REVIEW ARTICLE

Prognostic Factors in Heat Wave–Related Deaths

A Meta-analysis

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Background: Although identifying individuals who are at increased risk of dying during heat waves and instituting protective measures represent an established strategy, the evidence supporting the components of this strategy and their strengths has yet to be evaluated. We conducted a meta-analysis of observational studies on risk and protective factors in heat wave–related deaths.

Methods: Using the OVID interface, we searched Medline (1966-2006) and CINHAL (1982-2006) databases. The Web sites of the World Health Organization, Institut National de Veille Sanitaire, and Centers for Disease Control and Prevention were also visited. The search terms included *heat wave*, *heat stroke*, *heatstroke*, *sunstroke*, and *heat stress disorders*. Eligible studies were case-control or cohort studies. Odds ratios (ORs) and information on study quality were abstracted by 2 investigators independently. Six case-control studies involving 1065 heat wave–related deaths were identified.

Results: Being confined to bed (OR, 6.44; 95% confidence interval [CI], 4.5-9.2), not leaving home daily (OR, 3.35; 95% CI, 1.6-6.9), and being unable to care for oneself (OR, 2.97; 95% CI, 1.8-4.8) were associated with the highest risk of death during heat waves. Preexisting psychiatric illness (OR, 3.61; 95% CI, 1.3-9.8) tripled the risk of death, followed by cardiovascular (OR, 2.48; 95% CI, 1.3-4.8) and pulmonary (OR, 1.61; 95% CI, 1.2-2.1) illness. Working home air-conditioning (OR, 0.23; 95% CI, 0.1-0.6), visiting cool environments (OR, 0.34; 95% CI, 0.2-0.5), and increasing social contact (OR, 0.40; 95% CI, 0.2-0.8) were strongly associated with better outcomes. Taking extra showers or baths (OR, 0.32; 95% CI, 0.1-1.1) and using fans (OR, 0.60; 95% CI, 0.4-1.1) were associated with a trend toward lower risk of death.

Conclusion: The present study identified several prognostic factors that could help to detect those individuals who are at highest risk during heat waves and to provide a basis for potential risk-reducing interventions in the setting of heat waves.

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THE HEAT WAVE THAT AFfected Europe during the summer of 2003 led to 22 000 to 45 000 excess deaths.[1-3] A more recent estimation revised these figures to an unprecedented 70 000 excess deaths.[4] France alone recorded 14 800 deaths in 9 days, and one-third of the deaths were attributed to heatstroke, a lethal condition that is characterized by a rapid increase in core temperature to more than 40°C and widespread multiple organ tissue injury.[5-8] Detailed analysis of excess deaths revealed that, in addition to heatstroke, common medical conditions, such as cardiovascular and pulmonary or psychiatric illnesses, are aggravated by heat and thus contribute to the mortality rate.[1,3,5,9] Sophisticated climate models predict increasing frequency and severity of heat waves; therefore, the incidence of heat-related death could increase if proactive measures to address this threat are not adopted.[2,10]

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During heat waves, most victims are found dead at home; eg, in France in August 2003, 8584 victims (58%) died without the benefit of hospital care, and in the summer of 1980 in the United States, 103 of 156 persons (61%) with heatstroke were hospitalized or found dead within 1 day of the reported onset of illness.[3,5,9] Moreover, by the time the patients reach the hospital, the mortality from heatstroke can approach 60%, and survivors may sustain permanent neurologic damage.[7,8] These observations suggest that prevention is central to any public health strategy.

Several methods of intervention are considered crucial to reducing mortality and morbidity; they consist of identifying individuals at increased risk of dying during a heat wave and directing protective measures toward them.[6,11,12] These protective measures include establishing contact with the isolated elderly population to ensure that vulnerable individuals without domestic air-conditioning spend some hours in a cool environment, increase fluid intake, take extra showers or baths, and reduce outside activities.[11,12] Although these various approaches are now established, supporting evidence for their effectiveness has yet to be evaluated.

Systematic review of randomized controlled trials is increasingly popular in assessing the value of intervention in health care.[13] Studies of risk factors or health interventions associated with heat wave–related mortality are virtually impossible to randomize. They are unethical and impractical as they require follow-up on elderly persons in precarious health and social conditions during exposure to severe environmental heat.[13] Observational studies are therefore more appropriate and hence more commonly available.[13] The goal of the present study was to conduct a meta-analysis of observational studies on the risk and protective factors in heat wave–related death, from the perspective of providing an evidence-based framework for health intervention.

