ORIGINAL ARTICLE

The Effects of Climate Change on Patients With Chronic Lung Disease

A Systematic Literature Review

Christian Witt*, André Jean Schubert*, Melissa Jehn, Alfred Holzgreve, Uta Liebers, Wilfried Endlicher, Dieter Scherer

SUMMARY

Background: Ever since higher overall mortality rates due to heat stress were reported during the European heat waves of 2003 and 2006, the relation between heat waves and disease-specific events has been an object of scientific study. The effects of heat waves on the morbidity and mortality of persons with chronic lung disease remain unclear.

Methods: We conducted a systematic search using PubMed, the Cochrane Library, and Google Advanced Search to identify relevant studies published between 1990 and 2015. The reference lists of the primarily included articles were searched for further pertinent articles. All articles were selected according to the PRISMA guidelines. The heat-wave-related relative excess mortality was descriptively expressed as a mean daily rate ratio ([incidence 1]/[incidence 2]), and the cumulative excess risk (CER) was expressed in percent.

Results: 33 studies with evaluable raw data concerning the effect of heat waves on patients with chronic lung disease (chronic obstructive pulmonary disease, bronchial asthma, pulmonary arterial hypertension, and idiopathic pulmonary fibrosis) were analyzed in this review. By deriving statistics from the overall data set, we arrived at the conclusion that future heat waves will—with at least 90% probability—result in a mean daily excess mortality (expressed as a rate ratio) of at least 1.018, and—with 50% probability—in a mean daily excess mortality of at least 1.028. These figures correspond, respectively, to 1.8% and 2.8% rises in the daily risk of death.

Conclusion: Heat waves significantly increase morbidity and mortality in patients with chronic lung disease. The argument that the excess mortality during heat waves is compensated for by a decrease in mortality in the subsequent weeks/months (mortality displacement) should not be used as an excuse for delay in implementing adaptive strategies to protect lung patients from this risk to their health.

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Berlin is a metropolis that is situated in the transition zone from an oceanic to a continental climate. In the past decade, the city has experienced three severe heat waves: in 2006, 2010, and 2013 (1). Since the industrial revolution, between 1901 and 2005, the average temperature in Europe has risen by 0.90°C (2, 3). This is widely attributed to an increased production of carbon dioxide and other greenhouse gases, as well as with a raised concentration of ozone and fine dust particles in the environmental air (4–5).

According to data from the 16 most important climate models, from 2050 about 50% of all summers will be accompanied by heat waves. Summers that ranged among the very hottest of summers during the 1950s will become the norm in the 2090s and, according to model calculations, they will occur in 7 out of every 10 years (6, 7).

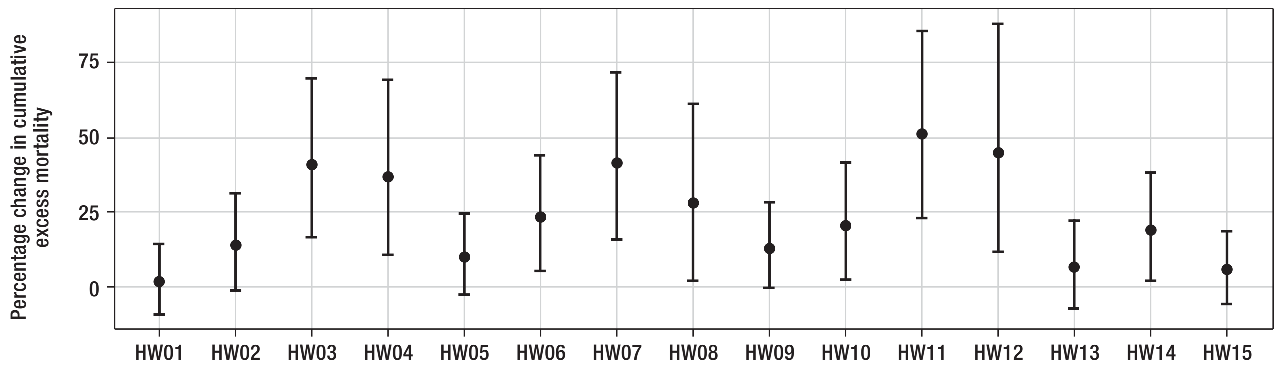
The historical heat waves have been investigated in many studies. According to such studies, 692 persons died in Chicago in 1995 from the consequences of heat; an estimated 50 000 died in Russia in 2010; and in the whole of Europe, the number of fatalities in the summer of 2003 was about 70 000 (8–11). The 2003 heat wave in Europe was extreme in terms of its course and number of fatalities: 15 000 in France, 9000 in Italy, 7000 in Germany, 6000 in Spain, 2000 in the UK, and more than 500 in the Netherlands (11–14).

