

## Vulnerability to Heat-related Mortality

Author(s): Tarik Benmarhnia, Séverine Deguen, Jay S. Kaufman and Audrey Smargiassi

Source: *Epidemiology*, November 2015, Vol. 26, No. 6 (November 2015), pp. 781-793

Published by: Lippincott Williams & Wilkins

Stable URL: <https://www.jstor.org/stable/10.2307/26511729>

### REFERENCES

Linked references are available on JSTOR for this article:

[https://www.jstor.org/stable/10.2307/26511729?seq=1&cid=pdf-reference#references\\_tab\\_contents](https://www.jstor.org/stable/10.2307/26511729?seq=1&cid=pdf-reference#references_tab_contents)

You may need to log in to JSTOR to access the linked references.

---

JSTOR is a not-for-profit service that helps scholars, researchers, and students discover, use, and build upon a wide range of content in a trusted digital archive. We use information technology and tools to increase productivity and facilitate new forms of scholarship. For more information about JSTOR, please contact [support@jstor.org](mailto:support@jstor.org).

Your use of the JSTOR archive indicates your acceptance of the Terms & Conditions of Use, available at <https://about.jstor.org/terms>



Lippincott Williams & Wilkins is collaborating with JSTOR to digitize, preserve and extend access to *Epidemiology*

JSTOR

# Vulnerability to Heat-related Mortality

## A Systematic Review, Meta-analysis, and Meta-regression Analysis

Tarik Benmarhnia,<sup>a,b</sup> Séverine Deguen,<sup>b,c</sup> Jay S. Kaufman,<sup>d</sup> and Audrey Smargiassi<sup>a,e</sup>

**Background:** Addressing vulnerability to heat-related mortality is a necessary step in the development of policies dictated by heat action plans. We aimed to provide a systematic assessment of the epidemiologic evidence regarding vulnerability to heat-related mortality.

**Methods:** Studies assessing the association between high ambient temperature or heat waves and mortality among different subgroups and published between January 1980 and August 2014 were selected. Estimates of association for all the included subgroups were extracted. We assessed the presence of heterogeneous effects between subgroups conducting Cochran *Q* tests. We conducted random effect meta-analyses of ratios of relative risks (RRR) for high ambient temperature studies. We performed random effects meta-regression analyses to investigate factors associated with the magnitude of the RRR.

**Results:** Sixty-one studies were included. Using the Cochran *Q* test, we consistently found evidence of vulnerability for the elderly ages >85 years. We found a pooled RRR of 0.99 (95% confidence interval [CI] = 0.97, 1.01) for male sex, 1.02 (95% CI = 1.01, 1.03) for age >65 years, 1.04 (95% CI = 1.02, 1.07) for ages >75 years, 1.03 (95% CI = 1.01, 1.05) for low individual socioeconomic status (SES), and 1.01 (95% CI = 0.99, 1.02) for low ecologic SES.

**Conclusions:** We found strongest evidence of heat-related vulnerability for the elderly ages >65 and >75 years and low SES groups (at the individual level). Studies are needed to clarify if other subgroups (e.g., children, people living alone) are also vulnerable to heat to inform public health programs.

(*Epidemiology* 2015;26: 781–793)

Submitted 20 November 2014; accepted 30 July 2015.

From the <sup>a</sup>Université de Montréal, Département de Santé Environnementale et Santé au Travail, Montréal, QC, Canada; <sup>b</sup>Ecole des Hautes Etudes en Santé Publique (EHESP) School of Public Health, Rennes, Sorbonne-Paris Cité, France; <sup>c</sup>INSERM U1085 (IRSET), Rennes, France; <sup>d</sup>Department of Epidemiology, Biostatistics, and Occupational Health, McGill University, Montreal, QC, Canada; and <sup>e</sup>Institut National de Santé Publique du Québec, Montréal, QC, Canada.

Supported by the EHESP School of Public Health and the School of Public Health of the University of Montreal.

The authors report no conflicts of interest.

**SDC** Supplemental digital content is available through direct URL citations in the HTML and PDF versions of this article ([www.epidem.com](http://www.epidem.com)).

This content is not peer-reviewed or copy-edited; it is the sole responsibility of the authors.

Correspondence: Audrey Smargiassi, Département de Santé Environnementale et Santé au Travail, École de Santé Publique, Université de Montréal, Pavillon Marguerite d'Youville, C.P. 6128, Succursale Centre-Ville, Montréal, QC, Canada H3C 3J7. E-mail: [audrey.smargiassi@umontreal.ca](mailto:audrey.smargiassi@umontreal.ca).

Copyright © 2015 Wolters Kluwer Health, Inc. All rights reserved.

ISSN: 1044-3983/15/2606-0781

DOI: 10.1097/EDE.0000000000000375

Rising temperatures, and their impact on human mortality, are a primary public health concern in the context of climate change. Studies of heat and mortality have increased during the past two decades, particularly with the documentation of prominent events including heat waves in Chicago in 1995<sup>1</sup> and in Western Europe in 2003.<sup>2</sup> In the heat-related mortality literature, it is typical to distinguish two types of heat exposures: first, increases in ambient temperatures which can be defined as periods of high temperatures over single days, associated with mortality, and second, consecutive days of high heat also known as heat-wave days, where population mortality is greater than on nonheat-wave days. Many literature reviews<sup>3–8</sup> have examined the evidence for associations of mortality with elevated ambient temperatures, focusing on the variation of heat effect thresholds or heat slopes, as a measure of effect size.<sup>7</sup>

In epidemiologic studies of heat-related mortality, various subgroups have been identified as being more severely impacted, and are therefore defined as “vulnerable.”<sup>9,10</sup> Vulnerability is often used synonymously with susceptibility, although they are sometimes used to refer to separate processes related to whether the impacts are from external factors or intrinsic.<sup>11</sup> Vulnerability can thus be defined as “the condition of having one or more interacting causes already and therefore being susceptible to the effect of the other”<sup>11</sup> or as “a greater likelihood of an adverse outcome given a specific exposure, compared with the general population, including both host (individual) and environmental (contextual) factors.”<sup>12</sup> Factors that mark greater vulnerability are modifiers of the association between an exposure and mortality, whenever the causal effect of the exposure of interest differs across levels of the modifying factor. Thus, there would be greater vulnerability in some subgroup whenever the causal effect of heat on mortality across two or more strata is heterogeneous.

Several individual or contextual subgroup characteristics marking greater vulnerability have been documented in the past decade of epidemiologic research. Individual vulnerability factors include age (elderly, children),<sup>3,13</sup> sex, and socioeconomic factors (education, ethnicity, income, or social isolation).<sup>4</sup> Contextual vulnerability factors include urban design (micro heat islands, population density), neighborhood (or ecologic) socioeconomic and community factors, and material conditions (air conditioning). These subgroups have

mostly been identified in studies on the relationship between temperature, or heat waves, and mortality, using stratified analyses.

Addressing vulnerability to heat-related mortality is a necessary step in the development of heat action plans,<sup>14</sup> to orient specific actions toward sensible subgroups.<sup>15,16</sup> The need to consider vulnerable populations in heat action plans and other related policies is well recognized.<sup>9,17,18</sup> The international epidemiologic literature can provide insights to orient policies dictated by heat action plans.

Yet, no study to date has systematically assessed the epidemiologic evidence concerning the characterization of vulnerable subgroups in the peer-reviewed heat-related mortality literature. The aim of this review is thus to systematically assess heterogeneity in the heat mortality associations with respect to individual and contextual population characteristics.

## METHODS

### Search Strategy

We identified peer-reviewed epidemiologic studies investigating potential heterogeneity in the associations between either high ambient temperature, or heat waves, and mortality, published between January 1980 and August 2014 in English. The search was conducted in September 2013 with an update in January 2015. The strategy used to conduct this review, in accordance with the PRISMA guidelines,<sup>19</sup> consisted of grouping keywords representing three categories: heat, mortality, and vulnerability (or heterogeneity). Keywords, titles, and abstracts were searched in PubMed and Elsevier Embase on the Ovid SP portal and in Web of Science as well. No restriction was put on the geographical location. The keywords used for this review were: (Heat OR climate OR environmental change OR heat stress OR hot weather OR high temperature OR heat effect OR hot effect OR hot temperature OR extreme temperature OR temperature) AND (Mortality OR health OR risk OR deaths) AND (vulnerability OR modif\* OR interaction OR susceptibility OR stratification OR differ\* OR hetero\*), where \* indicates any combination of subsequent letters.

### Selection of Studies

First, we screened manually the abstracts of all studies selected in the literature search according to the following exclusion criteria:

- (1) Studies without estimation of an association between mortality and heat.
- (2) Studies reporting associations between mortality and heat only for the entire population and not for subgroups constituting vulnerability (as described in the introduction).
- (3) Studies not performed on human populations.
- (4) Commentaries, editorials, or review articles.