METHODS

SEARCH STRATEGY

A computerized literature search was performed on the Medline database to cover the period from January 1966 to March 2006. The search was also performed on the CINHAL (Cumulative Index to Nursing and Allied Health Literature) database for the period 1982 to 2006 using the OVID interface. The Web sites of the World Health Organization, European Center for Environment and Health (www.euro.who.int), the Institut National de Veille Sanitaire (www.invs.sante.fr/display/?doc=surveillance/canicule/alerte.htm), and the Centers for Disease Control and Prevention (www.bt.cdc.gov/disasters/extremeheat/index.asp) were visited, and guidelines on health interventions for heat were examined and cross-checked for references used to establish the guidelines. The bibliography of retrieved articles was also checked. The search was limited to human studies without language restriction, using the following Medical Subject Heading (MeSH) terms: *heat wave*, *heat stroke*, *heatstroke*, *sunstroke*, and *heat stress disorders*. The references were downloaded into a reference manager, Endnote version 9 (Thomson Research Soft, Philadelphia, Pennsylvania).

STUDY SELECTION

Two investigators (A.B. and M.D.) independently evaluated the retrieved articles and made selections based on 2 criteria: (1) the population studied should have comprised patients whose death was attributed to heat wave; and (2) the risk and/or protective factors should have been examined in heat wave–related fatalities and controls, and odds ratios (ORs) and 95% confidence intervals (CIs) should have been generated (**Figure 1**). To be included in the analysis, each factor should have been determined in at least 3 independent studies.

END POINTS AND DEFINITIONS

Heat-Related Death

Heat-related death is defined as death in which exposure to a high ambient temperature either caused or contributed to death.[14] It includes (1) premortem or postmortem evidence of a body temperature equal to 40.6°C or higher; (2) if the body temperature is lower, evidence of changes in mental status and increased liver and muscle enzyme levels; and (3) when body temperature is not available, evidence of high environmental temperature at the time of death and exclusion of other causes of death. In the first 2 categories, death is certified as heatstroke or hyperthermia, and in the third, it is listed as a secondary cause of death.

All-Causes Death During Heat Waves

All-causes death during heat waves is defined as heat-related death and death resulting from common causes during heat waves. Analysis of deaths during heat waves revealed that 12% to 100% of the additional deaths were attributable to common medical conditions, particularly preexisting cardiovascular and psychiatric illnesses, without fulfilling the criteria of heat-related death as described in the previous subsection.[1,3,9,15-20]

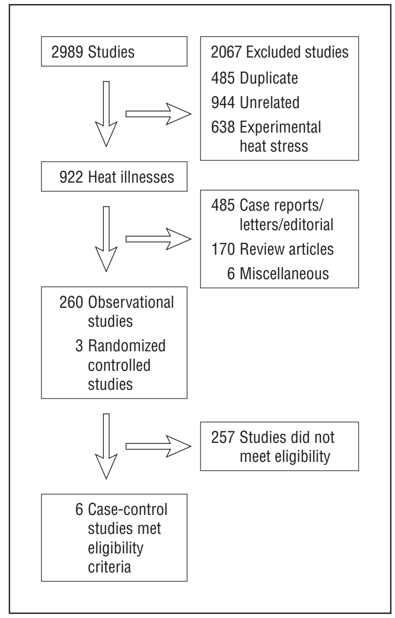

Figure 1. Flow diagram of the selection process.

Risk and Protective Factors During Heat Waves

Risk and protective factors during heat waves were classified according to their OR. A factor represents risk when the OR is greater than 1 and is protective when the OR is less than 1.

DATA EXTRACTION

Data were extracted by 2 of us (A.B. and M.D.) using a predefined review spreadsheet. Any difference was resolved by discussion to reach consensus among the investigators.

STUDY APPRAISAL

Study quality was assessed according to the following published criteria[13]: an explicit statement of the problem under study; a description of the considered study outcome; an explanation of how case patients and control subjects were selected; a description of the type of exposure or intervention; and information on data collection, analytic methods, and sample size. To circumvent subjective assessment, we did not generate an overall quality score; instead, we used an explicit description of the limitations of each individual study.

