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Relation between Elevated Ambient Temperature and Mortality: A Review of the Epidemiologic Evidence

Rupa Basu and Jonathan M. Samet

From the Department of Epidemiology, Bloomberg School of Public Health, Johns Hopkins University, Baltimore, MD.

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INTRODUCTION

The effect of elevated temperature on mortality is a public health threat of considerable magnitude. Every year, a large number of hospitalizations and deaths occur in association with exposure to elevated ambient temperatures (1, 2). An average of 400 deaths annually are counted as directly related to heat in the United States, with the highest death rates occurring in persons aged 65 years or more (3). The actual magnitude of heat-related mortality may be notably greater than what has been reported, since we do not have widely accepted criteria for determining heat-related death (4, 5–7), and heat may not be listed on the death certificate as causing or contributing to death. Persons living in urban environments may be at particularly increased risk for mortality from ambient heat exposure, since urban areas typically have higher heat indexes (combinations of temperature and humidity (8)) than surrounding suburban or rural areas, a phenomenon known as the "urban heat island effect" (9). Moreover, urban areas retain heat during the night more efficiently (10). Thus, as the US population becomes more urbanized and the number of elderly people continues to increase (11), the threat of heat-related mortality will probably become more severe. Many of these deaths may be preventable with adequate warning and an appropriate response to heat emergencies, but preventive efforts are complicated by the short time interval that may elapse between high temperature exposure and death. Thus, prevention programs must be based around prospective and rapid identification of high-risk conditions and persons. We carried out this review to assess the current epidemiologic evidence available for this purpose.

Observations on heat and mortality have been reported since the early decades of the 20th century. Among the classic studies, Gover (12) examined excess deaths associated with elevated ambient temperature exposure in 86 US cities from 1925 to 1937 and summarized findings from other early heat-wave studies. The northern central states (Ohio, Indiana, Illinois, Missouri, Iowa, and Nebraska) were most often affected by mortality subsequent to heat waves, followed by the states in the Northeast; the South and the Pacific Coast were least affected. Further early evidence for an association between ambient heat exposure and mortality came from studies of Army recruits conducted in the 1940s and 1950s (13, 14), and several studies published in the 1970s described possible physiologic mechanisms for heat stroke following exercise during periods of high ambient temperature (15, 16). The courses of several heat waves occurring prior to 1970 have been explored to identify risk factors for heat-related mortality. For example, Bridger et al. (17) examined mortality following heat waves that occurred in St. Louis, Missouri, in 1936, 1953, 1954, 1955, and 1966. For 1936, they found that persons aged 40–80 years had the greatest risk of mortality, whereas in 1966, the majority of deaths occurred among males, Whites, and persons aged 60–90 years, most likely reflecting the increase in life expectancy over the decades. More recent studies have added an emphasis on longer-term relations between weather and mortality to the more focused studies of heat waves.

Because of the projected consequences of global warming (18, 19) and the increased frequency and intensity of heat waves (20), heat-related mortality may achieve greater public health significance during the coming decades (21, 22). Over the past century, the overall global surface temperature has increased by 0.7–1.4°F, and the global sea level has risen 4–10 inches (10–25 cm) from the melting of the polar ice caps (18). Major predicted health effects of long-term climatic change include skin and eye damage from increased exposure to ultraviolet radiation, increased incidence of respiratory and cardiovascular diseases, increased incidence of vector-borne and water-borne diseases, and heat-related morbidity and mortality (18). Models of the relation between temperature and mortality are needed to predict the consequences of global warming, particularly for those most vulnerable and least able to adapt. Observational data on temperature and mortality are essential for developing these models. A further use of these models is in predicting

Correspondence to Dr. Rupa Basu, Office of Policy, Economics, and Innovation, Environmental Protection Agency, 1200 Pennsylvania Avenue NW, MC 1809T, Washington, DC 20460 (e-mail: basu.rupa@epa.gov).

dangerous heat conditions so that preventive steps can be taken (23).

REVIEW OF THE LITERATURE

Because the demographic picture in the United States has changed, particularly since the 1970s—including longer life expectancy, increased racial diversity in cities, and increased availability of air conditioning—we chose to limit the focus of our review to studies conducted after 1970, to more appropriately define current risk characteristics. Additionally, these years include the newer studies that have used time-series methods. The published literature was identified using the MEDLINE database (1970 to the present), covering recent US and international studies examining heat waves or other ambient heat-related exposures and subsequent mortality, and the Johns Hopkins University's Welch Library. The search was limited to English-language studies of humans in biomedical research; because of the interdisciplinary nature of heat-related mortality, it is covered by a variety of disciplines beyond medicine and public health, including meteorology, and our coverage does not extend comprehensively into those areas. Keywords and terms used for the search included "temperature," "high ambient temperature," "heat wave," "cardiovascular and respiratory mortality," and "mortality." Studies focusing only on winter or the effects of cold temperatures were excluded. A total of 98 references that addressed the general issues associated with heat-related mortality were included. Forty-nine studies specifically addressing mortality due to heat waves or high ambient temperatures had been published in peer-reviewed and indexed journals since 1970.

METHODOLOGICAL ISSUES

In evaluating studies of temperature and mortality, the following methodological issues should be considered: 1) assessment of exposure and outcome measures; 2) selection of an appropriate study design; and 3) use of statistical models to describe the temperature-mortality relation.

Exposure assessment

The heat stress experienced across day and night determines risk for heat-related mortality (24). In the epidemiologic studies, ambient temperature and/or dew point temperature is generally used as the exposure measure, serving as a surrogate indicator of heat stress. The microenvironmental model, which has been widely applied in assessing exposure to air pollution (25), considers personal exposure to pollution as the time-weighted sum of pollutant concentrations in the places where time is spent, referred to as microenvironments. Extending this model to heat or temperature, temperatures in the various locations where people spend their time determines their personal exposure to heat (26). A study of heat stress or temperature effects can also be carried out in a place-based investigation (27), which assesses the stress of being in particular places instead of the stress of particular people in them.