We examined remaining articles from the previous step in full. In this second step, we further screened studies or

assessments within studies (i.e., by vulnerability subgroups) based on the following exclusion criteria:

- (1) Studies or vulnerability subgroups (within a study) with either no comparison group or no reference group. If a study assessed only one of the strata for a given vulnerability factor, it was not possible to assess heterogeneity, thus such estimates were not considered. For instance, if a study assessed the association among individuals of 65 years and older, without giving the corresponding association for the 0–64 years age group, this study was excluded.
- (2) Studies not reporting a nonheat-wave reference period (i.e., when the heat exposure did not vary) were also excluded. These studies were excluded because they were not estimating a heat-wave effect, by comparing heat-wave days with nonheat-wave days across different subgroups, but rather associations across different subgroups during heat-wave periods solely.
- (3) When the vulnerability subgroups considered were assessed only once in all of the final set of selected papers without distinguishing ambient temperature and heat-waves studies (e.g., body mass index in Xu et al.,<sup>20</sup> depression in Stafoggia et al.,<sup>10</sup> and smoking in Madrigano et al.<sup>21</sup>).
- (4) When subcategories of outcomes, such as cause of death or place of death, were considered as vulnerability factors. We excluded these subgroups as, based on the definition of vulnerability we use, they cannot logically modify the associations between heat and mortality.

In addition, the reference sections of studies identified as described above were searched, and pertinent references not initially identified were thus added. Where published literature reviews on heat-related health effects were cited in these reference lists, we additionally searched their references: the reference lists of eight reviews on temperature effects in children,<sup>13,22</sup> the elderly,<sup>3</sup> and general population<sup>4,5,7,8,23</sup> were thus searched by hand.

We separated the articles finally selected into two categories: (1) studies investigating associations of high ambient temperature with mortality and (2) studies investigating associations of heat waves with mortality.

### Data Extraction

From the selected studies, we extracted the estimates of association (e.g., relative risk [RR], incidence rate ratios [IRR], or odds ratio) for all the included subpopulations. The estimates were obtained from the published tables, figures (when it was possible to precisely determine the estimates of association from the published material), through text descriptions, supplemental material, and when accessible from the original data. When different lag effects were presented, we systematically used estimates of association between heat and mortality for the shortest lag effects presented. We then

documented the location of the studies, their time period, study design, the temperature exposure variable, and the following vulnerability factors (see details in Supplemental Material: eTable 1; <http://links.lww.com/EDE/A964>): (1) sex; (2) age: elderly and children; (3) individual and ecologic socioeconomic status (SES); (4) urban design and housing: intraurban heat variations, air conditioning, and population density; and (5) marital status.

### Heterogeneity Assessment Using the Cochran Q Test

To assess whether there was a heterogeneous association with high temperatures between subgroups, we conducted a Cochran *Q* test (see eAppendix 1 for details; <http://links.lww.com/EDE/A964>). We considered the presence of heterogeneity at the 10% level of significance.<sup>24,25</sup> When estimates for all groups combined were not reported, we calculated them as described in the supplemental material (eAppendix 1; <http://links.lww.com/EDE/A964>; for example, if a study presented estimates for men and women without presenting the estimate for both sexes combined). When analyses were conducted in the same study for different cities or for different time periods (e.g., different heat waves), we assessed the heterogeneity between different subgroups separately; for this reason, the number of strata comparisons is greater than the number of studies finally included. When more than two strata were presented, we compared only the two extreme groups. For example, if the heat associations were presented by quintiles of SES, we compared the least deprived group (first quintile) to the most deprived group (fifth quintile). For ethnic groups, we only compared White persons with Black persons or with non-White persons and we did not include Hispanic persons in the comparisons (as this group was only assessed in one study<sup>26</sup>). In one study,<sup>27</sup> many employment status categories were presented, and we only compared unemployed with white collar.

### Heterogeneity Assessment Using a Meta-analysis

In parallel to the heterogeneity assessment described above, we conducted a meta-analysis. We included only high ambient temperature studies. We did not conduct a meta-analysis for heat-wave studies since the study designs and methods were not comparable with one another. The minimum number of studies required to conduct a meta-analysis was fixed at 10.<sup>28,29</sup> We considered sex, age (more than 65 and more than 75), and SES (individual and ecologic definitions separately) subgroups. To compare subgroups within selected studies, we used the natural logarithm of the ratio of RR values (RRR; or analogous estimates of association) for the two compared subgroups (e.g.,  $RR_{men}/RR_{women}$ ) as described by Altman and Bland<sup>30</sup> or Bassler et al.<sup>31</sup> The formula used to calculate the standard errors of the ratios is presented in the eAppendix 1 (<http://links.lww.com/EDE/A964>). Moreover, for the studies that reported contrast definition by comparing two percentiles of temperature distributions, the highest percentile was always

above the 95th percentile. We used random-effects models to account for heterogeneity between studies. To assess heterogeneity of the  $\ln(RRR)$ s across individual studies, we used the  $I^2$  statistic ( $I^2 > 50\%$  was used as a threshold).<sup>29,32</sup> Publication bias was assessed with funnel plots and Egger's regression model.<sup>33</sup>

### Meta-regression Analysis

To investigate factors associated with the magnitude of the RRR, we performed random effects meta-regression analyses in which the dependent variable was the  $\ln(RRR)$  and independent variables were: study design (i.e., case-crossover or time series), continent (i.e., Europe, America, Asia, and Australia), and contrast definition (i.e., percentage increase comparing two percentiles of the temperature distribution or percent changes associated with degree units increases above a city specific threshold) for sex and age >65 years; the continent and the contrast definition for age >75 years; study design, continent, and contrast definition for SES. We also investigated in all meta-regression analysis the separate associations with the following variables: local temperature, using the yearly summer temperature average for single cities, and when multiple cities were assessed simultaneously, the average for all the cities was considered; latitude, creating four groups of latitude positions: (1) 60°N to 30°N, (2) 30°N to equator, (3) equator to 30°S, and (4) 30°S to 60°S; and study period, including the median year of study period (as indicated in Table) as indicator of change of heat associations over time.

We conducted a meta-regression for each variable separately. We estimated from these meta-regressions the regression coefficients (betas and 95% confidence interval [CI]), the  $R^2$  statistic (which represents the proportion of between-study variance explained by the covariate), the residual  $I^2$  (which represents after adjustment for the predictors, a measure of the percentage of the residual variation that is attributable to between-study heterogeneity), and the adjusted pooled RRR (and 95% CI).

## RESULTS

### Selection of Studies

Altogether the abstracts of 299 articles were assessed and 111 underwent in-depth review, with 61 studies fulfilling the inclusion criteria. Figure 1 presents the inclusion and exclusion of studies. Among the 111 articles retained based on the first exclusion criteria with abstract screening, 43 studies were excluded entirely because they did not report a comparison group. Among them, three studies<sup>88–90</sup> were excluded because they used a case-only design that did not permit the comparison of different subgroups, and seven studies were excluded because they only assessed the spatial variability of heat-related mortality. Eight studies were excluded because they showed variation only according to cities or regions. Among the 61 remaining studies, seven were identified through reference searching. Two studies were excluded