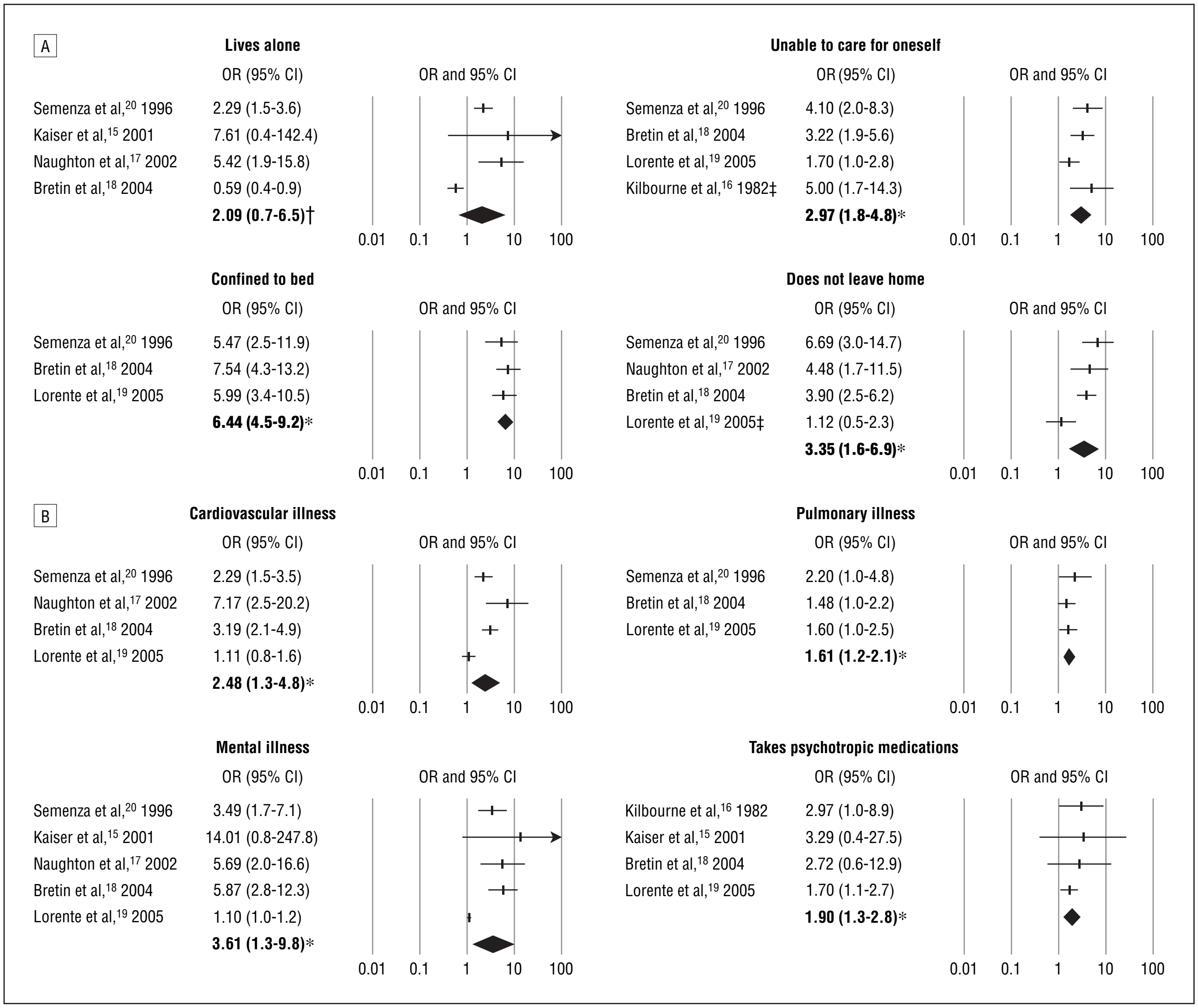

Figure 2. A, Individual summary odds ratios (ORs) and 95% confidence intervals (CIs) for social conditions and general health risk factors in all-causes deaths during heat waves using random-effects model. *$P<.001$. †$P>.05$. ‡Reciprocal OR calculated for unable to care for oneself (from able to care for oneself) and for does not leave home (from leaves home). B, Individual and summary ORs and 95% CIs for preexisting medical condition risk factors in all-causes deaths during heat waves using random-effects model. *$P<.01$.