According to the future scenarios predicted in climate studies, the effects of climate change will be experienced as:

- An increase in the number of extreme climate events
- A deterioration in air quality as a result of increased levels of ozone, particles, and pollen
- An increase in diseases that are transmitted through contaminated food and water
- A change in the incidence and prevalence of infectious diseases as a result of shifts in the distribution of vectors.

Different climate models looking at death rates estimate an annual increase in heat-related mortality from 5.4–6/100 000 between 1980 and 1998, to 5.8–15.1/100 000 for 2020 and 7.3–35.6/100 000 from 2050 (15).

FIGURE 1



Effect of heat wave definitions on cumulative excess mortality risk of total heat wave (HW) in Nanjing, China (17) for the 15 most commonly used HW models

Scientific assessment is made difficult by the fact that no consensus exists on the definition of "heat wave." There is consensus that unusually hot weather over several days is the prerequisite of a heat wave, but the many studies on the subject of heat waves use different meteorological criteria, which makes direct comparisons difficult (16). *Figure 1* uses Nanjing in China as an example of how the choice of definition of heat wave affects study results. Employing different heat wave definitions that are commonly used resulted in a substantial shift in the correlation between heat wave and mortality. Applying the most widely used heat wave models 1–15 sequentially to the sum of all hot days reveals ranges that are difficult to classify (a minimum of 6 and a maximum of 95 days of heat wave for Nanjing, China). Since 2013, however, heat wave model 11, defined as 4 or more consecutive days with an average daily temperature above the 98th percentile, seems to have tended to be the dominant model (17, 18).

Effects on lung disease

The lungs are in direct contact with the environment and are a sort of portal organ of climate change (Witt C: Die Lungen als Portalorgan des Klimawandels – ein Faktor für die Arbeitsmedizin? Forum Atemwege; 54. Jahrestagung der DGAUM 2014 [The lungs as a portal organ of climate change: a factor for occupational medicine? Airways forum; 54th annual meeting of the German Society for Occupational and Environmental Medicine 2014]). The extent of the influence of heat stress depends on:

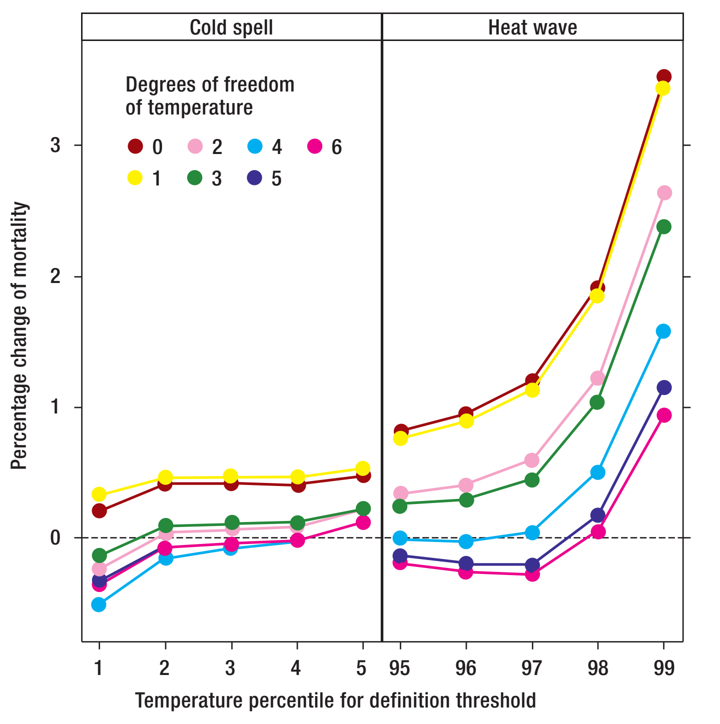
- Biological sensitivity (genetic disposition, chronic medication treatment/use)
- Geographical factors (climate extremes, urban heat islands)
- Socioeconomic variables (family status, social status, lifestyle, living conditions) (19).