**TABLE.** Characteristics of High Ambient Temperature (n = 41) and Heat-wave (n = 20) Studies Included in the Review

Studies	Location	Published	Period	Study Design	Ambient Temperature Measure	Vulnerability Subgroups Included
High ambient temperature studies						
Almeida et al. <sup>34</sup>	Portugal	2013	2000–2004	Time series	Daily maximum apparent T°	Age
Baccini et al. <sup>35</sup>	12 countries in Europe	2008	1990–2000	Time series	Daily maximum apparent T° (except for the city of Barcelona where daily mean apparent T° was used)	Age
Bai et al. <sup>36</sup>	Tibet	2014	2008–2012	Time series	Daily mean T°	Sex, age, individual SES (education)
Basu & Ostro <sup>26</sup>	USA	2008	1999–2003	Case-crossover	Daily mean apparent T°	Age, individual SES (ethnic group)
Bell et al. <sup>37</sup>	Brazil, Chile, and Mexico	2008	1998–2002	Case-crossover	Daily mean apparent T°	Sex, age, individual SES (education)
Benmarhnia et al. <sup>38</sup>	France	2014	2004–2009	Time series	Daily mean T°	Sex, age, ecologic SES
Breitner et al. <sup>39</sup>	Germany	2014	1990–2006	Time series	Daily mean apparent T°	Age
Burkart et al. <sup>40</sup>	Bangladesh	2013	2008	Time series	Universal thermal climate index (b)	Sex, age (elderly and children), population density (ecologic), ecologic SES
Chan et al. <sup>41</sup>	People's Republic of China	2012	1998–2006	Time series	Daily mean T°	Sex, age, individual and ecologic SES, population density (ecologic), marital status
Egondi et al. <sup>42</sup>	Kenya	2012	2003–2008	Time series	Daily minimum and maximum T°	Sex
Goggins et al. <sup>43</sup>	People's Republic of China	2012	2001–2009	Time series	Daily mean T°	Ecologic SES, intraurban heat variations (ecologic),
Goggins et al. <sup>44</sup>	People's Republic of China	2013	1999–2008	Time series	Daily mean T°	Age
Gomez-Alcebo et al. <sup>45</sup>	Spain	2012	2003–2006	Time series	Daily mean, maximum and minimum T°	Sex, age
Gouveia et al. <sup>46</sup>	Brazil	2003	1991–1994	Time series	Daily mean, maximum and minimum T°	Age (elderly and children), ecologic SES
Hajat et al. <sup>47</sup>	Brazil, England, and India	2005	1991–2004	Time series	Daily minimum and maximum T°	Age (elderly and children)
Hajat et al. <sup>48</sup>	England	2007	1993–2003	Time series	Daily minimum and maximum T°	Sex, age, ecologic SES
Huang et al. <sup>49</sup>	People's Republic of China	2014	2008–2011	Time series	Daily maximum and minimum T°	Sex, age
Ishigami et al. <sup>50</sup>	England, Hungary, and Italy	2008	1993–2004	Time series	Daily mean T°	Ecologic SES
Kim & Joh <sup>51</sup>	South Korea	2006	2000–2002	Time series	Daily maximum T°	Individual SES (income)
Leone et al. <sup>52</sup>	7 Mediterranean countries	2013	1991–2007	Time series	Daily maximum apparent T°	Age (elderly and children)
Ma et al. <sup>53</sup>	People's Republic of China	2012	2001–2004	Time series	Daily average T°	Sex, age (elderly), individual SES
Madrigano et al. <sup>21</sup>	USA	2013	1995–2003	Case-crossover	Daily apparent T° <sup>a</sup>	Sex, age, individual SES (ethnic group, income), ecologic SES (% poverty), population density(ecologic), intraurban heat variations (ecologic)
Medina-Ramon & Schwartz <sup>54</sup>	USA	2007	1989–2000	Case-crossover	Daily maximum T°	Air conditioning (ecologic), population density (ecologic)
Muggeo & Hajat <sup>55</sup>	Chile and Italy	2009	1989–1991; 1997–2001	Time series	Daily mean T°	Age

(Continued)

TABLE. (Continued)

Studies	Location	Published	Period	Study Design	Ambient Temperature Measure	Vulnerability Subgroups Included
O'Neill et al. <sup>56</sup>	USA	2003	1986–1993	Time series	Daily mean apparent T°	Sex, age, individual SES (ethnic group, education)
O'Neill et al. <sup>57</sup>	USA	2005	1986–1994	Time series	Daily mean apparent T°	Individual SES (ethnic group)
Rocklov et al. <sup>58</sup>	Sweden	2011	1990–2002	Time series	Daily maximum apparent T°	Age
Rocklov et al. <sup>59</sup>	Sweden	2014	1990–2003	Time series	Daily maximum apparent T°	Sex, age, ecologic SES (wealth)
Smargiassi et al. <sup>60</sup>	Canada	2009	1990–2003	Case-crossover	Daily mean T°	Ecologic SES (lodging value), Intraurban heat variations (ecologic)
Son et al. <sup>61</sup>	South Korea	2011	2000–2007	Time series	Daily mean T°	Sex, age (elderly), individual SES (education)
Stafoggia et al. <sup>10</sup>	Italy	2006	1997–2003	Case-crossover	Daily mean apparent T°	Sex, age (elderly), individual SES (income), marital status
Stafoggia et al. <sup>62</sup>	Italy	2008	1997–2004	Case-crossover	Daily mean apparent T°	Sex, age (elderly), individual SES (income), marital status
Urban et al. <sup>63</sup>	Czech Republic	2013	1994–2009	Time series	Daily mean T°	Sex
Vaneckova et al. <sup>64</sup>	Australia	2008	1993–2004	Time series	Daily maximum T°	Age (elderly)
Wang et al. <sup>65</sup>	People's Republic of China	2013	2005–2008	Time series	Daily mean T°	Sex, age (elderly), individual SES (education)
Wang et al. <sup>66</sup>	Australia	2014	1995–2000	Time series	Daily mean T°	Age (elderly)
Wu et al. <sup>67</sup>	People's Republic of China	2013	2006–2010	Time series	Daily mean T°	Age
Xu et al. <sup>20</sup>	People's Republic of China	2013	1998–2009	Time series	Daily mean apparent T°	Sex
Yang et al. <sup>27</sup>	People's Republic of China	2012	2003–2007	Time series	Daily mean T°	Sex, age (elderly), individual SES (education, occupation)
Yu et al. <sup>68</sup>	Australia	2010	1996–2004	Time series	Daily mean T°	Sex, age (elderly), ecologic SES)
Yu et al. <sup>69</sup>	Australia	2011	1996–2004	Time series	Daily mean T°	Age (elderly)
Heat-wave studies						
Anderson & Bell <sup>70b</sup>	USA	2009	1987–2000	Time series	Two consecutive days with mean T° above the 99.5th percentile	Age (elderly)
Basagana et al. <sup>71</sup>	Spain	2011	1983–2006	Case-crossover	Days with maximum T° above the 95th percentile	Age (children)
Borell et al. <sup>72</sup>	Spain	2006	2003	Descriptive	NA	Individual SES (education)
Fouillet et al. <sup>73</sup>	France	2006	2003	Descriptive	NA	Sex, age (elderly and children), marital status
Huang et al. <sup>74</sup>	People's Republic of China	2010	2003	Descriptive	Three consecutive days with maximum T° > 35°C	Sex, age (elderly and children)
Hutter et al. <sup>75</sup>	Austria	2007	1998–2004	Time series	Three consecutive days with mean T° > 30°C	Sex
Kyseli et al. <sup>76</sup>	South Korea	2009	1991–2005	Descriptive	Three consecutive days with a daily heat index >33°C	Sex, age (elderly)
Lan et al. <sup>77</sup>	People's Republic of China	2012	2009–2010	Descriptive	Days with maximum T° above the 98th percentile	Sex, age (elderly)
Medina- Ramon et al. <sup>54</sup>	USA	2007	1989–2000	Case-crossover	Days with maximum T° above the 99th percentile	Air conditioning (ecologic), population density (ecologic)
Nitschke et al. <sup>78</sup>	Australia	2007	1993–2004	Descriptive	Three consecutive days with max T° > 35°C	Age (elderly and children)
Nitschke et al. <sup>79</sup>	Australia	2011	1993–2009	Descriptive	Three consecutive days with max T° > 35°C	Age (elderly and children)
Rey et al. <sup>80</sup>	France	2009	2000–2003	Descriptive	NA	Ecologic SES (deprivation index)
Robine et al. <sup>81</sup>	16 European countries	2012	1998–2003	Descriptive	NA	Sex

(Continued)

TABLE. (Continued)

Studies	Location	Published	Period	Study Design	Ambient Temperature Measure	Vulnerability Subgroups Included
Rocklov et al. <sup>59</sup>	Sweden	2014	1990–2002	Time series	Days with maximum T° above the 98th percentile	Sex, age, individual SES (wealth)
Rooney et al. <sup>82</sup>	England and Wales	1998	1995	Descriptive	NA	Sex, age (elderly)
Schifano et al. <sup>83</sup>	Italy	2009	2005–2007	Time series	A heat-wave episode was defined when daily maximum T° rises above a monthly threshold	Sex, ecologic SES, marital status
Son et al. <sup>84</sup>	South Korea	2012	2000–2007	Time series	Two consecutive days with mean T° above the 98th percentile	Sex, age (elderly), individual SES (education)
Tian et al. <sup>85</sup>	People's Republic of China	2013	2000–2011	Time series	Days with maximum T° above the 99th percentile	Sex, age (elderly)
Tong et al. <sup>86</sup>	Australia	2014	1988–2009	Time series	Two consecutive days with mean T° above the 99th percentile (except Sydney: 95th percentile)	Sex, age (elderly)
Xu et al. <sup>87</sup>	Spain	2013	1999–2006	Case-crossover	Days with maximum T° above the 95th percentile	Age (elderly), ecologic SES, intraurban heat variations (ecologic), air conditioning (ecologic)

<sup>a</sup>Extreme temperature was also used in this study but we only included estimates for daily apparent temperature.

<sup>b</sup>The study by Anderson & Bell<sup>70</sup> was retained only for heat-waves studies. For the high ambient temperature effects, the results they present do not meet our inclusion criterion. NA indicates not available; SES, socioeconomic status; T°, temperature.

because it was impossible to precisely determine the estimates of association from the published material.

### Description of Selected Studies

The characteristics of the included studies are presented in the Table. All the studies were published between 1998 and 2014. Twenty-four studies were conducted in Europe, 12 in North America, 19 in Asia, seven in Australia, one in Africa, and two studies that assessed multiple regions.