Since measuring the daily dynamic ambient temperature exposure of all participants in a study or a representative sample of participants is impractical and expensive, epidemiologists have used ambient temperatures measured at weather stations as an exposure index. These indexes generally combine temperature and humidity, using recorded temperature (dry bulb temperature), wet bulb temperature, dew point temperature, a heat index consisting of temperature and humidity, changes in temperature, or air mass approaches. Outdoor temperature has been used as a surrogate for personal exposure to heat, even though people in developed countries generally spend most of their time indoors (25). This ecologic temperature measure assumes that all persons who are in a specified geographic area experience the same exposure. While this approach is made feasible by readily available data, some degree of misclassification of individual personal exposures is inherent. The extent of misclassification resulting from using temperature exposure data provided by weather stations will depend on the extent to which ambient and microenvironmental temperatures are correlated. Adaptive behaviors such as use of air conditioning will affect the association between ambient temperatures and indoor temperatures and increase variation in heat exposure among persons at a particular ambient temperature. The recorded ecologic temperature of a specified geographic area (e.g., a city) may not accurately represent the actual temperature exposure of each individual in that area (28). However, for the purposes of population-based analyses, ambient temperature is the strongest determinant of variation over time in the exposure of populations to heat.

In assessing associations of temperature with mortality, investigators must also consider the temperature variables and lag structure. For example, maximum, minimum, or average temperature might be used and the association of mortality with temperature considered at different lag times. Investigators have used a variety of measures, including the average temperature and the maximum temperature. With regard to lag structure, researchers have explored a number of possibilities for the relation between exposure time and response. Specific choices of exposure lag times are covered in the tables. An extensive body of literature on the physiologic consequences of heat exposure and adaptation exists, and the evidence indicates that short-term exposures are most appropriate (18, 29, 30).

In examining the effect of heat waves, the timing of these episodes across the summer months must be considered. Heat waves occurring early in the summer or spring often result in more deaths than heat waves occurring later in the summer (6, 12, 31). Thus, the most vulnerable persons may be affected by heat waves occurring early in the summer, leaving less susceptible persons alive later in the summer (i.e., loss of susceptibles). Alternatively, vulnerable persons who survive heat waves through the later summer months may have acquired physiologic adaptations or implemented behavioral changes following their initial exposure to high ambient temperatures (6, 12). However, adaptations to sudden extreme temperatures are unlikely.

Outcome assessment

Since heat-related mortality is subject to misclassification and generally only a few deaths are directly coded as being caused by heat, researchers have often used total mortality or cause-specific mortality as the outcome measure. The use of deaths specifically assigned to heat-related causes is problematic, because definitions of heat-related mortality vary by location and no widely accepted systematic criteria currently exist for classifying them (4, 6). The National Association of Medical Examiners Ad Hoc Committee suggests defining deaths as attributable to heat stroke or hyperthermia if body temperature at the time of death was at least 105°F and/or the deceased person had a clinical history of changes in mental status and elevated levels of liver and muscle enzymes (5). If body temperature cannot be established, a heat-related diagnosis should be listed as the cause of death or a contributing cause if the ambient temperature was elevated at the time of death. With such uncertainty, however, heat is often not reported as the underlying cause of death on death certificates, and incidence may thus be severely underestimated (7). Cardiovascular, respiratory, and/or cerebrovascular diseases are commonly reported as the underlying cause of death, because persons with these preexisting diseases are more susceptible to death during heat waves (e.g., death from myocardial infarction, stroke, pneumonia, and/or hyperthermia) (32–34). Donoghue et al. defined a heat-related death as "a death in which exposure to high ambient temperature either caused the death or significantly contributed to it" (5, p. 11), although other study-specific definitions and criteria exist. Using an outcome measure defined by the exposure (e.g., heat-related death) may lead to a differential information bias, resulting in overestimation of mortality attributable to heat waves, since deaths are expected following a heat wave and are therefore more likely to be reported as heat-related.

As with studies of air pollution and mortality, the potential effect of "harvesting" should be considered in studies of temperature and mortality. "Harvesting" refers to a brief temporal advancement of death among persons who are already ill or frail and at high risk of dying. Through examination of intermediate- and long-term effects, rather than only short-term effects, time domains are assessed in which the impact of harvesting is reduced (35, 36).

Statistical modeling

Statistical models are applied to examine the temperature-mortality relation, using various definitions for temperature exposure and mortality outcomes. These models represent the relation between temperature and other weather indicators and risk of heat-related mortality. In many studies, a J- or U-shaped curve has been found appropriate to describe the association, with elevated mortality being observed at temperature extremes and relatively lower mortality at moderate temperatures (30, 37–39). Thus, statistical models that do not assume linearity are needed to flexibly characterize the association (30, 37, 40–42). A polynomial term may be used to model mortality across all temperatures, although it may be challenging to determine the most appropriate model to fit the data. Alternatively, two linear models may be used, one to describe the negative slope associated with colder temperatures and another to account for the positive slope generally observed with hotter temperatures. Analyzing temperature extremes may be feasible, if an appropriate cutoff temperature can be selected to separate the effects of excessively hot and cold temperatures. Finally, stratifying the analysis by month or season would also ensure that temperatures were similar enough to assume linearity within each stratum.

Study designs

A variety of study designs can be used to assess the effects of mortality following heat waves and to characterize the association between elevated temperature and mortality. Descriptive studies (studies of heat waves and mapping studies) and case-control studies characterizing risk factors for heat waves have been employed; more recently, common analytical techniques, including the time-series and case-crossover study designs, have been used.

