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

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Summary

Background Identifying how greenspace impacts the temperature-mortality relationship in urban environments is crucial, especially given climate change and rapid urbanization. However, the effect modification of greenspace on heat-related mortality has been typically focused on a localized area or single country. This study examined the heat-mortality relationship among different greenspace levels in a global setting.

Methods We collected daily ambient temperature and mortality data for 452 locations in 24 countries and used Enhanced Vegetation Index (EVI) as the greenspace measurement. We used distributed lag non-linear model to estimate the heat-mortality relationship in each city and the estimates were pooled adjusting for city-specific average temperature, city-specific temperature range, city-specific population density, and gross domestic product (GDP). The effect modification of greenspace was evaluated by comparing the heat-related mortality risk for different greenspace groups (low, medium, and high), which were divided into terciles among 452 locations.

Findings Cities with high greenspace value had the lowest heat-mortality relative risk of 1·19 (95% CI: 1·13, 1·25), while the heat-related relative risk was 1·46 (95% CI: 1·31, 1·62) for cities with low greenspace when comparing the 99th temperature and the minimum mortality temperature. A 20% increase of greenspace is associated with a 9·02% (95% CI: 8·88, 9·16) decrease in the heat-related attributable fraction, and if this association is causal (which is not within the scope of this study to assess), such a reduction could save approximately 933 excess deaths per year in 24 countries.

Interpretation Our findings can inform communities on the potential health benefits of greenspaces in the urban environment and mitigation measures regarding the impacts of climate change.

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Keywords: Greenspace; Heat; Mortality; Effect modification

Introduction

Currently, more than half of the world's population live in urban areas and this population is expected to increase,[1] therefore it is critical to understand the results created by the urban environment.[2] Urbanization plays an important role in driving surface warming at the local scale generating the urban heat island (UHI) effect and extreme weather events, such as heatwave.[3–5] In particular, as exposure to high temperature increases due to climate change and the UHI effect, the sustainability of the rapidly growing urban environment around the world is being threatened.[6–8] 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).[9] The temperature-mortality relationship varies across countries, cities, and climatic regions due to various geographic and socioeconomic factors.[10,11] Therefore, identifying the potential factors of the urban environment that affect the temperature-mortality relationship in different urban settings is critical to mitigate health impacts due to climate change.

Urbanization increases impervious surfaces in urban and suburban areas, as buildings, concrete, and asphalt

Research in context

Evidence before this study

Urbanization and climate change have resulted in changes to the urban environment, including the urban heat island effect and contributions to other extreme weather events. Recently, as metropolitan areas have become denser due to rapid urbanization, environmental problems such as high temperatures are also worsening. Many studies showed that high temperatures increase health risks, including mortality. Therefore, identifying factors that could mitigate the high-temperature conditions in urban environments are a crucial part of climate change mitigation strategies. Many studies found that urban green spaces may play an important role in mitigating heat. Specifically, large green spaces have shown a significant and positive cooling effect. Vegetation can promote air convection through shading and evapotranspiration, which indicates that dense vegetation can lower air temperature. Therefore, more greenspace could result in lower temperatures during the warm season, which would lower exposure to high temperatures that impact human health. Importantly, while greenspace can lower exposure to heat, this study examined how greenspace modifies the heat-health relationship. Some studies have investigated this issue. For example, studies found that heat-related mortality and ambulance calls are negatively correlated with the amount of greenspace coverage. However, most previous work on how greenspace modifies the heat-health relationship was based on one country or region. Research is needed on a global scale to understand how greenspace in urban areas among different countries, with different populations, levels of urbanization, and types of greenspace, can modify the relationship between extreme temperatures and health. As climate change is anticipated to increase temperatures and the associated health consequences worldwide, greenspace may be a plausible mitigation strategy for cities in order to address heat-related health impacts at present and in the future.

Added value of this study

In this study, we explored the effect modification of greenspace on the heat-mortality relationship on a global scale. With a dataset of 452 locations from 24 countries located in various climate zones and continents, this study incorporated variability in greenspace, temperature, and population characteristics. We found that, based on 452 locations, the heat-mortality risks differed with greenspace category and the cities with higher greenspace values had lower heat-mortality risk than those with lower greenspace values.

Implications of all the available evidence

Our findings provide evidence that higher greenspace reduces the heat-related mortality, which is similar to other previous smaller studies, and our study results were consistent in different countries around various climate zones. These findings indicate that disparate greenspace levels, temperature, and environment settings should be considered when developing policies and strategies in climate change mitigation and public health adaptation. This study adds to the existing literature that greenspace can reduce the urban heat island effect, by providing evidence for the theory that greenspace can also lower the heat-mortality association, and documents such impacts on a global scale.

trap heat and contribute to the warming effect.[12] However, within these urbanized settings, vegetation is recognized as a crucial factor in changing the micro- and macro- climate.[13] A study conducted in China found that the highest mean land surface temperature (LST) were buildings and roads, and greenspace had a good cooling effect.[14] Also, the greenspace patch intensity was negatively correlated with UHI intensity in Illinois-Indiana-Ohio, United States.[15] Measured air temperature in 62 parks and forests of Leipzig, Germany, showed that the cooling effect of parks and forests increased as the green area increased.[16] Vegetation lowers the temperature close to the surface through shading, evapotranspiration, and absorbing solar radiation through photosynthesis.[17]