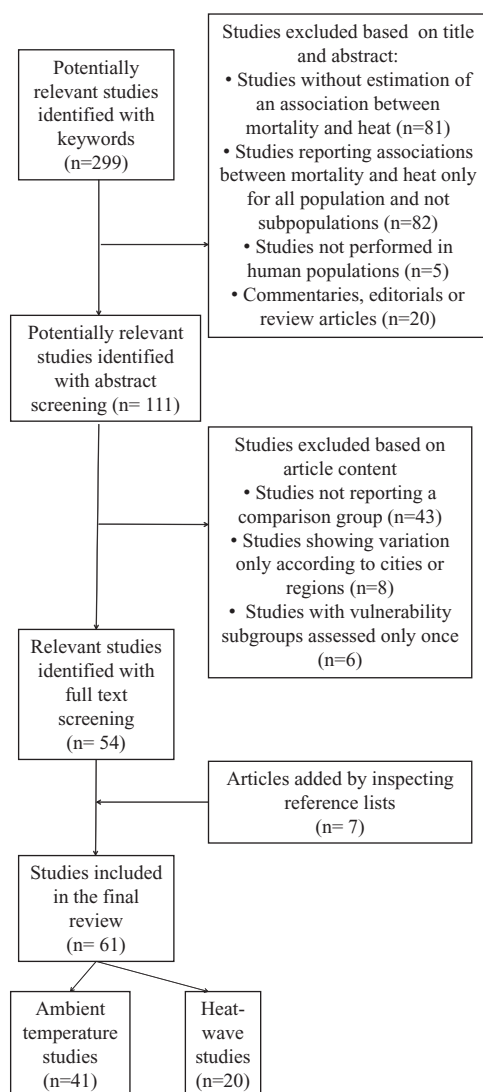
Forty-one studies retained assessed the association of high ambient temperature (Table) with mortality. Among these studies, 35 used a time-series design and six used a case-crossover design. Various contrast definitions between mortality and high ambient temperature were reported: 27 studies assessed the relationship by reporting percent changes or RR (or IRR) associated with degree unit increases (1°C, 3°C, 10°C, 10°F) above a city-specific threshold, and 14 reported percent increase or RR or odds ratios comparing two percentiles of temperature distributions.

Twenty of the retained studies assessed the association of heat waves (Table) with mortality. The definitions were very different from one study to another<sup>3,4</sup> as described in Table. Two types of definition have been used: one criterion requires 2 or 3 consecutive days with a specific temperature threshold, whereas the other criterion is based on single days above a temperature threshold. Among these studies, 10 used a descriptive design in which observed mortality rates during heat-wave days were compared with mortality rates during nonheat-wave

days across different subgroups. Seven studies used a time-series design, and three used a case-crossover design (Table). Various contrast definitions between mortality and heat waves were reported. Seven studies reported this relationship by a percent increase on heat-wave days compared with nonheat-wave days, and 13 with RR, IRR, or excess mortality rates for heat-wave days compared with nonheat-wave days.

### Heterogeneity Findings

We systematically compared all the included subgroup estimates of association between heat and mortality, separately for high ambient temperature (eTable 2; <http://links.lww.com/EDE/A964>) and for heat-wave studies (eTable 3; <http://links.lww.com/EDE/A964>). A description of the stratified estimates included in the review is presented in supplemental eTable 4 (<http://links.lww.com/EDE/A964>) for high ambient temperature studies and eTable 5 (<http://links.lww.com/EDE/A964>) for heat-waves studies. For studies of the association between high ambient temperature and mortality, we consistently found evidence of vulnerability for one subgroup: populations living in areas characterized by a low percentage of households having central air conditioning. For studies on the association between heat waves and mortality, we consistently found evidence of vulnerability for the following three subgroups: elderly persons above 85 years of age, populations living in hot places, and individuals who were not married (used as a proxy for social isolation<sup>41</sup>). Heterogeneity was not always found for



**FIGURE 1.** Flowchart outlining study selection. Nota Bene: two studies<sup>59,70</sup> investigated both ambient temperature and heat waves.

other subgroups studied, such as SES subgroups or children. Nonetheless when heterogeneity was found from studies on the association between temperature and mortality, the following subgroups were always identified as vulnerable: elderly persons by every age cut-point examined, low individual SES groups, populations living in high density areas, and unmarried individuals. The comparison of heterogeneity findings between high ambient temperature and heat-waves studies is presented in eTable 6 (<http://links.lww.com/EDE/A964>).

## Meta-analysis Results

We conducted meta-analyses of the  $\ln(RRR)$  for sex, age (more than 65 and more than 75 years), and SES (individual and ecologic separately) only on studies of high ambient temperature. We found that the pooled RRR for male sex was 0.99 (95% CI = 0.97, 1.01; eFigure 1; <http://links.lww.com/EDE/A964>).

A964). We found that the pooled ratio of RRs for individuals ages >65 years, compared with adults ages between 15 and 64 years was 1.02 (95% CI = 1.01, 1.03; Figure 2), and that the pooled ratio of RRs for those ages >75 years, compared with adults ages between 15 and 74 years was 1.04 (95% CI = 1.02, 1.07; eFigure 2; <http://links.lww.com/EDE/A964>). For SES measured at the individual level, we found that the pooled RRR for low SES compared with high SES groups was 1.03 (95% CI = 1.01, 1.05; Figure 3). For SES measured at the ecologic level, we found that the pooled RRR for low SES compared with high SES groups was 1.01 (95% CI = 0.99, 1.02; eFigure 3; <http://links.lww.com/EDE/A964>). Evidence of bias (assessed with Egger's test) was apparent for studies that assessed sex and age >75 years as vulnerable factors, but not for age >65 years and SES (eFigures 4–8; <http://links.lww.com/EDE/A964>).

## Meta-regression Results

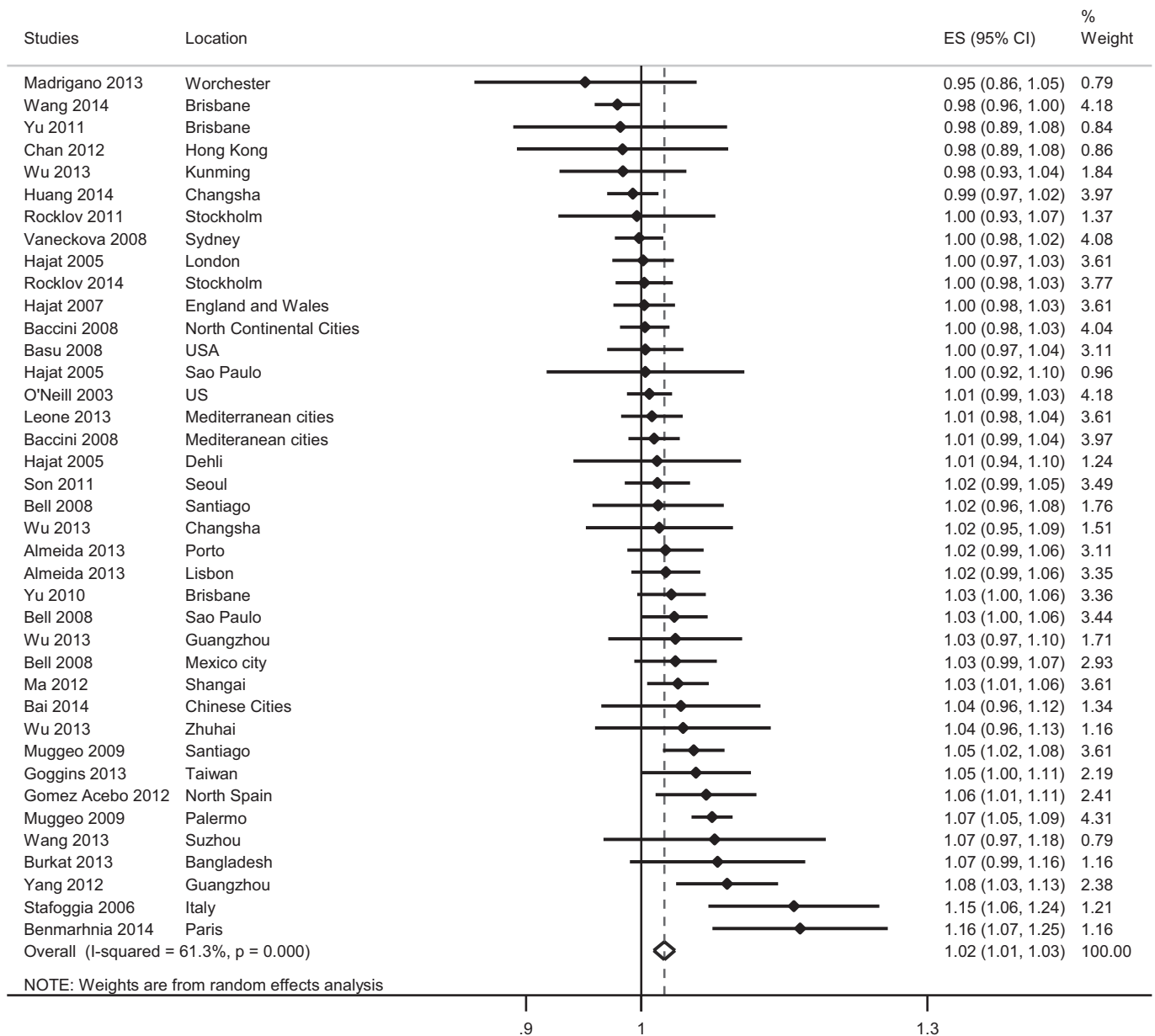
The large heterogeneity (all  $I^2 > 50\%$ ) found in the pooled RRR suggests the existence of study characteristics influencing this variability. We conducted meta-regression analyses to assess the influence of different study characteristics on meta-analysis heterogeneity. Of the study characteristics assessed for articles exploring age >75 years, only the contrast definition was a significant factor in explaining heterogeneity in the pooled RRR, such that the use of a percentage increase comparing two percentiles of the temperature distribution was associated with a higher vulnerability for the elderly. This suggests that when studies used a percentage increase as the contrast definition they were more likely to find vulnerability differences by age as compared with using the comparison of two percentiles of the temperature distribution. For individual SES studies, contrast definition was also related to the heterogeneity in the pooled RRR. Similarly to older age, the use of a percentage increase as the contrast was associated with higher vulnerability for low individual SES groups. Finally, we did not find that local temperature, latitude, or study period were related to the heterogeneity in the pooled RRR in any of the meta-regression conducted (eTables 7–11; <http://links.lww.com/EDE/A964>). The pooled estimate for the ratios for age >75 years versus younger age groups, adjusted for the contrast definition, was 1.11 (95% CI = 1.05, 1.17). The pooled ratio for low versus high SES measured at the individual level, adjusted for measures of associations, was 1.05 (95% CI = 1.03, 1.07). It is interesting to note that for individual SES, adjustment for the contrast definition decreased the  $I^2$  to 50%, which we define as a low degree of heterogeneity in the pooled RRR. The meta-regression results for individual SES and ecologic SES are, respectively, presented in eTables 7 and 8 (<http://links.lww.com/EDE/A964>) and other meta-regression results for sex, ages >65 and >75 years are presented in eTables 9–11 (<http://links.lww.com/EDE/A964>).