DATA ANALYSIS

The summary ORs and 95% CIs were determined from the selected studies. The reciprocal of the OR was occasionally calculated as indicated in **Figure 2**A and **Figure 3** and the figure legends to maintain uniformity of the interpretation of the ORs and 95% CIs of a studied factor. The summary ORs and 95% CIs were calculated using both fixed- and random-effects models. The choice between these 2 models was based on the Cochran Q χ^2 test of heterogeneity. Subgroup and sensitivity analyses were performed to explore the potential sources of heterogeneity according to the case definition group (all-cause and heat-related mortality), type of studies (population based and retirement home based), and settings (United States and France). For each factor, a Forest plot was produced. All calculations and graphical representations were performed using a commercially available meta-analysis software program (Comprehensive Meta Analysis, version 2; Biostat Inc, Englewood, New Jersey).

RESULTS

SEARCH RESULT

The initial search using a broad strategy identified 2989 references (Figure 1), from which 922 titles and abstracts were selected after elimination of duplicate citations, references unrelated to heat illnesses, and studies consisting solely of experimental research. The 922 references represented 3 randomized controlled studies (that assessed the cooling techniques) and 260 observational studies, of which 6, all case-control studies, met the eligibility criteria and were subjected to analysis.[15-20] Four studies were in English and were identified in PubMed, and 2 were in French and were published on the Institut National de Veille Sanitaire Web site.

CHARACTERISTICS OF THE STUDY POPULATION

The **Table** presents the characteristics of the 6 studies, which included 1148 case patients and 1485 control subjects, covering American and European populations. Five studies were population based[15-18,20] and 1 was re-