Descriptive studies. Studies of heat waves and mapping studies (also known as exploratory ecologic studies) may be used for exploratory analyses of ambient temperature and mortality. A heat wave is an event that provides a well-defined period of extreme temperature with a high risk of adverse health effects and mortality (43). The effect of excessive ambient temperature for a specific city on multiple days may be examined to identify vulnerable populations and high-risk factors. Mortality counts or rates during a heat wave are generally compared with rates from several days prior to the heat wave or rates during the same time period in the previous year to assess the number of excess deaths attributable to the heat wave. Mapping studies examine disease rates in geographically defined regions to search for spatial patterns that suggest an environmental etiology for disease occurrence or mortality. In contrast to studies of heat waves, mapping studies consider longer time periods of temperature exposure and larger populations in multiple areas to explore the relation between ambient heat exposure and mortality in cross-sectional analyses (44, 45). However, they do not quantify the association between temperature and mortality (i.e., the percentage of mortality associated with a 1-degree increase in temperature).

Time-series studies. The time-series study is an efficient design for examining the temperature-mortality relation for populations in single or multiple geographic regions over a substantial time period (46). Mortality counts or rates are the outcome measures, while temperature measurements collected at consecutive, regular intervals over time (e.g., every hour or every day) are the predictor variables of interest. Potentially confounding factors include season and the prevalence of air pollutants. Aggregate hourly or daily information is required for exposures and outcomes, rather than individual data; this information can be acquired easily from publicly accessible national databases.

Case-crossover studies. The case-crossover study design, first described in 1991 (47), serves as an epidemiologic technique for assessing the relation between a quickly changing risk factor (e.g., air pollution or ambient tempera-

ture) and an acute event (e.g., myocardial infarction or mortality). For each person experiencing the outcome, two or more time periods are defined: 1) a case or hazard period representing the exposure period temporally and biologically relevant to the acute event and 2) one or more control periods representing the exposure experienced before and/or after the hazard period during an interval with equal opportunity for exposure. Because the case-crossover design allows each person in the study to act as his or her own control, confounding due to measured and unmeasured differences between individuals (e.g., age, genetics, socioeconomic status, health behaviors, and physiologic differences) is minimized, and effect modification by individual characteristics can be explored. Since people are only included in the study if they experience the outcome of interest, more severe cases leading to death may be excluded, a pattern known as the Neyman bias (48). A limitation of the case-crossover study design is that each individual's date of death, which may not be readily available, is required for analysis (43).

FINDINGS

Many investigators have addressed the risks of heat-related mortality in the United States and in other countries using the study designs discussed above. The study populations, outcome measures, and results from these studies are described in the tables and provide a basis for characterizing mortality risk associated with elevated ambient temperature. Table 1 details total mortality resulting from heat waves in descriptive analyses; table 2 focuses on mortality specific to cardiovascular and respiratory diseases; table 3 considers studies conducted in medical institutions; and table 4 summarizes the findings of temperature-mortality studies other than studies of heat-wave exposure that used cluster maps and time-series analyses.

Studies of heat waves

Studies conducted following heat waves in the 1970s, 1980s, and 1990s (32, 33) showed evidence of increased mortality from heat waves in various locales while identifying key risk factors for vulnerable populations, including age, race, gender, and high-risk behaviors. One of the most severe heat waves, the 1980 heat wave in St. Louis and Kansas City, Missouri, provided population-based data on the effects of ambient heat exposure on health risks and led to recommendations for preventing heat-related mortality (49). Failure to follow these recommendations may have contributed to excess mortality in Chicago, Illinois, following the 1995 heat wave (4). Table 1 summarizes the results of studies that examined risk factors for increases in mortality counts or rates following heat waves.

Demographic factors. The effects of age, race, and gender were examined in several studies of heat waves. Infants under 1 year of age and the elderly were reported to be at highest risk for mortality following heat waves (50). In some studies, persons over age 60 years were found to be at highest risk (51, 52), while other investigators reported the highest-risk age groups to be those over 65 years of age (52–56), 70 years of age (34, 41), or 75 years of age (4). In US studies, African Americans (4, 51, 57), persons living in inner cities and persons working in jobs requiring heavy labor (51, 57), and persons living in lower-income census tracts (53) were most affected; these categories served as surrogates for low socioeconomic status or higher temperature exposure. US cluster maps of persons aged 65 years or older from 1979–1985 revealed that urban residence, minority status, and low socioeconomic status were important predictors of high risk (44), supporting the results found in the studies of heat waves. Two US heat-wave studies showed that males were more often adversely affected than females (4), although a heat wave in England and Wales resulted in more female deaths (58). A 3:1 ratio for heat stroke was reported for non-Whites versus Whites following the 1980 heat wave in Missouri (53). However, other heat-wave studies reported no differences between males and females (33, 59) or between Whites and non-Whites (33, 59). Thus, heat-related mortality primarily affects the elderly, infants, and persons of lower socioeconomic status. The evidence for influences of race and gender has been inconsistent.

Behavioral risk factors. Some case-control studies were conducted following heat waves that occurred in the Midwest in 1980, 1995, and 1999 to identify behavioral risk factors associated with heat-related mortality. Living alone (60, 61), being confined to bed (61), using tranquilizers (62), having a mental illness (63), not leaving home daily (60), living on higher floors of multistory buildings (62), and being alcoholic (62) were associated with increased risk of heat-related mortality. The strongest protective factor was access to air conditioning in the home (60–63) and in other places (62), as well as having access to transportation (61), living in a residence surrounded by trees or shrubs (62), being able to care for oneself (62), engaging in vigorous physical activity (while reducing such activity during a heat wave) (62), and drinking extra fluids (62). In these studies, exposures may have been slightly overestimated for cases; controls would be likely to underestimate their exposures, since they were not adversely affected by the heat wave, and surrogate respondents for cases (e.g., neighbors or friends) might not remember accurately the health behaviors of persons who died (64). Nonetheless, important behavioral risk factors were identified for educating vulnerable populations and for targeting preventive efforts in high-risk cities. For example, the relatively younger age of the case population (<65 years) during the 1999 heat wave may have been a result of interventions in Chicago that targeted the elderly following the heat wave of 1995. Other investigations of heat waves in the Midwest in 1995 and 1999 reported similar risk factors (65–67). An analysis of autopsy reports in Australia from 1991–1998 found excessive clothing, prolonged sun exposure, acute alcohol intoxication, obesity, medication use, alcoholic liver disease, and possibly epilepsy to be predisposing factors for heat-related mortality (68).