## DISCUSSION

### Summary of Results

In this systematic review, we assessed the published evidence supporting the presence of subgroups vulnerable to





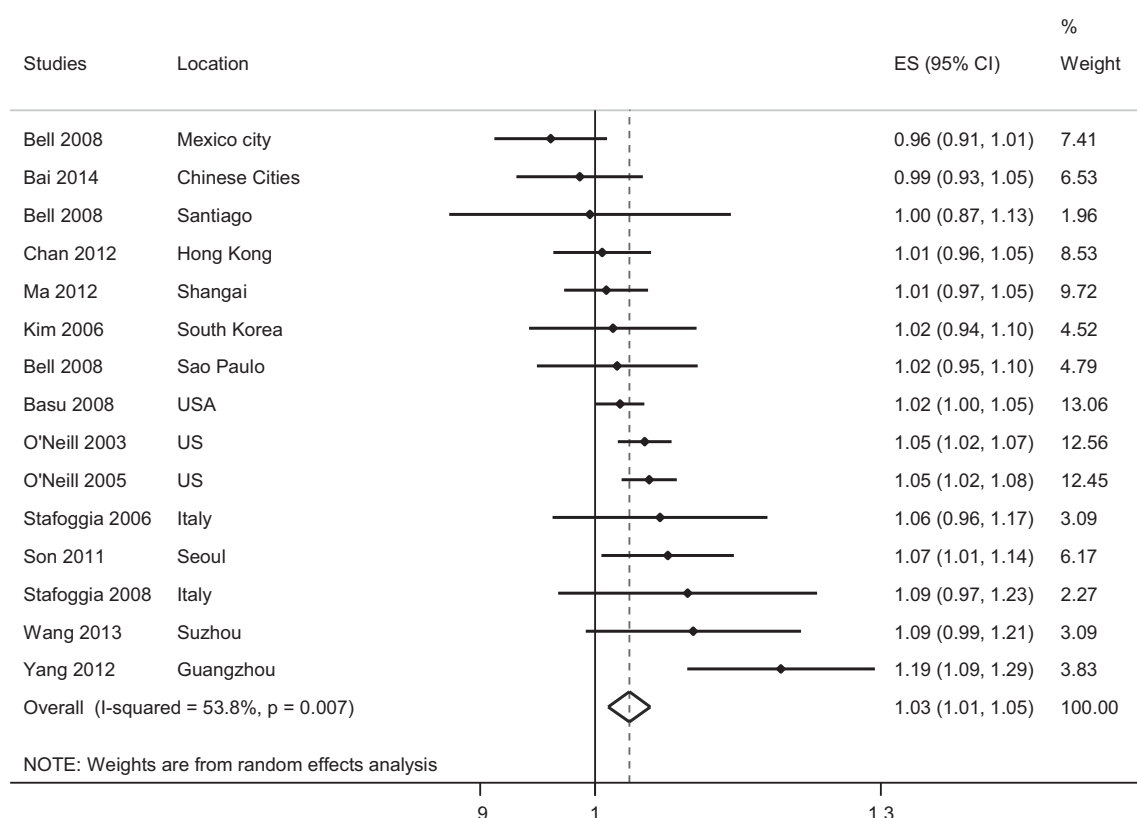
**FIGURE 2.** Meta-analysis of the ratio of the RRs according to ages 65+ (individuals ages >65 years, compared with adults ages between 15 and 64 years;  $RR_{65+}/RR_{15-64}$ ); n = 39 studies. ES indicates effect size; RR, relative risks.

heat-related mortality. Using Cochran's *Q* test, we found evidence of particular vulnerability for the most elderly and for populations living in areas characterized by a low percentage of households having central air conditioning. Vulnerability was also noted, in heat-wave studies, for populations living in hot places and for unmarried people, and in high ambient temperature studies, for people living in areas with a low percentage of households with central air conditioning, although very few assessments were available. On the other hand, results of the meta-analyses, focusing on high ambient temperature studies only, showed that elderly persons 65+ and 75+ years and low individual SES groups were

more vulnerable than their respective counterparts using the pooled estimate (RRR).

### Comparison of the Results with Current Knowledge

The results of this study can be compared with factors of vulnerability reported in various institutional guidelines, aimed at informing interventions for the prevention of heat-related mortality, such as the WHO heat action plan.<sup>91,92</sup> Heat action plans include heat warning systems during heat waves, plans for emergency measures, as well as actions aimed at reducing high ambient temperatures over the long term (e.g., greening activities).



**FIGURE 3.** Meta-analysis of the ratio of the RRs according to individual SES ( $RR_{lowSES}/RR_{highSES}$ );  $n = 15$  studies. ES indicates effect size; RR, relative risks; SES, socioeconomic status.

In the European WHO heat health action plan,<sup>91</sup> the vulnerable subgroups identified are the elderly, infants, and children, people with chronic diseases, people taking particular medications, people with low SES, and people in specific occupations. The identification of elderly people and those from low SES subgroups as being of particular vulnerability is concordant with our results. Lowe et al.,<sup>93</sup> in assessing the content of 12 European heat health action plans, also reported that in 11 out of 12 plans, the elderly, children, the chronically ill, and those on medication were considered vulnerable subgroups. Thus, it appears that some subgroups identified as vulnerable in both the heat action plans and in guidelines for planning were not assessed, or not reported as having heterogeneous associations with mortality, in this study. Other reviews addressed heat-related vulnerability. Bouchama et al.<sup>94</sup> conducted a meta-analysis of six case-control studies on heat-wave-related mortality, and found that both not leaving home daily and having a pre-existing illness were associated with higher risk, while greater social contact and having air conditioning were protective.

### Limitations of the Review

This review has some limitations. First, we excluded a number of studies because the statistical heterogeneity test could not be performed.

In epidemiologic studies addressing inequalities in the health effects of heat, such as those included in this review, the relative scale (e.g., risk ratio, incidence rate ratio, odds ratio, etc.) is most often used and the absolute scale (e.g., risk difference, incidence rate difference, etc.) is generally ignored.<sup>95</sup> However, baseline risks can differ considerably across different subgroups, as for elderly compared with younger adults. Using absolute measures when addressing vulnerabilities reflects not only differences in health impacts across different subgroups but also can be a more useful public health strategy, as risk difference corresponds directly to attributable cases.<sup>96,97</sup> Moreover, absolute measures will often highlight different patterns of inequalities between subgroups than relative measures.<sup>96,98</sup>

We conducted meta-analyses only for high ambient temperature studies to minimize the differences between study designs and methods of analysis. Still, we found considerable heterogeneity between studies (all  $I^2 > 50\%$ ), which makes complicates the interpretation of a single summary estimate.<sup>28,99</sup> Hence, we conducted meta-regression analyses to investigate factors associated with the magnitude of the RRR, and found that only the inclusion of contrast definition reduced the  $I^2$  estimate to 50% for the individual SES meta-analysis.