Urban greenness can modify the ambient temperature and atmospheric moisture, which may change temperature-related health risks, with differences across locations.[18] Previous studies found that lower heat-related morbidity and mortality are associated with higher vegetation coverage.[19–21] Marginal increase in tree canopy (from <5% to >5%) was found to reduce about 80% of heat-related ambulance calls in Canada.[19] In Korea, heat-mortality risk was highest in regions with low greenspace values.[21] Also, in Barcelona, the effect of heat related mortality was higher in the census tracts with residents perceiving little surrounding greenness (RR=1·29, 95% CI 1·01 to 1·65).[20] However, most of the previous studies focused on one country or city. Evaluating the characteristics of the urban environment is important to understand the full spectrum of consequences for human health. Future research should consider different types of greenspace, including different forms of vegetation, to better understand their impact on the relationship between heat and health. Therefore, a global study is needed to understand how greenspaces among different countries modify the heat-mortality relationship. In this study, we explore the hypothesis that higher levels of greenspace are associated with lower heat-mortality risk. We evaluated the effects of urban vegetation on the heat-related mortality in a multi-city, multi-country dimension. We divided 452 locations from 24 countries into three groups based on urban vegetation of each location and estimated the heat-mortality relationship. Also, we estimated the potential attributable fraction change based on different increases in greenspace scenarios.

Methods

Ethics statement

Ethical approval was not required for the analysis of aggregated anonymized data from the MCC Collaborative Research Network database.

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.[22,23] We obtained daily time-series data of mortality (all-cause/ respiratory/ cardiovascular) and daily mean temperature for each of 452 locations in 24 countries during the 4 warmest months. 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 A00 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). A detailed description of the data by country is provided in the appendix (pp 2, 4). 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 S1.

For each city, we estimated greenness using the Enhanced Vegetation Index (EVI) and Normalized Difference Vegetation Index (NDVI) from the Moderate Resolution Imaging Spectroradiometer product MOD13Q1. The specific details regarding greenspace calculations are described in the appendix (pp 2,3). The average of the calculated EVI values through the observation period was used as the representative greenness index of each city. 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 divided the 452 cities into three groups based on greenspace values as low, medium, and high with approximately one-third of the locations in each category. There were 151 cities in the high greenspace group (EVI $\geq$ 0·42; NDVI $\geq$ 0·62), 150 cities in the medium greenspace group (0·33$\leq$ EVI $<$0·42; 0·51$\leq$ NDVI $<$0·62), and 151 cities in the low greenspace group (EVI $<$ 0·33; NDVI $<$ 0·51). The specific locations for each greenspace group are shown in Table S1. We conducted a two-stage seasonal analysis using time-series data for each different greenspace group. 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.[22,23]

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 4 warmest 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). 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 flexible exposure-response relationship and 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 50th and 90th 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. Previous studies assessing heat-mortality relationship have used a 10-day lag period, since the lag effect of heat is mostly captured in 0-10 day lag period whereas the cold effect lasts for 0-25 lag days,[24,25] although the lag structure used varies by study. Choices of modelling assumptions and lag days are based on a previous multi-country study.[22,23] The first-stage analysis was performed with the R packages *dlnm*.

Second-stage pooled analysis. In the second stage analysis, we performed meta-regression with random effects using the location-specific estimates from the first-stage analysis (heat-mortality RRs).[26] The basic characteristics of potential meta-predictors for different greenspace is shown in Table S2. This table has summaries of the following variables: latitude, summer mean temperature, temperature range, humidity, GDP, population density, $PM_{2.5}$, and unemployment. We provide these values overall (across all cities) and separately for each of the three categories of greenness (low, medium, and high) for both EVI and NDVI. Based on the effect of each meta-predictors in the meta-regression separately, the meta-predictors adjusted in the final model were selected (Table S3). City-specific average temperature, city-specific temperature range, city-specific population density, and GDP were adjusted as meta-predictors in a multivariate meta-regression, and random effects for the indicator obtained by the combination of climate zones and country was considered.

The minimum mortality temperature (MMT) is the temperature at which risk of mortality is lowest, which we obtained from the non-linear heat-mortality relationship curve. This indicator is commonly used in temperature-mortality studies and the details of this method are provided elsewhere.[10,27] The city-specific temperature at which the mortality is minimum (i.e. the MMT), was derived from the best linear unbiased prediction of the overall cumulative exposure-response curve for each location. We derived the pooled heat-mortality relative risk (RR) comparing the 99th temperature percentile to the minimum mortality temperature (MMT) for each greenspace group (high, medium, low).

Estimation of city-specific heat attributable fraction. We calculated the fraction of deaths attributable to non-optimum temperatures (i.e., different from MMT) in each location using the first-stage cumulative exposure-response association. This is described in a previous study.[28] Mortality attributable to heat was computed by summing the heat-related deaths occurring in days with temperatures higher than the MMT, and then dividing by the total number of deaths. The empirical confidence interval (95% Cis) of attributable risk was obtained empirically through 1,000 Monte Carlo simulations, assuming a multivariate normal distribution of the best linear unbiased predictions of the first-stage reduced coefficients.

We have computed heat attributable fraction change and excess deaths by different greenspace scenarios: 1%, 10%, and 20% increase of greenspace in all cities compared to the cities' original greenspace value. We used a multivariable meta-regression model using the AF as the response variable to compute the AF change for different greenspace scenarios.