Lag times. A number of studies have explored temporal patterns of association between temperature exposures over antecedent days and risk on a particular day—that is, the lag time or lag structure. Various lag times have been reported for the strongest association of heat with mortality, ranging from the same day (29) to 3 days following a heat wave (50). Furthermore, a run of at least 3 consecutive days of elevated

TABLE 1. Results from descriptive studies analyzing risk factors for increases in mortality following heat waves

Study population (reference no.)	Exposure	Outcome	Results
Three September heat waves in Los Angeles, California, 1939, 1955, and 1963 (29)	Daily temperature ≥100°F; compared with 1947 "normal" temperatures	Daily no. of deaths	Death counts were higher with increasing temperature and age; lag time between maximum temperature and maximum mortality was ~1 day
Heat waves in New York City during the summers of 1972 and 1973 (59)	Heat wave for each year	No. of deaths	Increase in deaths after several days of excessively warm weather and on the day following the hottest day; ischemic heart disease and age ≥65 years most prominent
All age groups in New York (January 1965–December 1968) and England and Wales (1970–1971) (32)	Mean monthly temperatures based on daily temperatures (>68°F, also <50°F)	Daily deaths from myocardial infarction, stroke, and pneumonia	Short-term (1–2 days) exposure had little effect; medium-term (7–10 days) and longer-term (>3 weeks) exposures were associated with very significant changes in death rates; stronger effect seen in the elderly
Heat wave in New York City, August 1995 (33)	Daily maximum air temperatures	Daily mortality (all-cause and type-specific)	Elderly of both sexes were at greatest risk; no difference seen by race or gender; ischemic heart disease was most prominent
Heat wave in Birmingham, England, June 24, 1976–July 8, 1976 (34)	Several weather variables (mean daily temperature above 72°F)	Daily no. of deaths	No. of deaths increased by nearly 20% (and by >30% from July 3 to July 5); excess seen primarily in elderly men and women (aged 70–79 years) with CVD* or cerebrovascular disease
Heat wave in Memphis, Tennessee, June 25, 1980–July 20, 1980 (51)	Average daily temperatures	Heat-related deaths and other mortality outcomes (e.g., type-specific mortality, all-cause mortality, death from natural causes, DOA* rate)	Elderly (aged ≥60 years), poor, Black, inner-city residents were at greatest risk; 83 heat-related deaths in July 1980 vs. 0 in July 1979; statistically significant increase in total and CVD mortality rates and DOA rate; rise in emergency room visits 3 days prior to rise in heat-related deaths
Heat wave in St. Louis and Kansas City, Missouri, July 1980 (53)	Daily maximum temperatures	Heat-related illnesses and deaths from heat stroke	Deaths from all causes increased by 57% and 64% in St. Louis and Kansas City, respectively, and by only 10% in rural areas; greatest risk was seen for elderly (aged ≥65 years), non-Whites, and those of lower SES*
Case-control study; 156 cases with heat stroke or a close friend/family member and 462 controls matched by age, sex, and neighborhood (62)	St. Louis and Kansas City, Missouri heat wave (July 1980)	Fatal and nonfatal heat stroke	Alcoholism, living on higher floors of multistory buildings, and using major tranquilizers increased risk; spending time at home or in other places with air conditioning, living in a residence shaded by trees, being able to care for oneself, being able to undertake vigorous physical activity (and reducing activity during heat waves), and taking extra fluids decreased risk
Heat waves in Texas, June 18, 1980–August 27, 1980 (57)	Afternoon temperatures in excess of 100°F	Heat-related deaths	Males, elderly, Blacks, and persons engaged in heavy labor were at greatest risk; related to lower SES
Heat wave in Chicago, Illinois, July 12, 1995–July 16, 1995; 465 heat-related deaths, July 11, 1995–July 27, 1995 (4)	Heat index (temperature and humidity)	Deaths from hyperthermia (core body temperature ≥105°F)	Males, Blacks, and persons aged ≥75 years were at greatest risk; highest mortality was observed 2 days after heat index peaked; excess CVD deaths
Case-control study; 339 relatives, neighbors, or friends of persons who died and 339 controls matched by age and neighborhood (61)	Chicago, Illinois heat wave, July 12, 1995–July 16, 1995	Heat-related and CVD deaths	Persons confined to bed (OR* = 8.2, 95% CI*: 3.1, 22.0) or living alone (OR = 2.3, 95% CI: 1.2, 4.4) were at increased risk; having a working air conditioner (OR = 0.3, 95% CI: 0.2, 0.6) and having access to transportation (OR = 0.3, 95% CI: 0.1, 0.5) were associated with decreased risk
Heat wave in England, Wales, and Greater London, United Kingdom, July 1995–August 1995 (58)	5-day heat wave	Excess mortality	619 extra deaths (8.9% increase, 95% CI: 6.4, 11.3%) compared with moving average of 31 days for that period in all age groups; mostly women and persons with respiratory and cerebrovascular diseases; attributed >60% of total excess mortality
Heat wave in the northeastern United States, July 4, 1993–July 14, 1993 (55)	Extremely hot weather	Mortality rates compared with June 8, 1993–June 18, 1993	26% increase in total mortality and 98% increase in CVD mortality in Philadelphia, Pennsylvania
Case-control study; 17 cases from surrogate information and 34 controls matched by neighborhood (63)	Cincinnati, Ohio heat wave, summer 1999	Heat-related deaths	Having a mental illness increased risk (OR = 14.0, 95% CI: 1.8, 633); having a working air conditioner decreased risk (OR = 0.03, 95% CI: 0, 0.2)
Heat waves in Milwaukee, Wisconsin, in 1995 and 1999 (93)	Comparison of heat waves	Heat-related deaths and EMS* visits	At least 49% fewer heat-related deaths and EMS visits in 1999 than in 1995; may have been partly due to changes in public health preparedness
Case-control study; 63 cases from surrogate information and 77 controls matched by age and neighborhood (60)	Chicago, Illinois heat wave, summer 1999	Heat-related deaths	Living alone (OR = 8.1, 95% CI: 1.4, 48.1) and not leaving home daily (OR = 5.8, 95% CI: 1.5, 22.0) increased risk; having a working air conditioner decreased risk (OR = 0.2, 95% CI: 0.1, 0.7)

* CVD, cardiovascular disease; DOA, dead on arrival; SES, socioeconomic status; OR, odds ratio; CI, confidence interval; EMS, emergency medical services.

temperature and humidity was associated with increased mortality in Barcelona, Spain (54). The most significant rates of death from myocardial infarction, stroke, and pneumonia were observed with longer-term (>3 weeks) elevated mean temperatures as compared with shorter-term (1–2 days) or medium-term (7–10 days) elevated temperatures (32).