However, other study-related factors that were not assessed in this review, such as population age and sex

structures, presence of local heat action plans or population's resilience facing hot temperatures,<sup>7</sup> could explain some of the residual heterogeneity. We also did not assess the influence of lag effects. Yet, mortality displacement (i.e., when a proportion of excess deaths that occur during a hot day are deaths that would have occurred in the subsequent days or weeks, even without the hot day) could be heterogeneous because of subgroups in different populations. Further studies may address this matter. Finally, it is worth noting that in addition to the previous factors that can affect heterogeneity between studies, the differences between two subgroups within a study's population can impact heterogeneity between studies as well. For instance, the magnitude of socioeconomic inequalities can differ widely between two cities over the world, so that the comparison of the lowest to highest groups can reflect completely different degrees of disparity.

We assessed socioeconomic vulnerability to heat, considering together income, education, immigration status, deprivation composite indexes, and other ecologic or individual characteristics, assuming that they represent the comparable measures of social hierarchy. However, the various individual and/or ecologic socioeconomic measures may not represent the same social dimension.<sup>100–103</sup> For example, education may influence the understanding of preventive messages, while income may limit access to air conditioning.

We considered vulnerability factors independently as assessed in the majority of the studies since many of the factors considered are highly correlated. Yet, when assessing vulnerability according to sex, for example, it is possible that sex differences in age distribution could explain some of this heterogeneity.

Finally, as many vulnerability definitions exist, the one adopted in our study could be disputed.<sup>104,105</sup> We chose an epidemiologic definition (i.e., effect measure modification) to identify factors of vulnerability to heat, but vulnerability can encompass other dimensions beyond this definition, such as the notion of social trajectory.<sup>105</sup> Also, in the literature reviewed in this article, vulnerability factors were considered separately, but it is reasonable to think that several modifying factors might interact synergistically in the heat-related mortality relationship.

## Recommendations for Studies on the Relationship Between Heat and Death

We noted some limitations in the selected studies of our review, so here we present recommendations to guide further research on heat-related mortality vulnerability. As noted above, the absolute scale is rarely used in this context; therefore, we encourage integrating risk differences in case-crossover designs for example. To do so, we recommend that future studies estimate risk differences directly from logistic regressions. The use of novel inequality measures in time-series analyses is also encouraged, such as use

of the index of disparity,<sup>106</sup> or simple measurement of differences in daily death counts between two subgroups as outcomes.<sup>98,107</sup>

We excluded both cause of death and place of death as modifying factors as they are subcategories of the mortality outcome. In the studies reviewed, causes of death for instance were used as proxies for existing cardiovascular or respiratory diseases. We argue that this is an inappropriate proxy as these factors are themselves due to heat (i.e., stratification for factors affected by exposure). Even if association estimates across these strata are observed to be heterogeneous, they do not constitute a modifying factor in the same sense. This point should be further explored using appropriately designed studies with prospective data, in which the diagnosis of a pre-existing illness is used, as was undertaken in a recent article on elderly persons.<sup>108</sup>

Some effect modifiers were difficult to assess in this study due to the lack of published examples. These include marital status or living in hot places (e.g., micro heat islands), and could be addressed in the future studies.

We found that contrast definition can influence the heterogeneity between studies. Further studies may assess effect modification using different contrast definitions, as sensitivity analyses.

The causal pathways linking vulnerability factors (i.e., modifying factors) are complex and need further consideration. More effort is needed toward the inclusion of causal inference methods to properly consider the role of measured individual or contextual determinants in the heat-related mortality studies, and their synergic influence. Using directed acyclic graphs can be useful for identifying inappropriate practices in causal structures investigating vulnerable subgroups to heat-related mortality,<sup>109,110</sup> as illustrated with respect to confounding in two recent articles.<sup>111,112</sup> Methodologic developments are also required since the distinction between individual and contextual factors remains unclear, and methods used to date do not permit one to elucidate the association of place characteristics with individual outcomes while accounting for nonindependence of observations.<sup>113,114</sup>

## CONCLUSIONS

While the link between excess heat and mortality is well established, the needed fundamental evidence on heat-vulnerable subgroups remains incomplete. Knowledge about vulnerable subgroups is essential for the success of public health programs,<sup>15,16,115</sup> and is necessary for the application of blended intervention strategies, such as proportionate universalism and targeting within universalism.<sup>116,117</sup> Where specific interventions are planned to reduce health impacts in vulnerable populations or territories, such as adapted campaigns or urban modifications, misclassification of vulnerability status may challenge intervention effectiveness and implementation success.

## ACKNOWLEDGMENTS

The authors are grateful to Lena Dolman for her useful comments and contribution in editing this article.