The effect modification was estimated by comparing heat-related RR for different greenspace group (high, medium, and low greenspace) and AF change for three greenspace scenarios (1%, 10%, and 20% increase in greenspace). Analysis was also conducted separately for all-cause, respiratory, and cardiovascular mortality. Statistical analyses were performed in R software (version 4.0.3) and the R package *mixmeta* was used.

Statistics

The dataset used in this study is a time-series dataset with no specific sample size (i.e., all mortalities were included). Similarly, we did not use a randomized population but rather the whole study population for these cities. Thus, we did not add sentences on sample size determination or randomization. Data were aggregated at the city level and individual-level data or identifying information was not included. Cities without meteorological information (e.g., mean temperature) were excluded from the study.

Role of the funders

The funders of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

During 2000 to 2018 for the warm season (four warmest months for each city), mean temperature was highest for Southeastern Asia (29·13°C) and lowest for Northern Europe at 15·92°C. Based on the cities included, Southern Europe had the highest daily death counts for all-cause, cardiovascular, and respiratory mortality for a single city (35·70, 14·77, and 3·46 deaths/-day, respectively; Table 1). For the study cities, Southeastern Asia had the highest greenspace mean value (EVI of 0·46), whereas Western Asia had the lowest greenspace value with 0·09. For NDVI, Eastern Asia had the highest mean value of 0·65 and Western Asia had the lowest at 0·13. Specific summary for each city is presented in Table S4 and Table S5.

The geographical distribution, average mean temperature, and mean greenspace values (EVI) of the 452 locations represent the various regions included in this study, which include different climatic conditions from Northern Europe to Southeast Asia (Figure 1). Greenspace levels were higher in the East Asian continent and lower in the European continent. The mean NDVI values for each location are displayed in Figure S1.

The overall correlation between EVI and NDVI was 0·96. These greenness metrics were highly correlated at different temperature strata (high and low) as shown in Figure S2. We used EVI for our main analysis and conducted sensitivity analysis using NDVI. The correlation between EVI and mean temperature was 0.21 and 0.13 for NDVI and mean temperature.

The cumulative temperature-mortality association for different greenspace group is represented in Figure 2. Cities with low greenspace value (EVI<0·33) had a higher heat-related mortality risk compared to cities with high greenspace value (EVI ≥0·42) for summer temperature above 50 percentiles. The overall pooled heat-mortality relative risk (99th temperature vs. MMT) was 1·29 (95% CI: 1·23, 1·36). Heat-mortality relative risk was 1·46 (1·31, 1·62) in cities with low greenspace and 1·19 (1·13, 1·25) for high greenspace group (Table 2). We have examined effect modification of the heat-mortality relationship by greenspace as a continuous variable in Table 2. One interquartile range (IQR) increase in EVI (IQR: 0·145) was associated with a reduction of 12·44% (95%CI: 6·17, 18·3) in heat-mortality relative risk (comparing the 99th temperature percentile to the MMT), and one IQR increase in NDVI (0·194) was associated with a decrease 6·6% (0·1, 12·6) of heat-mortality relative risk (Table S6). The temperature-mortality curve (Figure S3), and the heat-mortality relative risk change was similar for NDVI (Table S6). Also, the heat-mortality relative risk was highest in low greenspace cities and lowest among the high greenspace group for cardiovascular and respiratory mortality, which is similar to all-cause mortality.

The pooled AF resulting from the temperature above MMT was 2·47% (95% CI: 2·26, 2·69). We compared the heat-related attributable fraction by different greenspace scenarios: 1) 1% increase (increase range: 0·0005, 0·006), 2) 10% increase (increase range: 0·005, 0·06),

Region	Number of cities	Temperature °C		Deaths/day [mean across cities]			Greenspace	
		Mean (SD)	Minimum, Maximum	All-cause	Cardiovascular	Respiratory	EVI, Mean (SD)	NDVI, Mean (SD)
Global	452	22·71 (4·42)	14·07, 30·18	19·30	5·00	2·20	0·34 (0·10)	0·53 (0·15)
Americas	132	22·37 (4·65)	15·50, 26·85	17·84	5·25	1·69	0·36 (0·06)	0·54 (0·07)
Northern America	119	20·64 (2·62)	15·84, 25·46	15·65	4·80	1·35	0·36 (0·07)	0·56 (0·08)
Latin America and the Caribbean	13	24·10 (6·69)	15·16, 28·23	20·02	5·70	2·04	0·35 (0·05)	0·52 (0·06)
Europe	130	18·81 (1·22)	16·51, 20·31	18·71	7·36	1·45	0·31 (0·06)	0·52 (0·09)
Northern Europe	7	15·92 (0·19)	15·72, 16·11	15·80	6·13	0·83	0·36 (0·05)	0·64 (0·09)
Southern Europe	42	23·74 (2·15)	18·48, 25·12	35·70	14·77	3·46	0·21 (0·07)	0·35 (0·12)
Western Europe	70	17·69 (1·29)	15·54, 20·20	11·50	3·10	0·85	0·29 (0·05)	0·47 (0·07)
Central Europe	11	17·89 (1·23)	16·29, 19·80	11·85	5·45	0·65	0·39 (0·07)	0·62 (0·09)
Africa	42	22·31 (2·37)	15·04, 27·56	27·30	4·00	3·10	0·26 (0·10)	0·45 (0·15)
Asia	148	27·01 (0·62)	25·97, 28·48	29·82	8·12	2·48	0·32 (0·07)	0·43 (0·08)
Western Asia	1	25·88 (-)	-	33·50	10·70	1·60	0·09 (-)	0·13 (-)
Eastern Asia	84	26·02 (0·66)	23·87, 26·94	31·65	6·65	3·00	0·42 (0·06)	0·65 (0·08)
South-eastern Asia	63	29·13 (0·57)	28·07, 30·01	24·30	7·00	2·85	0·46 (0·07)	0·63 (0·07)

