortality. Greenspace affects various causes of mortality through mental health, social engagement, physical activity, and air pollution. This could link to possible effect modification of the temperature-mortality relationship.

The study results suggest that higher greenspace results in protective effects on heat-related mortality in most regions. The total heat-related mortality attributable fraction increased as the

greenspace level decreased. However, this relationship could have geographical variability. UK and Canada with the lowest mean temperatures (16.34°C and 17.29°C, respectively) had a relatively small attributable fraction related to heat compared to other countries, and countries in Europe (Spain, France, and Italy) showed a high attributable fraction with a low greenspace level. Hot regions, such as Thailand and Brazil, had an average heat-related mortality attributable fraction (0.27 and 0.19, respectively) with moderate greenspace level (EVI: 0.41, 0.28; NDVI: 0.57, 0.48). Since our dataset includes various climate regions and countries, these findings could contribute to efforts to estimate the global impact of climate change in different greenspace level settings.

There are some limitations to this study. Observation periods and data collection procedures are not the same in all countries. Since different countries have different protocols and logistics, and although we used government records for air pollution, all countries do not have a consistent data collection process. However, the two-stage analytical framework used in this study included indicators for countries as meta-predictors in the second-stage meta-regression, which could account for any structural difference across countries as the fixed-effects indicators. This approach was used in similar multi-city multi-country settings.<sup>42</sup> Many previous studies used a single metric for greenspace, while in this study we used EVI for our main analysis and NDVI for sensitivity analysis. Satellite measured vegetation is widely used in various greenspace studies, but these measures lack assessment of the quality of greenspace and could lack accuracy in some regions. Also, there are limitations in EVI and NDVI for representing the greenspace itself. These indexes do not cover accessibility of green space, different types of vegetation, or the specific land cover characteristics that might be an important factor. However, studies validating EVI and NDVI have shown high performance in epidemiology study settings.<sup>53, 54</sup> Also, this study did not consider the

different urbanization level among cities and countries, although all our study areas are urban centers. Despite these limitations, this study assessed the effect modification of heat-related mortality in a worldwide setting. This allows incorporation of different temperature, greenness values, and climate settings while examining the effect modification of greenspace on the temperature-mortality relationship.

This study shows that increasing the amount of greenspace could be one of the strategies to counteract the adverse effects of heat in urban areas. Therefore, the greening policy for health benefits should consider implementing green structures such as urban parks in urban planning.