## REFERENCES

1. Semenza JC, Rubin CH, Falter KH, et al. Heat-related deaths during the July 1995 heat wave in Chicago. *N Engl J Med*. 1996;335:84–90.
2. Kovats RS, Kristie LE. Heatwaves and public health in Europe. *Eur J Public Health*. 2006;16:592–599.
3. Åström DO, Forsberg B, Rocklöv J. Heat wave impact on morbidity and mortality in the elderly population: a review of recent studies. *Maturitas*. 2011;69:99–105.
4. Basu R. High ambient temperature and mortality: a review of epidemiologic studies from 2001 to 2008. *Environ Health*. 2009;8:40.
5. Basu R, Samet JM. Relation between elevated ambient temperature and mortality: a review of the epidemiologic evidence. *Epidemiol Rev*. 2002;24:190–202.
6. Gosling SN, Lowe JA, McGregor GR, Pelling M, Malamud BD. Associations between elevated atmospheric temperature and human mortality: a critical review of the literature. *Clim Change*. 2009;92:299–341.
7. Hajat S, Kosatky T. Heat-related mortality: a review and exploration of heterogeneity. *J Epidemiol Community Health*. 2010;64:753–760.
8. Romero-Lankao P, Qin H, Dickinson K. Urban vulnerability to temperature-related hazards: a meta-analysis and meta-knowledge approach. *Global Environmental Change*. 2012;22:670–683.
9. McMichael AJ, Wilkinson P, Kovats RS, et al. International study of temperature, heat and urban mortality: the “ISOTHURM” project. *Int J Epidemiol*. 2008;37:1121–1131.
10. Stafoggia M, Forastiere F, Agostini D, et al. Vulnerability to heat-related mortality: a multicity, population-based, case-crossover analysis. *Epidemiology*. 2006;17:315–323.
11. Kuh D, Ben-Shlomo Y, Lynch J, Hallqvist J, Power C. Life course epidemiology. *J Epidemiol Community Health*. 2003;57:778–783.
12. Brook RD, Rajagopalan S, Pope CA 3rd, et al.; American Heart Association Council on Epidemiology and Prevention, Council on the Kidney in Cardiovascular Disease, and Council on Nutrition, Physical Activity and Metabolism. Particulate matter air pollution and cardiovascular disease: an update to the scientific statement from the American Heart Association. *Circulation*. 2010;121:2331–2378.
13. Xu Z, Etzel RA, Su H, Huang C, Guo Y, Tong S. Impact of ambient temperature on children's health: a systematic review. *Environ Res*. 2012;117:120–131.
14. Sari Kovats R, Menne B, Ebi KL. *Methods of assessing human health vulnerability and public health adaptation to climate change*, WHO, 2003.
15. Benach J, Malmusi D, Yasui Y, Martínez JM, Muntaner C. Beyond Rose's strategies: a typology of scenarios of policy impact on population health and health inequalities. *Int J Health Serv*. 2011;41:1–9.
16. Frohlich KL, Potvin L. Transcending the known in public health practice: the inequality paradox: the population approach and vulnerable populations. *Am J Public Health*. 2008;98:216–221.
17. Bassil KL, Cole DC. Effectiveness of public health interventions in reducing morbidity and mortality during heat episodes: a structured review. *Int J Environ Res Public Health*. 2010;7:991–1001.
18. Toloo G, FitzGerald G, Aitken P, Verrall K, Tong S. Evaluating the effectiveness of heat warning systems: systematic review of epidemiological evidence. *Int J Public Health*. 2013;58:667–681.
19. Moher D, Liberati A, Tetzlaff J, Altman DG; PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Ann Intern Med*. 2009;151:264–269, W64.
20. Xu W, Thach TQ, Chau YK, et al. Thermal stress associated mortality risk and effect modification by sex and obesity in an elderly cohort of Chinese in Hong Kong. *Environ Pollut*. 2013;178:288–293.
21. Madrigano J, Mittleman MA, Baccarelli A, et al. Temperature, myocardial infarction, and mortality: effect modification by individual- and area-level characteristics. *Epidemiology*. 2013;24:439–446.
22. Xu Z, Sheffield PE, Su H, Wang X, Bi Y, Tong S. The impact of heat waves on children's health: a systematic review. *Int J Biometeorol*. 2014;58:239–247.
23. Hansen A, Bi L, Saniotis A, Nitschke M. Vulnerability to extreme heat and climate change: is ethnicity a factor? *Glob Health Action*. 2013;6:21364.
24. Kaufman JS, MacLehose RF. Which of these things is not like the others? *Cancer*. 2013;119:4216–4222.
25. Shah AS, Langrish JP, Nair H, et al. Global association of air pollution and heart failure: a systematic review and meta-analysis. *Lancet*. 2013;382:1039–1048.
26. Basu R, Ostro BD. A multicounty analysis identifying the populations vulnerable to mortality associated with high ambient temperature in California. *Am J Epidemiol*. 2008;168:632–637.
27. Yang J, Ou CQ, Ding Y, Zhou YX, Chen PY. Daily temperature and mortality: a study of distributed lag non-linear effect and effect modification in Guangzhou. *Environ Health*. 2012;11:63.
28. Garg AX, Hackam D, Tonelli M. Systematic review and meta-analysis: when one study is just not enough. *Clin J Am Soc Nephrol*. 2008;3:253–260.
29. Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. *Stat Med*. 2002;21:1539–1558.
30. Altman DG, Bland JM. Interaction revisited: the difference between two estimates. *BMJ*. 2003;326:219.
31. Bassler D, Briel M, Montori VM, et al.; STOPIT-2 Study Group. Stopping randomized trials early for benefit and estimation of treatment effects: systematic review and meta-regression analysis. *JAMA*. 2010;303:1180–1187.
32. Reid IR, Bolland MJ, Grey A. Effects of vitamin D supplements on bone mineral density: a systematic review and meta-analysis. *Lancet*. 2014;383:146–155.
33. Egger M, Davey Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. *BMJ*. 1997;315:629–634.
34. Almeida S, Casimiro E, Analitis A. Short-term effects of summer temperatures on mortality in Portugal: a time-series analysis. *J Toxicol Environ Health A*. 2013;76:422–428.
35. Baccini M, Biggeri A, Accetta G, et al. Heat effects on mortality in 15 European cities. *Epidemiology*. 2008;19:711–719.
36. Bai L, Cirendunzhu, Woodward A, Dawa, Xiraoruodeng, Liu Q. Temperature and mortality on the roof of the world: a time-series analysis in three Tibetan counties, China. *Sci Total Environ*. 2014;485–486:41–48.
37. Bell ML, O'Neill MS, Ranjit N, Borja-Aburto VH, Cifuentes LA, Gouveia NC. Vulnerability to heat-related mortality in Latin America: a case-crossover study in Sao Paulo, Brazil, Santiago, Chile and Mexico City, Mexico. *Int J Epidemiol*. 2008;37:796–804.
38. Benmarhnia T, Oulhote Y, Petit C, et al. Chronic air pollution and social deprivation as modifiers of the association between high temperature and daily mortality. *Environ Health*. 2014;13:53.
39. Breiher S, Wolf K, Devlin RB, Diaz-Sanchez D, Peters A, Schneider A. Short-term effects of air temperature on mortality and effect modification by air pollution in three cities of Bavaria, Germany: a time-series analysis. *Sci Total Environ*. 2014;485–486:49–61.
40. Burkart K, Breiher S, Schneider A, Khan MM, Krämer A, Endlicher W. An analysis of heat effects in different subpopulations of Bangladesh. *Int J Biometeorol*. 2014;58:227–237.
41. Chan EY, Goggins WB, Kim JJ, Griffiths SM. A study of intracity variation of temperature-related mortality and socioeconomic status among the Chinese population in Hong Kong. *J Epidemiol Community Health*. 2012;66:322–327.
42. Egondi T, Kyobutungi C, Kovats S, Muindi K, Ettarh R, Rocklöv J. Time-series analysis of weather and mortality patterns in Nairobi's informal settlements. *Glob Health Action*. 2012;5:23–32.
43. Goggins WB, Chan EY, Ng E, Ren C, Chen L. Effect modification of the association between short-term meteorological factors and mortality by urban heat islands in Hong Kong. *PLoS One*. 2012;7:e38551.
44. Goggins WB, Ren C, Ng E, Yang C, Chan EY. Effect modification of the association between meteorological variables and mortality by urban climatic conditions in the tropical city of Kaohsiung, Taiwan. *Geospat Health*. 2013;8:37–44.
45. Gómez-Acebo I, Llorca J, Rodríguez-Cundín P, Dierssen-Sotos T. Extreme temperatures and mortality in the North of Spain. *Int J Public Health*. 2012;57:305–313.
46. Gouveia N, Hajat S, Armstrong B. Socioeconomic differentials in the temperature-mortality relationship in São Paulo, Brazil. *Int J Epidemiol*. 2003;32:390–397.
47. Hajat S, Armstrong BG, Gouveia N, Wilkinson P. Mortality displacement of heat-related deaths: a comparison of Delhi, São Paulo, and London. *Epidemiology*. 2005;16:613–620.