***Table 1:* Summary of mean temperatures, number of deaths/day, and greenspace for 24 countries by continent and region.**

*Note: "-" indicates there were no available dataset for the specific region. Not all regions had multiple cities.

and 3) 20% increase (increase range: 0·01, 0·11). A decrease of 0·8% (95% CI: 0·7, 0·9) was expected when there is an 1% increase of greenspace in all cities (Table 3). A 20% increase of greenspace in all cities is associated to reduce heat-related all-cause mortality by 9% (95% CI: 8·9, 9·2). Similarly, 1% to 20% increase in NDVI in all cities expected to decrease heat-related attributable fraction 0·5 ~ 9·2% (Table S7).

Total 10,323 heat attributable deaths per year among 24 countries were expected to reduce approximately 50 heat attributable deaths per year when greenspace increase 1% and may be associated in reducing approximately 933 heat attributable deaths per year when greenspace increase 20% (Table S8). The excess deaths by different NDVI increase scenarios was comparable to EVI. Heat-related mortality for cardiovascular and respiratory mortality had a higher decrease in attributable fraction and excess deaths compared to all-cause mortality.

Our sensitivity analyses results indicate that our main findings are robust under different heat-mortality relative risk: 1) 99^{th} percentile vs 75^{th} temperature percentile and 2) 99^{th} percentile vs 90^{th} temperature percentile (Table S9). Also, the heat-mortality relative risk (99^{th} vs MMT) for all-cause mortality by different greenspace level (high, medium, and high) were similar when adjusting different parameters for the meta-predictors in a multivariate meta-regression: 1) adjusting for city-specific average temperature, city-specific temperature range, and population density as meta-predictors, 2) adjusting for city-specific average temperature, city-specific temperature range, and GDP as meta-predictors, 3) adjusting for city-specific average temperature, city-specific temperature range, and $PM_{2.5}$ as meta-predictors, 4) adjusting for city-specific average temperature and city-specific temperature range, 5) adjusting for region as categorical variable, city-specific average temperature, and city-specific temperature range, and 6) adjusting for Gini index. city-specific average temperature, and city-specific temperature range (Table S10).

Discussion

This study investigated the effect modification of greenspace on the heat-mortality relationship in 452 locations within 24 countries. To our knowledge, this study is the largest epidemiological study investigating greenspace as an effect modifier of heat-related mortality. We found that greenspace modifies the heat-related mortality for all-cause and cardiovascular diseases. Increase in greenspace was associated with protective effects on the heat-mortality relationship for all-cause and cardiovascular mortality.

Our results are consistent with 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