TABLE 2. Results from studies of heat-related mortality specific to cardiovascular and respiratory diseases

Study population (reference no.)	Exposure	Outcome	Results
England and Wales (years not available) (70)	Temperature indicators	Respiratory disease, arteriosclerotic disease, and total no. of deaths	Temperatures above 68°F increased CVD* mortality by 0.5–15.1%, depending on age and specific disease; no gender difference; stronger in elderly
Durban and Johannesburg, South Africa, 1968–1971 (50)	Seasonal variations in temperature	Total, CVD, respiratory, and diabetes mortality	Seasonal variations in mortality among infants aged <1 year and the elderly; related to total mortality and to CVD, respiratory, and diabetes incidence and mortality
Greater London, England, April 1965–December 1972 (52)	Short spells of hot weather during summers (not heat waves)	Mortality	Persons aged ≥60 years were high-risk group; peak mortality observed in deaths from respiratory disease (1968), CVD (1968, 1969, and 1970), and cerebrovascular disease (1970)
Persons aged 70–74 years in England and Wales, 1964–1984 (69)	Summer months (July–September)	All-cause, respiratory disease, coronary disease, and cerebrovascular disease mortality	No significant change from 1964 to 1974, then a decrease from 1974 to 1984 ($p < 0.001$)
The Netherlands, 1979–1987 (37)	Daily temperatures above 68–78°F	Daily mortality rates	26% of unexplained heat-related mortality due to CVD from increased stress on respiratory and circulatory systems
Taiwan, 1981–1991 (42)	Outdoor temperature	CVD mortality	U-shaped temperature-mortality relation (from coronary artery disease (22% excess) and cerebral infarction (66%)—90°F vs. 81–85°F), especially in elderly
Total population resident in Barcelona, Spain, 1985–1989 (54)	Minimum and maximum temperatures, dew point temperature, relative humidity	CVD, respiratory disease, and total mortality; mortality in persons aged >65 years	CVD mortality rose by 4.6% (4.2% in summer) and respiratory mortality by 21.6% (13.2% in summer)
Valencia, Spain, 1991–1993 (41)	Variations in ambient temperature	Daily mortality (total and specific causes)	Effect of temperature was greatest in persons aged >70 years and in cases of death from circulatory and respiratory causes; statistically significant temperature-mortality relation
Time-series study in the Netherlands, 1979–1997 (38)	Daily temperature (average of maximum and minimum temperatures)	Daily mortality (total, malignant neoplasms, respiratory disease, and CVD) in persons aged ≥65 years	V-like relation between temperature and mortality; mortality from all causes increased during heat waves, particularly respiratory mortality; 12.1% average total excess mortality during heat waves (39.8 deaths/day)
Time-series study in Madrid, Spain, January 1, 1986–December 31, 1987 (98)	Daily maximum and minimum temperatures, daily relative humidity	Daily mortality (total, respiratory, and circulatory) among persons aged ≥65 years	Total mortality increased up to 28.4% for every degree above 98°F, particularly among women aged >75 years; temperature effects were enhanced by humidity
Time-series study in Seville, Spain, during the summer months of 1986–1997 (98)	Maximum daily temperature, relative humidity (7:00 a.m.)	Daily mortality (total and cause-specific) in persons aged ≥65 years	Total mortality increased up to 51% for every degree above 106°F among persons aged >75 years; effects were more noticeable for CVD and women

* CVD, cardiovascular disease.

Studies of cardiovascular and respiratory disease mortality

In studies of heat waves and elevated temperature, cardiovascular diseases (37, 42, 50, 52, 54, 69), respiratory diseases (37, 41, 50, 52, 54, 69, 70), and cerebrovascular diseases (42, 52, 69) were prominent causes of death. Table 2 summarizes the findings of studies that examined heat-related mortality specific to these causes. Most deaths occurred in persons with preexisting disease, such as ischemic heart disease, stroke, or respiratory illnesses, although one study found that patients with less severe respiratory diseases were also at risk (37). The main underlying mechanism is that stress on the cardiovascular and respiratory systems increases during periods of high ambient temperature, especially among elderly persons with limited adaptive responses. In elderly persons, the ability to thermoregulate body temperatures is reduced (71), and sweating thresholds are generally elevated in comparison with younger persons (72). When body heat production is greater than necessary to maintain a normal body temperature, blood flow from the body core to the skin increases, and heat is transferred more rapidly to the external environment. As a result, blood pressure may increase initially, and heart and respiratory rates increase (24).