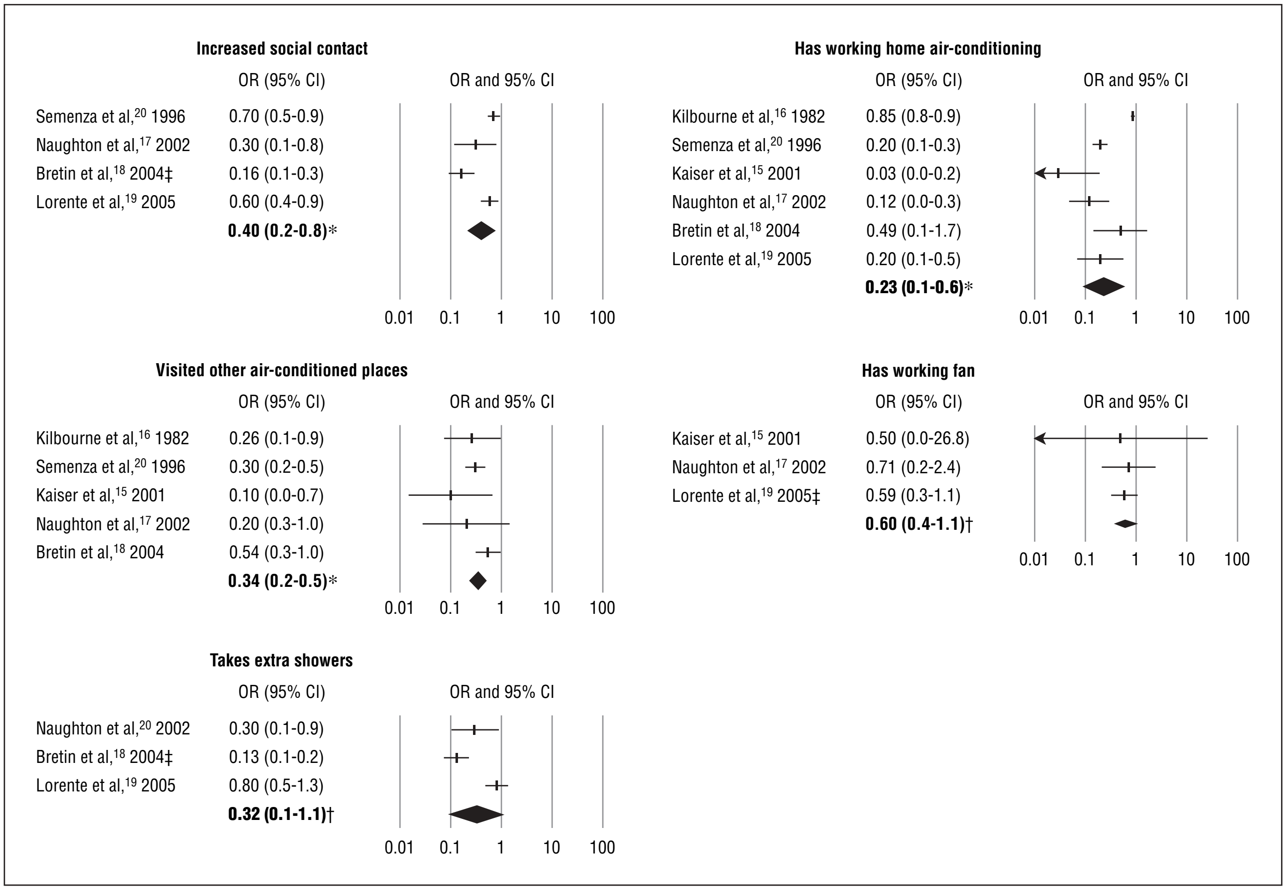

Figure 3. Individual and summary odds ratios (ORs) and 95% confidence intervals (CIs) for protective factors in all-causes deaths during heat waves using random-effects model. $^*P<.001$. $^\dagger P>.05$. ‡Reciprocal OR calculated for increased social contact (from no social contact), takes showers or baths more than once a day (from once per day, every 2 days, once a week, or never), and has a working fan (from does not have a working fan).

tirement home based.[19] All studies described a clear strategy for identifying cases. The studies included all deaths that occurred during heat waves; however, 1 study included both fatal and nonfatal heatstroke, but only the fatal heatstroke cases (n=73) were analyzed .[16] The cause of death was based on the death certificates in 4 studies[15-17,20] and on clinical criteria in 2 studies.[18,19] Among the 1065 case patients, heat was noted as the immediate or contributive cause of death in 573 cases (53.8%), while cardiovascular illness and other causes of death, with no reference to heat, were noted in 492 cases (46.2%).[15-18,20] All but 1 study[15] used age- and neighborhood-matched controls, and in 2 studies, the controls were also matched according to sex.[16,18] The assessment, particularly the limitations, of each study is shown in the Table and includes small sample size or insufficient matching of case patients and control subjects as well as the use of an outcome that was lacking specificity.

ANALYSIS OF ALL-CAUSES DEATH DURING HEAT WAVE

The Cochran *Q* test revealed statistically significant heterogeneity in 7 of 13 risk and protective factors analyzed in the present study.[15-20] We elected to calculate the summary ORs using a conservative approach, ie, the random-effects model, for all factors.

Factors Associated With Higher Risk

Figure 2A shows that being confined to bed (OR, 6.44; 95% CI, 4.5-9.2; $P<.001$), not leaving home daily (OR, 3.35; 95% CI, 1.6-6.9; $P<.001$), and being unable to care for oneself (OR, 2.97; 95% CI, 1.8-4.8; $P<.001$) were associated with the highest risk of death during a heat wave. Living alone during a heat wave was associated with a trend toward increased risk of death but was not statistically significant (OR, 2.09; 95% CI, 0.7-6.5; $P=.20$). Figure 2B shows that among preexisting medical conditions, psychiatric illness (OR, 3.61; 95% CI, 1.3-9.8; $P<.01$) was the factor most strongly associated with death, followed by cardiovascular illness (OR, 2.48; 95% CI, 1.3-4.8; $P<.01$), taking psychotropic medications (OR, 1.90; 95% CI, 1.3-2.8; $P<.001$), and pulmonary illness (OR, 1.61; 95% CI, 1.2-2.1; $P<.001$).

Factors Associated With Lower Risk

Figure 3 shows that having working air-conditioning at home (OR, 0.23; 95% CI, 0.1-0.6; $P<.01$), visiting other air-conditioned environments (OR, 0.34; 95% CI, 0.2-0.5; $P<.001$), and participating in social activities (OR, 0.40; 95% CI, 0.2-0.8; $P<.01$) were associated with lower risk of death. Taking extra showers or baths (OR, 0.32; 95% CI, 0.1-1.1; $P=.07$) and using fan ventilation (OR, 0.60; 95% CI, 0.4-1.1; $P=.31$) during a heat wave were associated with a trend toward lower risk of death but were not

Table. Summary of Data From Studies for All-Causes Death During Heat Waves From 1966 to 2006