Numerous epidemiological studies have shown that heat stress has a negative effect on the disease course in patients with chronic lung disease and consequently results in increased hospital admission rates and fatality rates (2, 20, 21). Because of their lower ability to adapt, the group of persons older than 75, especially women, is most strongly affected—especially vulnerable, even (21).

Notably (*Figure 2*) the human body has adapted better to cold temperatures than to heat during the course of evolution. When low temperatures are falling in the lower range of the 5th percentile, mortality and morbidity rise far more moderately than when temperatures are rising above the 95th percentile.

We wish to use this opportunity to clarify a widespread misunderstanding relating to questions of climate change, heat waves, and cold spells. It is often proposed that global warming causes merely a diagnosis-related shift in mortality—away from low temperatures and towards extreme temperatures as a pathological substrate. What is correct, however, is that both extremes will widen further and occur in increasingly pronounced form. The risk of death during cold waves will remain about the same while that during heat waves will likely further increase in future (22). This does not mean that the current status quo should be misunderstood: it is correct that cumulatively, the biggest increases in mortality can be explained by moderately warm and cold environmental temperatures (between 3% and 97% of the average annual temperature), whereas the largest proportion of excess mortality correlates with moderately low (above the 3rd percentile) temperatures (23). The individual days of heat or heat waves that are truly deadly are currently still rare events. In the range of the 97th percentile, increases in excess mortality of 0.4–3.4% per degree Celsius increase can be observed, whereas below the 3rd percentile, excess mortality does not increase in cold temperatures.

FIGURE 2



Mortality increase per 1 °C in cold spells and heat waves (felt temperature and environmental temperature) (29)

Pathophysiologically, heat stress—in combination with a higher degree of pollution in the environmental air—leads to an inflammation of the bronchial mucosa and lowers the bronchoconstriction threshold. The accompanying fluid loss additionally contributes to subsequent changes in perfusion and ventilation. A number of different noxious substances, such as greenhouse gases, NO_2, SO_2, and O_3, cause acute as well as chronic injury to lung tissue (24). A further factor is exposure to dust particles, among others to P2.5 and P10. Fine dust destroys the integrity of endothelial cells via the signal transduction pathways that depend on reactive oxygen derivates (ROS) and p38-activated protein kinase (p38-MAPK) and is involved in the pathogenesis of cardiopulmonary disorders (25, 26). The synergistic interaction of heat and concentrations of noxious/toxic substances in the air leads to exacerbations, especially of asthma and chronic obstructive pulmonary disease (COPD) (27). The importance of hot air as a pathological substrate of bronchoconstriction has been shown in animal experiments. Lung tissue localized TRPV receptors mediate bronchoconstriction at temperatures far below the tissue-toxic threshold of 42°C (28, 29).

Materials and methods

The present article is based on a systematic literature search according to the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (30). Only studies that focused exclusively on mortality and morbidity in chronic lung disease were included. The size of the study population did not influence inclusion, to ensure that the bias of very large studies (31) is not given too much weight. The *eFigure* and the *eBox* provide detailed information on the search strategy (selection stages and inclusion process).

Statistical analysis

All values shown as mean relative excess risks (Re1R) of mortality and morbidity as rate ratios (RR) where this value was not reported directly. Where reported as cumulative excess risk (CER), we recalculated as Re1R, reported as RR, if the relevant information (duration of heat wave, additive method: yes/no?) was unequivocally available in the study. In the other scenario we reported CER as percentages and compared these with one another. We considered the sum of all included chronic lung diseases—in addition to COPD, this included asthma, pulmonary arterial hypertension, and lung fibrosis. We used SPSS version 22 for our statistical analysis. Using the available datasets, we grouped the upper and lower limits of the confidence interval (CI, 90% to 95%) and the mean values and studied these for the normal distribution and means for 95% CI. The method was descriptive. No additional new confidence intervals were constructed.