Studies of heat-related mortality in medical facilities

Medical institutions served as the sites of several studies examining the effects of ambient heat exposure in susceptible populations (table 3). These investigations provided a unique opportunity to study risk factors associated with heat-related illnesses, since medical facilities provide a controlled environment housing persons with severe disease. Investiga-

TABLE 3. Results from studies of heat-related mortality in medical facilities

Study population (reference no.)	Exposure	Outcome	Results
Medical records of inpatients at South Manchester University Hospital, Manchester, England, April 1976–July 1976 (73)	Peak daily temperature during heat wave	Weekly no. of deaths	Correlation coefficient = 0.87 ($p < 0.001$); no threshold or lag effect
Retrospective survey of four major teaching hospitals in Adelaide, South Australia, February 1993 (2)	10-day period with exceptionally high ambient temperature	All emergency department presentations (e.g., deaths, hospital admissions)	94 patients had heat-related illness (78% with heat exhaustion), 85% were aged >60 years, 20% were from institutional care; severity was related to preexisting conditions; mortality was 12%
872 patients in a large institution during a hot summer in England (year not stated) (76)	Ambient temperature	Hyperthermia	15.7% of persons aged <60 years developed hyperthermia vs. 18.9% of those aged 70–79 years, 28.3% of those aged 80–89 years ($p = 0.01$), and 50% of those aged ≥90 years ($p < 0.001$); women were more affected than men (25.6% vs. 16.9%); 29% in warmer wards vs. 17.2% in cooler ones ($p < 0.01$); 42.3% of bedridden group vs. 20.4% of semidependent group and 11.1% of mobile group ($p < 0.01$)
Nursing home patients in the Netherlands, 1993–1994 (1)	Weekly averages of daily temperatures	Mortality rates	Mortality rate 50% (95% confidence interval: 44%, 56%) greater than minimum rate during hottest weeks (78–86°F); patients with cardiovascular disease and respiratory conditions were at highest risk

tors have reported that the weekly number of deaths in a geriatric ward increased with peak daily temperature during a heat wave (73) and that psychiatric patients had twice the risk of dying during a heat wave than the general population (74) before air conditioning was readily available. In another study carried out in New York City, deaths in nursing homes without air conditioning were significantly greater than expected (75). Recent studies of patients in institutional care involved patients admitted to a hospital for treatment of hyperthermia (2, 76) or cardiorespiratory disease (1). With an age-related increase, women were more affected than men by marginal hyperthermia (evident if body temperatures reached 101°F on at least one occasion) (76). An association was also found between the incidence of hyperthermia and ambient temperature (29 percent of cases were in the warmer hospital wards on the top floor as compared with 17.2 percent in the cooler ground-floor wards) and with level of dependence (42.3 percent of the bedridden group and 20.4 percent of the semidependent group as compared with 11.1 percent of the mobile group). In another study, nursing-home patients with cardiovascular disease and respiratory conditions were found to be at greater risk of dying during heat waves, with a mortality rate that was 50 percent higher during the hottest weeks (78°F–86°F), compared with the lowest rates (1). Thus, identifying high-risk patients in medical facilities lacking sufficient air conditioning and taking appropriate measures to avoid hyperthermia are essential for decreasing mortality during heat waves.

Studies of the temperature-mortality relation

Further evidence of heat-related mortality comes from studies examining the relation between ambient temperature, rather than heat waves specifically, and mortality (table 4). These studies were able to examine the general risk of elevated temperature in multiple areas over long time periods, using ecologic study designs such as cluster mapping and time-series analyses. In defining temperature, users of these statistical techniques attempt to represent the effect of heat stress. Recent studies have quantified the risk of temperature-related mortality, developing methods for future studies. For example, Hales et al. (40) found that counts of all-cause mortality (1 percent, 95 percent confidence interval: 0.4, 2.1) and respiratory mortality (3 percent, 95 percent confidence interval: 0.1, 6.0) were associated with a 1.8°F increase in temperature in their time-series study conducted in New Zealand.

Seasonal effects. Some long-term studies suggested seasonal effects of temperature-related mortality. Seretakis et al. (45) found seasonal effects to decrease with time from 1937 to 1991 in New England and the southern US states, particularly with adequate heating and air conditioning. Mortality ratios decreased by 2 percent per year until 1970, especially in the New England states, where residents were less likely to be acclimatized to excessive ambient temperatures. A long-term study in England and Wales found no significant change in all-cause, respiratory, coronary, or cerebrovascular mortality among 70- to 74-year-olds in the summer months from 1964 to 1974 (69). From 1974 to 1984, these mortality outcomes decreased ($p < 0.001$), most likely because of lifestyle alterations such as increased access to air conditioning. Seasonal variations in mortality were evident in infants and the elderly but not in adolescents or young adults (50).

Threshold effect. Several temperature-mortality studies identified a minimum temperature above which effects of temperature on mortality were observed; these temperatures varied by location. In a study of 32 US cities, mortality from coronary heart disease and stroke was generally found to increase at temperatures greater than 60–70°F (77). Warmer-than-usual temperatures in six US states in July and August were linked to higher mortality in a time-series study, with both immediate and delayed effects (39). In Japan, the greatest risk of death occurred on days when peak daily

TABLE 4. Results from studies of the temperature-mortality relation other than studies of heat-wave exposure that used cluster maps and time-series analyses

Study population (reference no.)	Exposure	Outcome	Results
32 US cities, 1962–1966 (77)	Daily temperature and snowfall	Coronary heart disease and stroke deaths	Mortality generally rose at temperatures >60–70°F and temperatures <10°F
Cluster maps of persons aged ≥65 years in the United States, 1979–1985 (44)	Excessive heat	Mortality	Persons who were highly urbanized, non-White, or poor were at highest risk
Six US states (Massachusetts, Michigan, Washington, North Carolina, Mississippi, and Utah), 1921–1985 (39)	Monthly temperature fluctuations	Mortality	Warmer-than-usual temperatures in July and August were linked to higher mortality, with immediate and delayed effects
New England and the South, United States, 1937–1991 (45)	Seasonal patterns, environmental heat and cold	Coronary heart disease mortality, monthly mortality	Seasonal patterns have changed over time (with adequate heating and air conditioning); peak:trough ratio decreased by 2% per year until 1970, especially in New England
Heat-related deaths in Japan, 1968–1994 (78)	High ambient temperature	Mortality	Death was prone to occur above 101°F, with an exponential dependence on the no. of hot days; 50% of deaths occurred in children aged <4 years and elderly persons aged ≥70 years; results were similar in males and females
Time-series study of Christchurch, New Zealand, June 1988–December 1993 (40)	Daily weather	Daily no. of deaths	1.8°F increase was associated with a 1% (95% CI*: 0.4, 2.1%) increase in all-cause mortality and a 3% (95% CI: 0.1, 6%) increase in respiratory mortality; no evidence of interaction with air pollutants
Time-series study of 11 eastern cities in the United States, 1973–1994 (30)	Daily weather	Mortality	Temperature most strongly predicted mortality with a U-shaped relation, inverse relation with latitude (higher latitudes have lower minimum mortality temperatures)
Heat-mortality association in Toronto, Ontario, Canada, 1980–1996 (56)	Humidex (temperature and humidity) and apparent temperature	Excess mortality	Excess mortality with humidex 86–95°F (below current standard of 104°F); mortality for persons aged ≥65 years increased with higher humidex and apparent temperature
Time-series study in London, England, January 1976–December 1996 (79)	Daily temperature	Daily mortality	Average temperatures above the 97th percentile (70°F) resulted in an increase in deaths of 3.34% (95% CI: 2.47, 4.23%) for every 1° increase in average temperature; longest duration and highest temperature had greatest mortality effect