48. Hajat S, Kovats RS, Lachowycz K. Heat-related and cold-related deaths in England and Wales: who is at risk? *Occup Environ Med.* 2007;64:93–100.
49. Huang J, Wang J, Yu W. The lag effects and vulnerabilities of temperature effects on cardiovascular disease mortality in a subtropical climate zone in China. *Int J Environ Res Public Health.* 2014;11:3982–3994.
50. Ishigami A, Hajat S, Kovats RS, et al. An ecological time-series study of heat-related mortality in three European cities. *Environ Health.* 2008;7:1–7.
51. Kim Y, Joh S. A vulnerability study of the low-income elderly in the context of high temperature and mortality in Seoul, Korea. *Sci Total Environ.* 2006;371:82–88.
52. Leone M, D'Ippoliti D, De Sario M, et al. A time series study on the effects of heat on mortality and evaluation of heterogeneity into European and Eastern-Southern Mediterranean cities: results of EU CIRCE project. *Environ Health.* 2013;12:55.
53. Ma W, Yang C, Tan J, Song W, Chen B, Kan H. Modifiers of the temperature-mortality association in Shanghai, China. *Int J Biometeorol.* 2012;56:205–207.
54. Medina-Ramón M, Schwartz J. Temperature, temperature extremes, and mortality: a study of acclimatisation and effect modification in 50 US cities. *Occup Environ Med.* 2007;64:827–833.
55. Muggeo VM, Hajat S. Modelling the non-linear multiple-lag effects of ambient temperature on mortality in Santiago and Palermo: a constrained segmented distributed lag approach. *Occup Environ Med.* 2009;66:584–591.
56. O'Neill MS, Zanobetti A, Schwartz J. Modifiers of the temperature and mortality association in seven US cities. *Am J Epidemiol.* 2003;157:1074–1082.
57. O'Neill MS, Zanobetti A, Schwartz J. Disparities by race in heat-related mortality in four US cities: the role of air conditioning prevalence. *J Urban Health.* 2005;82:191–197.
58. Rocklöv J, Ebi K, Forsberg B. Mortality related to temperature and persistent extreme temperatures: a study of cause-specific and age-stratified mortality. *Occup Environ Med.* 2011;68:531–536.
59. Rocklöv J, Forsberg B, Ebi K, Bellander T. Susceptibility to mortality related to temperature and heat and cold wave duration in the population of Stockholm County, Sweden. *Global health action* 2014;7.
60. Smargiassi A, Goldberg MS, Plante C, Fournier M, Baudouin Y, Kosatsky T. Variation of daily warm season mortality as a function of micro-urban heat islands. *J Epidemiol Community Health.* 2009;63:659–664.
61. Son JY, Lee JT, Anderson GB, Bell ML. Vulnerability to temperature-related mortality in Seoul, Korea. *Environ Res Lett.* 2011;6:034027.
62. Stafoggia M, Forastiere F, Agostini D, et al. Factors affecting in-hospital heat-related mortality: a multi-city case-crossover analysis. *J Epidemiol Community Health.* 2008;62:209–215.
63. Urban A, Davidková H, Kysely J. Heat- and cold-stress effects on cardiovascular mortality and morbidity among urban and rural populations in the Czech Republic. *Int J Biometeorol.* 2014;58:1057–1068.
64. Vaneckova P, Beggs PJ, de Dear RJ, McCracken KW. Effect of temperature on mortality during the six warmer months in Sydney, Australia, between 1993 and 2004. *Environ Res.* 2008;108:361–369.
65. Wang C, Chen R, Kuang X, Duan X, Kan H. Temperature and daily mortality in Suzhou, China: a time series analysis. *Sci Total Environ.* 2014;466–467:985–990.
66. Wang L, Tong S, Toloo GS, Yu W. Submicrometer particles and their effects on the association between air temperature and mortality in Brisbane, Australia. *Environ Res.* 2014;128:70–77.
67. Wu W, Xiao Y, Li G, et al. Temperature-mortality relationship in four subtropical Chinese cities: a time-series study using a distributed lag non-linear model. *Sci Total Environ.* 2013;449:355–362.
68. Yu W, Vaneckova P, Mengersen K, Pan X, Tong S. Is the association between temperature and mortality modified by age, gender and socioeconomic status? *Sci Total Environ.* 2010;408:3513–3518.
69. Yu W, Mengersen K, Hu W, Guo Y, Pan X, Tong S. Assessing the relationship between global warming and mortality: lag effects of temperature fluctuations by age and mortality categories. *Environ Pollut.* 2011;159:1789–1793.
70. Anderson BG, Bell ML. Weather-related mortality: how heat, cold, and heat waves affect mortality in the United States. *Epidemiology.* 2009;20:205–213.
71. Basagaña X, Sartini C, Barrera-Gómez J, et al. Heat waves and cause-specific mortality at all ages. *Epidemiology.* 2011;22:765–772.
72. Borrell C, Mari-Dell'Olmo M, Rodríguez-Sanz M, et al. Socioeconomic position and excess mortality during the heat wave of 2003 in Barcelona. *Eur J Epidemiol.* 2006;21:633–640.
73. Fouillet A, Rey G, Laurent F, et al. Excess mortality related to the August 2003 heat wave in France. *Int Arch Occup Environ Health.* 2006;80:16–24.
74. Huang W, Kan H, Kovats S. The impact of the 2003 heat wave on mortality in Shanghai, China. *Sci Total Environ.* 2010;408:2418–2420.
75. Hutter HP, Moshammer H, Wallner P, Leitner B, Kundi M. Heatwaves in Vienna: effects on mortality. *Wien Klin Wochenschr.* 2007;119:223–227.
76. Kysely J, Kim J. Mortality during heat waves in South Korea, 1991 to 2005: how exceptional was the 1994 heat wave? *Climate Res.* 2009;38:105.
77. Lan L, Cui G, Yang C, et al. Increased mortality during the 2010 heat wave in Harbin, China. *Ecohealth.* 2012;9:310–314.
78. Nitschke M, Tucker GR, Bi P. Morbidity and mortality during heatwaves in metropolitan Adelaide. *Med J Aust.* 2007;187:662–665.
79. Nitschke M, Tucker GR, Hansen AL, Williams S, Zhang Y, Bi P. Impact of two recent extreme heat episodes on morbidity and mortality in Adelaide, South Australia: a case-series analysis. *Environ Health.* 2011;10:42.
80. Rey G, Fouillet A, Bessemoulin P, et al. Heat exposure and socio-economic vulnerability as synergistic factors in heat-wave-related mortality. *Eur J Epidemiol.* 2009;24:495–502.
81. Robine JM, Michel JP, Herrmann FR. Excess male mortality and age-specific mortality trajectories under different mortality conditions: a lesson from the heat wave of summer 2003. *Mech Ageing Dev.* 2012;133:378–386.
82. Rooney C, McMichael AJ, Kovats RS, Coleman MP. Excess mortality in England and Wales, and in Greater London, during the 1995 heatwave. *J Epidemiol Community Health.* 1998;52:482–486.
83. Schifano P, Cappai G, De Sario M, et al. Susceptibility to heat wave-related mortality: a follow-up study of a cohort of elderly in Rome. *Environ Health* 2009;8:1–14.
84. Son JY, Lee JT, Anderson GB, Bell ML. The impact of heat waves on mortality in seven major cities in Korea. *Environ Health Perspect.* 2012;120:566–571.
85. Tian Z, Li S, Zhang J, Guo Y. The characteristic of heat wave effects on coronary heart disease mortality in Beijing, China: a time series study. *PLoS One.* 2013;8:e77321.
86. Tong S, Wang XY, Yu W, Chen D, Wang X. The impact of heatwaves on mortality in Australia: a multicity study. *BMJ Open.* 2014;4:e003579.
87. 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;67:519–525.
88. Kosatsky T, Henderson SB, Pollock SL. Shifts in mortality during a hot weather event in Vancouver, British Columbia: rapid assessment with case-only analysis. *Am J Public Health.* 2012;102:2367–2371.
89. Medina-Ramón M, Zanobetti A, Cavanagh DP, Schwartz J. Extreme temperatures and mortality: assessing effect modification by personal characteristics and specific cause of death in a multi-city case-only analysis. *Environ Health Perspect.* 2006;114:1331–1336.
90. Schwartz J. Who is sensitive to extremes of temperature?: A case-only analysis. *Epidemiology.* 2005;16:67–72.
91. Matthies F, Bickler G, Marin NC, Hales S. *Heat-health action plans: guidance World Health Organization*, 2008.
92. WHO. *Climate change and health*, 2008.
93. 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;8:4623–4648.
94. Bouchama A, Dehbi M, Mohamed G, Matthies F, Shoukri M, Menne B. Prognostic factors in heat wave related deaths: a meta-analysis. *Arch Intern Med.* 2007;167:2170–2176.
95. King NB, Harper S, Young ME. Use of relative and absolute effect measures in reporting health inequalities: structured review. *BMJ.* 2012;345:e5774.
96. Lynch J, Davey Smith G, Harper S, Bainbridge K. Explaining the social gradient in coronary heart disease: comparing relative and absolute risk approaches. *J Epidemiol Community Health.* 2006;60:436–441.

97. Yang S, Platt RW, Dahhou M, Kramer MS. Do population-based interventions widen or narrow socioeconomic inequalities? The case of breastfeeding promotion. *Int J Epidemiol*. 2014;43:1284–1292.
98. Harper S, King NB, Meersman SC, Reichman ME, Breen N, Lynch J. Implicit value judgments in the measurement of health inequalities. *Milbank Q*. 2010;88:4–29.
99. Lau J, Ioannidis JP, Schmid CH. Summing up evidence: one answer is not always enough. *Lancet*. 1998;351:123–127.
100. Braveman PA, Cubbin C, Egerter S, et al. Socioeconomic status in health research: one size does not fit all. *JAMA*. 2005;294:2879–2888.
101. Galobardes B, Lynch J, Smith GD. Measuring socioeconomic position in health research. *Br Med Bull*. 2007;81:21–37.
102. Oakes JM, Rossi PH. The measurement of SES in health research: current practice and steps toward a new approach. *Soc Sci Med*. 2003;56:769–784.
103. Shavers VL. Measurement of socioeconomic status in health disparities research. *J Natl Med Assoc*. 2007;99:1013–1023.
104. Alwang J, Siegel PB, Jorgensen SL. Vulnerability: a view from different disciplines. *Social protection discussion paper series*, 2001.
105. Delor F, Hubert M. Revisiting the concept of ‘vulnerability’. *Soc Sci Med*. 2000;50:1557–1570.
106. Pearcy JN, Keppel KG. A summary measure of health disparity. *Public Health Rep*. 2002;117:273–280.
107. Benmarhnia T, Zunzunegui MV, Llacer A, Béland F. Impact of the economic crisis on the health of older persons in Spain: research clues based on an analysis of mortality. SESPAS report 2014. *Gac Sanit*. 2014;28(Suppl 1):137–141.
108. Zanobetti A, O’Neill MS, Gronlund CJ, Schwartz JD. Summer temperature variability and long-term survival among elderly people with chronic disease. *Proc Natl Acad Sci USA*. 2012;109:6608–6613.
109. Shrier I, Platt RW. Reducing bias through directed acyclic graphs. *BMC Med Res Methodol*. 2008;8:70.
110. VanderWeele TJ, Robins JM. Four types of effect modification: a classification based on directed acyclic graphs. *Epidemiology*. 2007;18:561–568.
111. Buckley JP, Samet JM, Richardson DB. Commentary: does air pollution confound studies of temperature? *Epidemiology*. 2014;25:242–245.
112. Reid CE, Snowden JM, Kontgis C, Tager IB. The role of ambient ozone in epidemiologic studies of heat-related mortality. *Environ Health Perspect*. 2012;120:1627–1630.
113. Greenland S. Principles of multilevel modelling. *Int J Epidemiol*. 2000;29:158–167.
114. Naess O, Piro FN, Nafstad P, Smith GD, Leyland AH. Air pollution, social deprivation, and mortality: a multilevel cohort study. *Epidemiology*. 2007;18:686–694.
115. Balbus JM, Malina C. Identifying vulnerable subpopulations for climate change health effects in the United States. *J Occup Environ Med*. 2009;51:33–37.
116. Lawrence E, Stoker R, Wolman H. The effects of beneficiary targeting on public support for social policies. *Policy Studies J*. 2013;41:199–216.
117. Skocpol T. Targeting within universalism: politically viable policies to combat poverty in the United States. In Jencks C, Peterson PE, eds. *The Urban Underclass*, Vol 411. Washington, DC: The Brookings Institution; 1991:437–459.