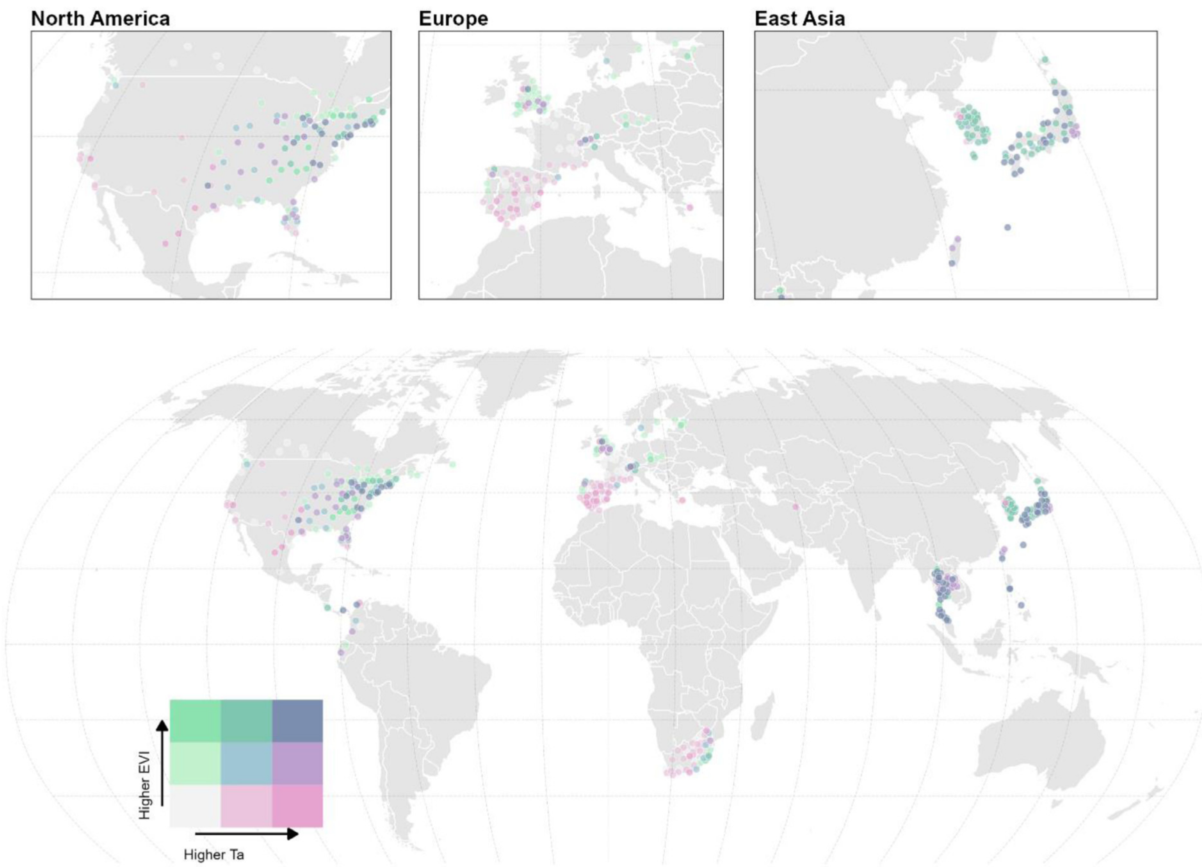

Figure 1. Map of the 452 locations included in the analysis with temperature and EVI.

Note: The locations represent metropolitan areas, provinces, or larger areas from 452 locations of 24 countries. Each color represents different range of the average greenspace value (EVI) shown in Table S2; and different ranges of average daily mean temperature shown in Table S1. High greenspace group (EVI $\geq$ 0·42), medium (0·33$\leq$ EVI $<$0·42), and low greenspace group (EVI $<$0·33); High temperature group ($T_a \geq$ 24·9), medium (20·6$\leq T_a <$24·9), and low temperature group ($T_a <$20·6).

increase in greenspace per 1,000 people could prevent 7·4 heat-related deaths.[29] In 17 Chinese cities, the heat-mortality effects were higher in cities with a low proportion of greenspace.[30] Urban greenspace was found to have a mitigating effect on heat-related mortality in the elderly population in Lisbon, Portugal.[31] However, few studies were conducted on a multi-country scale and also the existing literature largely focuses on total mortality rather than cause-specific mortality. A multi-country analysis with 340 cities, a subset of the location's cities used in this study, showed low heat mortality effects in cities with higher green area (square meters per million persons).[10] This result is consistent with our finding of effect modification on heat-related all-cause mortality. That study assessed green area in the year 2000 for only the metropolitan area for 340 cities in 22 countries. We calculated impacts on a larger scale (452 locations in 24 countries) and examined the greenspace in different categories for each city during the study period.

Urban parks and vegetations are approximately 1-2°C cooler than their urban surroundings, forming "park cool island" (PCI).[32] Previous studies found urban greenspace have cooling effects on their surroundings, mitigating the UHI effect.[33–36] Spronken-Smith and Oke et al. found that larger parks have stronger PCI effects,[35] and Shashua-Bar and Hoffman examined that tree-shaded area had the highest cooling effect.[36] Urban vegetation may reduce the extreme heat exposure, which would affect the temperature-related human morbidity and mortality. Many studies have shown that greenspace is associated with all-cause, respiratory, cardiovascular, heat-related mortality.[37–39] A national cohort in Canada showed a decreased all-cause mortality risk of 8-12% per IQR in exposure to greenspace (NDVI).[37] Also, the risk for respiratory and cardiovascular mortality decreased with increasing greenness with adjustment of socioeconomic and air pollution variables. A cohort study in the USA found that greenness was associated with reduced overall, cancer, respiratory

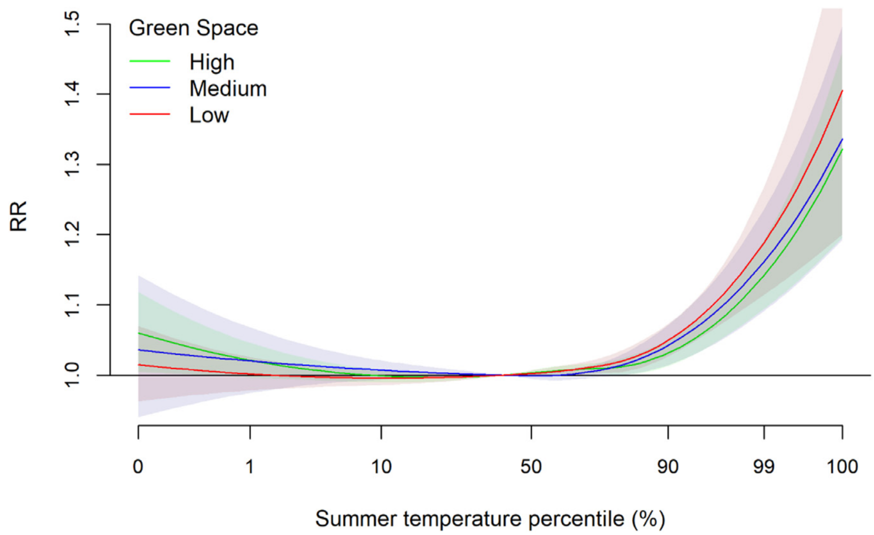

Figure 2. Overall cumulative temperature-mortality relationship by different greenspace level. The pooled relative risk was centered at the median temperatures (22·1°C); High greenspace group (EVI ≥ 0·42), medium (0·33≤ EVI <0·42), and low greenspace group (EVI <0·33).

and kidney disease mortality.[39] Higher exposure to greenspace is associated with decreased levels of depression, anxiety, and stress, and this could be linked to decreased mortality risk.[40,41] Greenspace affects various causes of mortality through mental health, social engagement, physical activity, and air pollution. Therefore, greenspace could modify vulnerability by reducing the risk. This is related to our study results, where we found significant effect modification of the association between heat and all-cause mortality with a lower mortality impact from heat in areas with higher greenness. 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 settings with various levels of greenspace.