* CI, confidence interval.

temperatures exceeded 100°F, with an exponential dependence on the number of hot days (78). A rise in heat-related deaths was observed at only 68°F in England, with average temperatures above the 97th percentile (70°F) producing an increase in deaths of 3.34 percent (95 percent confidence interval: 2.47, 4.23) for every 1.8°F increase in temperature above 70°F (79).

Latitude variations. As weather patterns and adaptive abilities vary by latitude, a differential effect of temperature on mortality has been found throughout the United States. Minimum mortality temperature (i.e., the inflection point of the U-shaped curve), defined as the temperature of the lowest temperature-associated mortality observed in a city, was shown to vary by latitude in a recent time-series study conducted by Curriero et al. (30). People who live in cities at higher latitudes, such as Chicago, Illinois, and Boston, Massachusetts, have lower minimum mortality temperatures, while people who live in cities at lower latitudes (e.g., Miami and Tampa, Florida) have higher thresholds for ambient temperature. Thus, people who reside in the northern United States may be at greater risk of dying from heat waves.

Kalkstein and colleagues have provided further insights into latitude variations (31, 80–83). In their 1989 study, Kalkstein and Davis (80) discussed the spatial variability within US metropolitan areas, suggesting that higher mortality was related to the summer season in warm, humid, and calm conditions, particularly in areas where hot weather is uncommon. Using seven spatial synoptic air masses to define temperature exposure—dry polar, dry temperate, dry tropical, moist polar, moist temperate, moist tropical, and transition—Kalkstein and Greene (83) recognized that each air mass varied on the basis of daily air temperature, dew point temperature, visibility, total cloud cover, sea-level air pressure, wind speed, and wind direction. They found that a hot and dry air mass had more influence on mortality in the eastern United States than in the southern states, where it is more commonly experienced, and that it may increase daily mortality by as much as 50 deaths in large eastern cities. Overall summer mortality was predicted to increase dramatically in the future, regardless of acclimatization to the increased warmth.

TABLE 5. Results from studies of the effect of the air pollution-temperature relation on mortality

Study population (reference no.)	Exposure	Outcome	Results
10 large cities in the United States, 1962–1965 (89)	Temperature, dew point, air pressure, air pollutants	Daily mortality	Exposure variables were accompanied by daily fluctuations in mortality in the northern and northeastern United States
Los Angeles County, California, 1970–1979 (84)	Weather factors (temperature, relative humidity) and air pollutants (carbon monoxide, sulfur dioxide, nitrogen dioxide, halocarbon, ozone, total suspended particulates)	Daily mortality (total, respiratory disease, and cardiovascular disease)	Positive association was observed for temperature, pollution, or both; sulfur dioxide, nitrogen dioxide, ozone, and relative humidity were nonsignificant
Summer synoptic categories in St. Louis, Missouri, 1964–1990 (81)	Weather, pollution concentrations	Daily mortality	Synoptic categories including long, consecutive days of hot, oppressive weather were associated with a continuing rise in mortality; people were more sensitive to weather than to pollutants
United States, Canada, China, and Egypt (years not stated) (31, 82)	Climate change	Heat-related mortality	Greatest impacts were seen in China and Egypt; in the United States, air pollution did not appear to impact daily mortality significantly when severe weather was present but had a slight influence otherwise
Mortality after a heat wave in Belgium, June 27, 1994–August 7, 1994 (88)	Temperature, relative humidity, and 24-hour concentrations of main air pollutants	Daily mortality compared with expected mortality during the summers of 1985–1993	Mortality increased by 9.4% in persons aged <65 years (236 excess deaths; $p < 0.001$) and by 13.2% in the elderly (1,168 excess deaths; $p < 0.001$); synergy between temperature (59–82°F) and ozone concentration (34.5–111.5 μg/m^3), both measured 1 day before
Barcelona, Spain, 1985–1991 (85)	Daily air pollutant values	Daily mortality (total, cardiovascular disease, and respiratory disease)	Nitrogen dioxide and ozone were positively related to elderly mortality (RR* = 1.05 and RR = 1.09, respectively) and cardiovascular disease mortality (RR = 1.07 and RR = 1.09) during the summer
APHEA* Project in Athens, Greece, 1975–1987 (86)	Sulfur dioxide, black smoke, carbon monoxide, temperature, relative humidity	Daily mortality	U-shaped relation of temperature and mortality; relative humidity was not significant; sulfur dioxide and temperature were significant (not black smoke or carbon monoxide)
12 European cities in the APHEA Project, 1991–1994 (87)	Sulfur dioxide, PM_{10}*, and possible confounding factors	Relative risk of death	Effects of sulfur dioxide and PM_{10} were stronger in summer and were mutually independent
Philadelphia, Pennsylvania, 1973–1980 (90)	Sulfur dioxide and total suspended particulates, weather (using four different models)	Daily mortality	Weather did not significantly modify effects of air pollutants

* RR, relative risk; APHEA, Air Pollution and Health: A European Approach; PM_{10}, particulate matter less than 10 μm in aerodynamic diameter.