Source (Country)	Population: Case Patients	Population: Control Subjects	Outcomes Measured	Limitations
Kilbourne et al (US),[16] 1982	156 Heatstroke survivors and nonsurvivors in 1980 St Louis and Kansas City, MO, heat wave	462 Age-, sex-, and neighborhood-matched subjects	Fatal and nonfatal heatstroke[a]	None
Semenza et al (US),[20] 1996	339 Nonsurvivors in 1995 Chicago, IL, heat wave	339 Age- and neighborhood-matched subjects	Heat wave–related death	None
Kaiser et al (US),[15] 2001	17 Nonsurvivors in 1999 Cincinnati, OH, heat wave	34 Neighborhood-matched subjects	Heat-related death	Small sample size; control subjects younger than case patients; percentage of women and blacks higher among case patients than among control subjects
Naughton et al (US),[17] 2002	63 Nonsurvivors in 1999 Chicago heat wave	77 Age- and neighborhood-matched subjects	Heat-related death	Percentage of preexisting medical illnesses higher among case patients than among control subjects
Bretin et al (Fr),[18] 2004	259 Nonsurvivors in 2003 European heat wave (aged ≥65 y and living at home)	259 Age-, sex-, and neighborhood-matched subjects	Heat wave–related death[b]	Selection of case patients based on clinical criteria
Lorente et al (Fr),[19] 2005	314 Nonsurvivors in 2003 European heat wave (living in retirement home)	314 Age- and retirement home–matched subjects	Heat wave–related death[c]	Selection of case patients based on clinical criteria

Abbreviations: Fr, France; US, United States.
[a] Only fatalities due to heatstroke (n = 73) were subjected to analysis.
[b] Mortality adjusted for age.
[c] Mortality adjusted for sex and inability to care for oneself.

statistically significant. There were insufficient data to assess other common recommendations, such as extra intake of fluid and reducing outdoor activity.

ANALYSIS OF HEAT-RELATED DEATH DURING HEAT WAVE

Of the 6 studies, 3 included solely heat-related death case patients (n=153), and 3 included heat-related cases combined with common causes of death during heat wave. The percentage of heat-related case patients was 46.1% (420 of 912) of the total case patients, all of whom were clearly identifiable, thus permitting their inclusion in the analysis. The summary ORs of risk and protective factors in heat-related deaths are comparable with those of all-causes death during heat waves (data not shown).

POPULATION-BASED VS RETIREMENT HOME–BASED CASE PATIENTS

Of the 6 studies, 5 used population-based case patients,[15-18,20] including 70.5% (751 of 1065) of patients, and 1 used retirement home–based case patients,[19] including 29.5% (314 of 1065) of patients. The Cochran *Q* test revealed statistically significant heterogeneity for 3 of the 9 factors studied. The risk of dying during a heat wave is reduced among persons who are unable to take adequate care of themselves (OR, 1.7; 95% CI, 1.0-2.8) and among those who have a preexisting cardiovascular (OR, 1.1; 95% CI, 0.8-1.5) or psychiatric illness (OR, 1.1; 95% CI, 1.0-1.2) when they are institutionalized in retirement homes compared with those who are not (OR, 3.7; 95% CI, 2.5-5.5; OR, 3.1; 95% CI, 2.0-5.0; and OR, 4.8; 95% CI, 3.0-7.6, respectively; $P<.001$).

STUDIES IN FRANCE COMPARED WITH STUDIES IN THE UNITED STATES

Of the 6 studies, 4 were performed in the United States[15-17,20] and 2 in France[18,19]; they included 492 (46.2%) and 573 (53.8%) case patients, respectively. No difference in the magnitude of the ORs was observed between the 2 groups, and the Cochran *Q* test revealed statistically significant heterogeneity for 1 factor only. In contrast to the United States, in France living alone was not associated with an increased risk of dying during a heat wave (OR, 3.0; 95% CI, 1.6-5.7; and OR, 0.6; 95% CI, 0.4-0.9, respectively; $P<.001$).

COMMENT

A meta-analysis of 6 case-control studies established the following evidence: First, social precariousness and poor general health, ie, being confined to bed ($P<.001$), unable to adequately care for self ($P<.001$) or to leave home daily ($P<.001$), or having a preexisting cardiovascular ($P<.01$), pulmonary ($P<.001$), or psychiatric ($P<.01$) condition, are significantly associated with death during a heat wave. Second, having working air-conditioning ($P<.01$) is the strongest protective factor, followed by access to an air-conditioned place for some hours ($P<.001$) and participating in social activities ($P<.01$) during a heat wave. There was a trend that showed taking extra showers or baths and use of a fan during a heat wave reduced the risk of dying, although the trend was not statistically significant. These findings are in agreement with those of previous descriptive observational studies and reinforce the notion that withdrawing this distinct population at risk from heat, even for a short time, is the cornerstone of any public health response during a severe heat wave.[9,11,12,17,21-23]