The factors impacting the heat-related human health have changed over time, through air conditioning, and interventions such as heat alerts and heat wave warning systems.[42] Also, land use, built environment, and people's behavior have changed resulting in spatiotemporal differences in heat-mortality relationship. The health benefits of greenspace should be considered with urban planning in relation to their impacts (costs, health and other societal benefits) for other interventions. Many cities have implemented early heat warning system and cooling centers, which are shown to reduce heat exposure.[43] However, the heat warning system has some drawbacks in notifying the vulnerable population and in evaluating the heatwaves.[44] Specifically, heat warning systems are difficult to operationalize for those who cannot be reached through emails, text message, and phone calls. Therefore, multiple strategies such as greenspace and heat warning systems may be useful to reduce the public health burden from high temperatures.

There are some strengths and 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, 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.[10] We used city-level spatial resolution, which could be too large to capture the effect modification of greenspace on temperature-mortality relationship precisely. The dataset used in this study is mainly focused on cities in an urban environment, which does not address non-urban settings, such as suburban and rural areas. Further, greenspace was investigated at the city level, which does not address within-city heterogeneity of greenspace. Considering how greenspace may modify the heat-mortality relationship at a smaller scale (e.g., neighborhood) could help identify the vulnerable populations with higher risks and inform policy-makers on which types of greenspace are most impactful. This could further help targeted interventions and reduce health inequalities by prioritizing resource and healthcare.[45] Detailed analysis is needed based on intra-urban variations regarding greenspace, the built environment, community characteristics (e.g., socio-economic status), air pollution, and temperature. Satellite measured vegetation is widely used in greenspace studies, but these measures lack assessment of the quality of greenspace and could lack accuracy in some regions. These indexes do

	% change in heat-mortality relative risk per IQR EVI	Heat-mortality relative risk			
		Pooled	Low Greenspace	Medium Greenspace	High Greenspace
All	−12.44 (−18.30, −6.17)	1·29 (1·23, 1·36)	1·46 (1·31, 1·62)	1·24 (1·15, 1·34)	1·19 (1·13, 1·25)
Cardiovascular	−14.46 (−22.71, −5.34)	1·37 (1·27, 1·47)	1·52 (1·31, 1·77)	1·34 (1·20, 1·49)	1·26 (1·16, 1·36)
Respiratory	−12.24 (−23.09, 0.14)	1·34 (1·22, 1·47)	1·63 (1·32, 2·00)	1·24 (1·05, 1·48)	1·20 (1·09, 1·33)

***Table 2*: Association between greenspace and heat-related mortality relative risk and overall pooled heat-mortality relative risk by different level of greenspace for cause specific mortality. Association between greenspace and heat-mortality risk is presented as a percentage change in heat-related RR per interquartile range increase in greenspace (IQR: 0·145 (EVI)), where heat-related mortality risk refers to the mortality risk at the 99th percentile of the warm season temperature vs mortality risk at the minimum mortality temperature (MMT); values: RR (95% confidence interval).**

	Pooled attributable fraction (%)	Greenspace scenarios		
		1% increase	10% increase	20% increase
All	2·47 (2·26, 2·69)	−0·5 (−0·6, −0·3)	−4·6 (−4·8, −4·5)	−9·0 (−9·2, −8·9)
Cardiovascular	2·96 (2·68, 3·26)	−0·6 (−0·8, −0·5)	−5·9 (−6·0, −5·7)	−11·2 (−11·3, −11·1)
Respiratory	3·92 (3·54, 4·33)	−0·7 (−0·8, −0·6)	−6·6 (−6·7, −6·5)	−12·4 (−12·5, −12·3)

***Table 3*: Attributable fraction change by different greenspace scenarios for cause specific mortality. Heat-related attributable fraction caused by temperature over MMT; values: % decrease in AF (95% confidence interval).**

not cover accessibility of greenspace, different types of vegetation, or the specific land cover characteristics that might be important factors. Future studies considering specific parks accessible to the surrounding area, the walkability to the specific greenspace, and shades form by trees should be conducted. However, studies validating EVI and NDVI have shown high performance in epidemiology study settings.[46] Huete et al. found that both EVI and NDVI demonstrated a good dynamic range for assessing the spatial and temporal variations in vegetation amount and condition.[46] Also, when evaluating the effect modification of greenspace, we calculated the average greenspace values throughout the observation period, which did not take into account the temporal change of greenspace. The study periods were different among countries for this study dataset, so we adjusted for temporal trend in the model. However, greenspace can change over time such as increasing greenspace with development of urban parks or decreasing greenspace through further urbanization. In future studies, considering the greenspace change over time could be considered in the analysis. 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. Also, this study examined different greenspace scenarios, presenting the decrease in heat-related attributable fraction and decrease in excess deaths, which could be useful information for the local policymakers. This study shows that increasing the amount of greenspace could be one of the strategies to counteract the adverse health effects of heat in urban areas. Therefore, policies for improving health in urban settings should consider implementing green structures such as urban parks in urban planning.