Effect of the relation between air pollutants and temperature on mortality

In many locations, patterns of air pollution are driven by the weather, and concentrations of pollutants may be associated with temperature. The relations among air pollutant levels, temperature, and mortality have been investigated in several studies (table 5). These studies have produced conflicting results, and it is uncertain whether air pollutants are confounders and/or effect modifiers (i.e., a synergistic effect) of the temperature-mortality association (84–88) or whether they have no effect on mortality with temperature (81, 89, 90). Thus, additional studies examining the effect of the relation between air pollutants and temperature on mortality are warranted.

SUMMARY AND FUTURE RESEARCH

To date, a number of studies have shown that mortality is increased during heat waves and that ambient heat exposures, primarily indexed by temperatures, are positively associated with mortality. Beginning with descriptive heat-wave and mapping studies that provided early evidence of heat-related mortality in specific cities, the scope of research has expanded to address heat and mortality in larger, more diverse populations in multiple areas using time-series and case-crossover analyses. The findings suggest that persons with preexisting cardiovascular and respiratory diseases have increased risk of death associated with ambient heat exposure and that risk is higher for several population groups, including the elderly, infants, and persons of low socioeconomic status. Other specific risk factors include lack of air conditioning, lack of access to transportation, living alone, using tranquilizers, having a mental illness, and living on higher floors of multistory buildings. Temperatures at lag times of 0–3 days have been observed to produce the maximum effect of mortality following heat waves, demonstrating that heat-related mortality is an acute event requiring timely intervention.

The studies of risk factors, along with related qualitative assessments, make clear that a convergence of individual and community characteristics places some people at high risk for heat-related mortality. Klinenberg (91) recently provided a comprehensive description of the Chicago heat wave of 1995, elegantly highlighting how an unusual period of high temperature resulted in striking excess mortality for particular people in specific neighborhoods in Chicago. The Chicago experience affords a powerful reminder that prevention efforts involve individuals and communities. The epidemiologic information derived from heat waves is useful for identifying persons at high risk, as shown in Semenza et al.'s (61) case-control study in Chicago.

The available information has long been sufficient to support a need for intervention and to indicate potential avenues for research. Some studies have focused on evaluating preventive efforts by comparing adverse effects of two successive heat waves in the same locale. In a comparison of the 1980 and 1995 heat waves in St. Louis, Missouri, the 1980 heat wave was more severe, with higher heat-related mortality (92). Nonetheless, persons residing in St. Louis remained at risk for heat-related mortality, despite increased use of air conditioning and preventive efforts. In another comparison of heat waves in 1995 and 1999 occurring in Milwaukee, Wisconsin, heat-related deaths and emergency medical service visits were reported to be at least 49 percent lower in 1999 than in 1995 (93). The decrease in associated mortality cannot be attributed to differences in temperature levels, and preventive efforts may have played a role in these reductions. Thus, city-specific interventions for heat-related mortality, like those established in Chicago (93) and Toronto (56), may be beneficial in preventing heat-related mortality. A "heat warning" watch for high-risk cities can be developed and implemented with the help of government health agencies, physicians, and neighborhood programs. Interventions may consist of: 1) implementation of a "buddy system" whereby a person on each street ensures that elderly and ill persons are remaining unharmed during a heat wave; 2) media broadcasts of a "heatline" telephone number for persons who are becoming ill from the heat; 3) suggestions to drink more fluids and to stay in air-conditioned places along with heat advisories; and 4) providing transportation to air-conditioned areas such as shopping centers during a heat wave (23).

Based primarily on previous US heat waves, the current National Weather Service guidelines suggest issuing a heat advisory whenever a daytime heat index reaches or exceeds 105°F and whenever a nighttime minimum ambient temperature greater than or equal to 80°F persists for at least 48 hours (94). However, these guidelines may be inadequate for preventing heat-related deaths in specific cities, since the evidence shows variation by location and region. Updated policies should be implemented on the basis of the latest research and surveillance findings. Elderly people living in urban environments, who are particularly vulnerable to the effects of heat stress, should be the focus of preventive efforts. Although previous studies have identified the elderly to be at an increased risk of heat-related mortality (4, 32, 33, 56, 59, 74), risk factors have not been characterized specifically for them. Adaptation to heat exposure may prevent some heat-related deaths, though not necessarily during periods of extreme heat. Thus, more research is needed to examine the relation between temperature and mortality, focusing on the elderly population.

Further research should better consider the multiple levels of factors that determine risk for heat-related adverse outcomes. Time-series studies at the population level link temperature or weather patterns to mortality while not considering community or individual characteristics and responses to heat. Multilevel designs could prove informative, if the requisite data on communities or neighborhoods could be obtained. For example, such designs have been applied recently to assess determinants of violence in Chicago neighborhoods (95). Hierarchical models developed for studies of air pollution could be extended to the investigation of heat as well (96). Acclimatization (i.e., people's ability to adapt to climate patterns that they commonly experience) can be addressed by conducting city-specific as well as regional analyses by season. The Eurowinter Study, assessing adaptation to cold across multiple countries in Europe, provides one useful research model (97).

With regard to climate change and health, gaps in the evidence identified in the recent US National Assessment Report need to be addressed (22). These include establishing the confounding and/or modifying effect of the relation between air pollutants and temperature on mortality, examining changes in infectious disease patterns resulting from weather changes, and conducting heat exposure assessment studies. Specifically, the health impacts of chronic exposure to high-level ozone and other air pollutants—particularly for persons with asthma or other chronic lung diseases—and the mechanisms responsible for promoting adverse health effects should be evaluated. Rates of water-borne, food-borne, vector-borne, and rodent-borne infectious diseases are likely to increase during periods of higher temperature and changes in weather patterns (e.g., greater rainfall in some areas and drought in others). Many detrimental effects of elevated ambient temperature have been identified, and these effects will probably worsen with global warming. Therefore, further research is required in order to bring these issues to public attention and to instigate policy changes.

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