Our meta-analysis has several limitations. The findings of a meta-analysis depend on the methodology and design of the individual studies, as their potential problems and biases may affect the pooled estimate of the ORs.[13] A potential bias of case-control studies is the necessity to rely on surrogates' postmortem reports, which may be inaccurate and lead to misclassification of risk factors, eg, underestimation or overestimation of social factors or preexisting medical conditions. Also, even though the control subjects in these studies were carefully matched to case patients, reluctance to disclose a full social or medical condition, eg, a history of psychiatric illness or dependence on medication, is a possibility and may result in imprecise ascertainment of risks or protective factors. Another possible source of bias is the fact that different definitions of case patients were grouped together, although segregated group analysis suggested that comparable risk and protective factors are at play during a heat wave, whether or not the observed outcome is clearly attributable to excessive heat exposure. Moreover, population- and retirement home–based studies were grouped together, which may have resulted in differences in terms of risk and protective factors. Being institutionalized clearly reduces the risk of death in patients who are unable to take adequate self-care or who have a preexisting cardiovascular or psychiatric condition. This finding is consistent with the hypothesis that, with appropriate help, the outcome of this vulnerable population, which is composed of individuals who are physically and cognitively impaired and who are thus potentially unable to drink enough fluids, to gain access to cool places without help, or to recognize symptoms of heat exposure during a heat wave, can improve dramatically. Finally, the population-based studies covered different geographic locations (the United States and France) and therefore different ethnic and social backgrounds, which may have added to the heterogeneity of the studies. It is noted that in all population-based studies in the United States, but not in France, living alone greatly increased the risk of dying during a heat wave, although the explanation for this difference is not immediately apparent. Nonetheless, to ensure consistency of the results, these potential sources of heterogeneity were clearly identified and accounted for. The consistency of the results was achieved by varying the approach of aggregation (French vs US studies, population-based and retirement home–based studies, and all-cause mortality and heat-related mortality) as well as by choosing the random-effects model, a more conservative approach that assumes that the effect on the outcome is not identical and follows an unknown distribution.

Despite these limitations, our meta-analysis has important implications for prevention. To our knowledge, this is the first study that has attempted to collect the scanty data that are available in the field of heat wave–related mortality and morbidity and to present them in an evidence-based framework. Also, the analysis provides pooled data for more than 1000 cases and controls and thus has sufficient power to estimate more accurately the risk factors and protective measures as well as the extent of their effect during a heat wave. The meta-analysis could help formulate recommendations for the prevention of heat wave–related mortality and morbidity. Finally, the present study has identified areas for further research. For instance, while the study shows that spending a few hours in a cool environment is protective, it does not provide quantitative information such as the number of hours needed. Likewise, other common recommendations, such as using a fan, drinking extra water, taking extra showers, and reducing outdoor activities, would need further evaluation, particularly as they are not without potential adverse effects. Encouragement to drink additional water during a heat wave has recently been associated with severe hyponatremia.[24] Likewise, taking extra showers or baths might increase the risk of falls and traumatic injury in the elderly population. Finally, fan ventilation, which is extremely popular, needs further study before definitive recommendations can be made, because fan ventilation might not be effective, as has been suggested in previous reports,[16,17,20] and may even be harmful if it is not properly used, as detailed elsewhere.[25] A fan induces air movement that increases evaporation and lowers skin temperature, but in warm environments increased wind speeds of hot air can actually raise the skin temperature and thus produce opposite results by increasing core body temperature.[25,26] Further studies assessing the risk and benefit of each intervention would therefore provide important information that may help to generate improved practice guidelines.

In conclusion, although our data should be interpreted cautiously because of the limited number of qualifying studies and the limitations inherent in case-control studies, the present meta-analysis identifies a population at greatest risk of dying during a heat wave, along with several potentially important prognostic factors that may help to stratify risks as well as to generate potentially efficacious interventions. We extended our literature search to March 2007 and found only 1 additional study on Medline that fulfilled the inclusion criteria. However, this study was reported on the Web site of the Institut National de Veille Sanitaire and was already included in the current meta-analysis (Bretin et al[18]). This new reference has been added to the reference list (Vandentorren et al[27]).

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