Results

Search results

33 relevant articles were identified by the literature search and the subsequent search of secondary sources (17, 20, 22, 24, 31–39, e1–e20). The evaluable RR mortality, RR morbidity, and CER mortality were selected for the purposes of the descriptive analysis. Articles excluded during the final selection process included 11 publications that were used to compare the literature searches. All articles included in our study were listed in the PubMed database. The primary remaining articles from Google Advanced (6 articles?) and the Cochrane Library (2 articles) were excluded during the first selection step because their topics were from different disciplines (ophthalmology and zoological medicine).

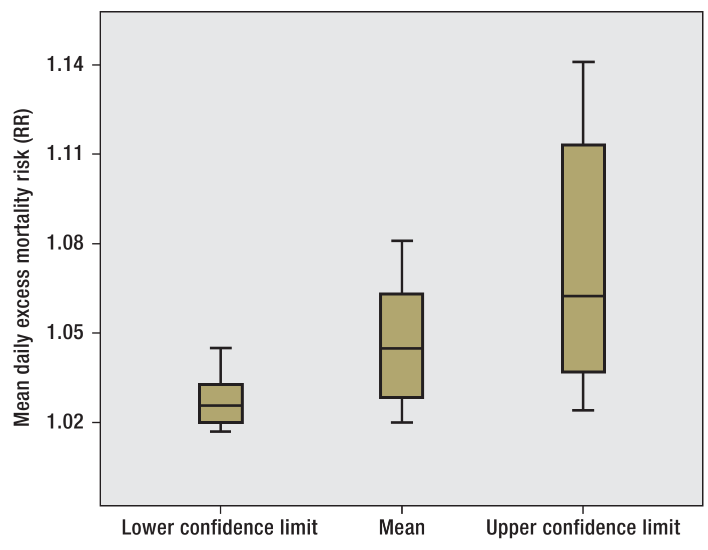
Results of the analysis

In all included articles, the excess mortality risk was between RR 1.018 and 1.082. This means that the risk of dying as a result of chronic lung disease during a heat wave was 1.8–8.2% higher per day than on days with temperatures in the range of the average summer temperature. Capping the top and bottom 25% of all values yields a daily excess mortality risk between 3% and 6.5% (RR 1.03–1.065; 95% CI 90% to 95%). More important than this finding is the conclusion that in the regions under study, future heat waves will—with at least 90% probability—result in a minimum daily excess mortality of 1.8% for patients with chronic lung disease. This value will be 2.8% with a residual probability of 50%. For the RR of the excess morality risk, no outliers were found below 1.0 (see boxplot in *Figure 3*). The conclusion is therefore highly significant.

In all samples of the included studies, the CER is 0–92%, the median half (after capping the top and bottom 25%) of all samples between 22% and 45% CER. 50% of all heat waves under study thus caused an increase in total mortality due to chronic lung disease of 22–45%.

The conclusion for morbidity is that in all samples of the relative mean daily morbidity risk for patients with chronic lung disease, the RR in the included studies is 1.0–1.09; the RR in the median half of all samples were 1.02–1.05. 50% of all heat waves studied were characterized by a daily increase in morbidity between RR 1.02 and RR 1.05. There are lower outliers. From the information of the grouped lower confidence intervals, we can deduce with a probability of at least 90% a mean daily excess morbidity risk of at least 50% for an RR >1.0 for future heat waves.

FIGURE 3



Boxplot comparison: confidence intervals (CI) [90; 95] of mean relative heatwave-related daily excess mortality risk (as rate ratio [RR]) for patients with chronic lung disease

Discussion

Study bias

For the topic of heat waves, which is associated with the geopolitical topic of climate change, the question of study biases is of particular importance. In the final step of the search we intentionally excluded studies consisting of political statements and studies that did not relate to raw data that had been statistically analyzed by the researchers themselves. We also made a conscious decision not to give weighting factors to the studies according to the size of their populations (in the order of 10 000 to 10 000 000), in order to prevent individual study bias as far as possible. Altogether, the cohorts in the included studies comprised more than 100 million persons from Europe, Asia, Australia, and America.