Contributors

H.M.C. and W.L. performed data analysis. H.M.C., W. L., Y.G, and M.L.B. contributed conceptualizing. S.H. provided resources (provision and production of study materials) and data curation (production of software code for exposure assessments). W.L., D.R., A.U., A.E., A.M.V., A.Z., A.G., A.Z., A.T., B.A., B.F., C.Í., C.Å., E.I., E.L., F.M., F.A., F.S., H.O. H.K., J.K., J.M., J.S., J.J., K. K., M.H.D., M.S.R., M.P., N.R., N.S., S.O., S.T., X.S., Y. L.G., Y.G., and M.L.B. provided essential data resources. H.M.C. drafted the first version. H.M.C. and M.L.B. performed writing the manuscript. H.M.C., W.L., A.U., A. G., A.T., B.A., E.L., F.S., S.T., and M.L.B. conducted editing and reviewing. H.M.C. and D.R. have developed the figures. A.G. and B.A. verified the underlying data. All authors have read and acknowledged the final manuscript.

Data sharing statement

Data was collected within the Multi-Country Multi-City (MCC) Collaborative Research Network under a data sharing agreement and cannot be made publicly available. Researchers can refer to MCC participants, who are listed as coauthors of this Article, for information on accessing the data for each country.

Declaration of interests

K.K is a member of the ERS Environment and Health Committee, of the WHO TAG and of the UKHSA COMEAP. M.B. received consulting fees from EPA Clean Air Scientific Advisory Board, honorarium as a speaker, grant reviewer or advisor from Boston University, Korea University, Organization of Teratology Information Specialists, NIH, Health Canada, PAC-10, UKRI, AXA Research Fund Fellowship, Harvard and University of Montana, travel reimbursement from Boston University, Harvard, University of Illinois and University of Texas, is an unpaid member of National Academies Panels and Committees, The Lancet Countdown, 5th National Climate assessment and John Hopkins University, Department of Environmental Health and Engineering Advisory Board. The other authors declare no competing interests.

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Supplementary materials

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References

1 UN. 2018 August 19, 2020. Available from: https://www.un.org/development/desa/en/news/population/2018-revision-of-world-urbanization-prospects.html.

2 Kuddus MA, Tynan E, McBryde E. Urbanization: a problem for the rich and the poor? *Public Health Rev*. 2020;41(1):1.

3 Manoli G, Fatichi S, Schläpfer M, et al. Magnitude of urban heat islands largely explained by climate and population. *Nature*. 2019;573(7772):55–60.

4 Watts N, Amann M, Arnell N, et al. The 2020 report of the Lancet Countdown on health and climate change: responding to converging crises. *Lancet North Am Ed*. 2021;397(10269):129–170.

5 Meehl GA, Tebaldi C. More intense, more frequent, and longer lasting heat waves in the 21st century. *Science*. 2004;305(5686):994–997.

6 Wouters H, De Ridder K, Poelmans L, et al. Heat stress increase under climate change twice as large in cities as in rural areas: a study for a densely populated midlatitude maritime region. *Geophys Res Lett*. 2017;44(17):8997–9007.

7 Matthews TK, Wilby RL, Murphy C. Communicating the deadly consequences of global warming for human heat stress. *Proc Natl Acad Sci*. 2017;114(15):3861–3866.

8 Tuholske C, Caylor K, Funk C, et al. Global urban population exposure to extreme heat. *Proc Natl Acad Sci*. 2021;118(41):e2024792118.

9 Armstrong BG, Chalabi Z, Fenn B, et al. Association of mortality with high temperatures in a temperate climate: England and Wales. *J Epidemiol Community Health*. 2011;65(4):340–345.

10 Sera F, Armstrong B, Tobias A, et al. How urban characteristics affect vulnerability to heat and cold: a multi-country analysis. *Int J Epidemiol*. 2019;48(4):1101–1112.

11 Guo Y, Li S, Zhang Y, et al. Extremely cold and hot temperatures increase the risk of ischaemic heart disease mortality: epidemiological evidence from China. *Heart*. 2013;99(3):195–203.

12 Coseo P, Larsen L. How factors of land use/land cover, building configuration, and adjacent heat sources and sinks explain Urban Heat Islands in Chicago. *Landsc Urban Plan*. 2014;125:117–129.

13 Wilby R. A review of climate change impacts on the built environment. *Built Environ*. 2007;33:31–45.

14 Zhao Z-Q, He B-J, Li L-G, Wang H-B, Darko A. Profile and concentric zonal analysis of relationships between land use/land cover and land surface temperature: case study of Shenyang, China. *Energy Build*. 2017;155:282–295.

15 Li X, Zhou W. Optimizing urban greenspace spatial pattern to mitigate urban heat island effects: extending understanding from local to the city scale. *Urban Forest Urban Green*. 2019;41:255–263.

16 Jaganmohan M, Knapp S, Buchmann CM, Schwarz N. The bigger, the better? The influence of urban green space design on cooling effects for residential areas. *J Environ Qual*. 2016;45(1):134–145.

17 Mathey J, Rößler S, Lehmann I, Bräuer A. Urban green spaces: potentials and constraints for urban adaptation to climate change. Resilient cities: cities and adaptation to climate change. 2011.

18 Hu L, Li Q. Greenspace, bluespace, and their interactive influence on urban thermal environments. *Environ Res Lett*. 2020;15(3):034041.

19 Graham DA, Vanos JK, Kenny NA, Brown RD. The relationship between neighbourhood tree canopy cover and heat-related ambulance calls during extreme heat events in Toronto, Canada. *Urban Forest Urban Green*. 2016;20:180–186.

20 Xu Y, Dadvand P, Barrera-Gómez J, et al. Differences on the effect of heat waves on mortality by sociodemographic and urban landscape characteristics. *J Epidemiol Community Health*. 2013;67(6):519–525.

21 Son J-Y, Lane KJ, Lee J-T, Bell ML. Urban vegetation and heat-related mortality in Seoul, Korea. *Environ Res*. 2016;151:728–733.

22 Gasparrini A, Guo Y, Hashizume M, et al. Temporal variation in heat−mortality associations: a multicountry study. *Environ Health Perspect*. 2015;123(11):1200–1207.

23 Gasparrini A, Guo Y, Sera F, et al. Projections of temperature-related excess mortality under climate change scenarios. *Lancet Planet Health*. 2017;1(9):e360–e367.

24 Guo Y, Gasparrini A, Armstrong BG, et al. Heat wave and mortality: a multicountry, multicommunity study. *Environ Health Perspect*. 2017;125(8):087006.

25 Anderson BG, Bell ML. Weather-related mortality: how heat, cold, and heat waves affect mortality in the United States. *Epidemiology*. 2009;20(2):205–213.

26 Sera F, Armstrong B, Blangiardo M, Gasparrini A. An extended mixed-effects framework for meta-analysis. *Stat Med*. 2019;38(29):5429–5444.

27 Gasparrini A, Guo Y, Hashizume M, et al. Mortality risk attributable to high and low ambient temperature: a multicounty observational study. *Lancet*. 2015;386(9991):369–375.

28 Gasparrini A, Leone M. Attributable risk from distributed lag models. *BMC Med Res Methodol*. 2014;14:55.
29 Dang TN, Van DQ, Kusaka H, Seposo XT, Honda Y. Green space and deaths attributable to the urban heat island effect in Ho Chi Minh City. *Am J Public Health*. 2018;108(S2):S137–S143.
30 Ma W, Chen R, Kan H. Temperature-related mortality in 17 large Chinese cities: how heat and cold affect mortality in China. *Environ Res*. 2014;134:127–133.
31 Burkart K, Meier F, Schneider A, et al. Modification of heat-related mortality in an elderly urban population by vegetation (urban green) and proximity to water (urban blue): evidence from Lisbon, Portugal. *Environ Health Perspect*. 2016;124(7):927–934.
32 Jáuregui E. Influence of a large urban park on temperature and convective precipitation in a tropical city. *Energy Build*. 1990;15(3-4):457–463.
33 Chang C-R, Li M-H, Chang S-D. A preliminary study on the local cool-island intensity of Taipei city parks. *Landsc Urban Plan*. 2007;80(4):386–395.
34 Cao X, Onishi A, Chen J, Imura H. Quantifying the cool island intensity of urban parks using ASTER and IKONOS data. *Landsc Urban Plan*. 2010;96(4):224–231.
35 Spronken-Smith R, Oke T. The thermal regime of urban parks in two cities with different summer climates. *Int J Remote Sens*. 1998;19(11):2085–2104.
36 Shashua-Bar L, Hoffman ME. Vegetation as a climatic component in the design of an urban street: an empirical model for predicting the cooling effect of urban green areas with trees. *Energy Build*. 2000;31(3):221–235.
37 Crouse DL, Pinault L, Balram A, et al. Urban greenness and mortality in Canada's largest cities: a national cohort study. *Lancet Planet Health*. 2017;1(7):e289–e297.
38 Villeneuve PJ, Jerrett M, Su JG, et al. A cohort study relating urban green space with mortality in Ontario, Canada. *Environ Res*. 2012;115:51–58.
39 James P, Hart JE, Banay RF, Laden F. Exposure to greenness and mortality in a nationwide prospective cohort study of women. *Environ Health Perspect*. 2016;124(9):1344–1352.
40 Gascon M, Triguero-Mas M, Martínez D, et al. Mental health benefits of long-term exposure to residential green and blue spaces: a systematic review. *Int J Environ Res Public Health*. 2015;12(4):4354–4379.
41 Maas J, van Dillen SME, Verheij RA, Groenewegen PP. Social contacts as a possible mechanism behind the relation between green space and health. *Health Place*. 2009;15(2):586–595.
42 Bobb JF, Peng RD, Bell ML, Dominici F. Heat-related mortality and adaptation to heat in the United States. *Environ Health Perspect*. 2014;122(8):811–816.
43 Stone B, Jr., Vargo J, Liu P, et al. Avoided heat-related mortality through climate adaptation strategies in three US cities. *PLoS One*. 2014;9(6):e100852.
44 Lowe D, Ebi KL, Forsberg B. Heatwave early warning systems and adaptation advice to reduce human health consequences of heatwaves. *Int J Environ Res Public Health*. 2011;8(12):4623–4648.
45 Fann N, Roman HA, Fulcher CM, et al. Maximizing health benefits and minimizing inequality: incorporating local-scale data in the design and evaluation of air quality policies. *Risk Anal*. 2011;31(6):908–922.
46 Huete A, Didan K, Miura T, Rodriguez EP, Gao X, Ferreira LG. Overview of the radiometric and biophysical performance of the MODIS vegetation indices. *Remote Sens Environ*. 2002;83(1):195–213.