Comparison with previous literature reviews

Earlier literature reviews showed an increase in mortality and morbidity due to chronic lung disease during and after heat waves (13, 18, e9, e21–e30). To very varying extents, chronic lung disease was given a particular status in terms of extra mortality peaks due to lag effects to hospital admission in COPD patients. The range of the confidence intervals in the included studies is large.

The critical scientific discussion has focused mainly on the dissent regarding the shift in mortality. This refers to the temporal shift in mortality—that is, a diagnosis-related displacement of the time of death (forwarded mortality, mortality displacement, harvesting effect). In the discussion of temporal mortality shifts, the arguments used focus almost exclusively on cold spells and heat waves.

For the time being, the statistical question relates exclusively to mortality—and not morbidity—due to heat waves. Segmenting the data from a selected study into its age group cohorts, for example, shows that the relative increases in mortality are largely accounted for by the older age groups (>75 years, occasionally >75 years plus COPD). Mortality rises in the younger cohort subsets often do not show any significant RR increases (e10). Since 2013 there have increasingly been voices claiming that the mortality increase during a heat wave is to be viewed as a single temporal mortality shift (e31). The countercurrent, so to speak, is now seeking to document temporal mortality shift phenomena over months and years after a heat wave or a cold spell (e32). The former group fully acknowledges the fact that in more strongly pronounced heat waves (for example, in France in 2003), mortality and morbidity will affect with increasing significance the cohorts with low morbidity. The question of whether a heat wave with a temporal mortality shift of a fortnight should be less relevant for health policy response than a shift of months or years is difficult to answer from an ethical perspective.

Limitations

This study was intended to provide access to fundamental terminologies and differences in opinion on the topic of “heat stress induced mortality/morbidity” and to render the data reported in the available studies into a shape that makes them statistically comparable. This was successfully done for the Re1R in the RR of mortality and morbidity and as the CER of mortality in patients with chronic lung disease.

Assessing the Re1R of morbidity and the CER of mortality clarifies the complex way in which the many variables affect the interpretation of the results. The residual risk that the lower confidence interval of the CER of mortality includes zero is 20%. This was not the case for the Re1R of mortality in the RR. Among the datasets of the Re1R of morbidity in the RR, the problematic datasets with very large confidence intervals and atypical morbidity values carry particular weight. The RR of morbidity in the Korean studies (2003–2006) (39), (2003–2008) (e10) and the data from Ljubljana (1997–1999) (e7, e8) are representative. The reasons for this lie in the different statistical processing of the data in different studies. It was obvious that a heat wave in the entire summer was studied that had already been preceded by a heat event.

More than 70% of all clusters of heat days do not reach the definition threshold for a heat wave (18). Of note: a drop in the RR of morbidity for the total cohort of persons with chronic lung disease (–0.2%, –7%, –3.8%, –9.2%), as well as an even higher drop in the RR within the anticipated most highly vulnerable group of the over-75-year-olds in Ljubljana (–4.6%) (e7). It is highly unlikely that during this heat wave, morbidity did not only fall, but that this reduction reflects precisely the expected increase.

Preventive measures

Preventive measures range from heat avoidance and adequate lifestyles among vulnerable patients to climate-adjusted medication treatment to protect against exacerbations (dosage adjustment). Adaptive strategies include innovative patient management, for example, by means of telemonitoring (lung function, ECG, Movelet-based tracking) and the creation of air-conditioned hospitals and housing for older persons. Consequently, priority should be given to studies aiming to identify groups that are vulnerable to heat stress. Central to this are heat monitoring and warning systems for the early detection of weather constellations that are hazardous to health (e33–e40). Distinction needs to be made between two systems: one is triggered if a defined mortality and morbidity index is reached, and the other reacts to ordinary weather forecasts that warn of heat waves.

Further initiatives include active (energy efficient stand-by air-conditioning units in hospital rooms and residences for older people) and passive prevention measures. The latter include architectural measures to improve the interior climate (for example, green building facades and roofs, architectural measures to protect against and reduce the rays of the sun, filters and seals) as well as town-planning measures (for example, parks and green spaces) (e41–e43).

In a study conducted at the Charité University Hospital in Berlin, which investigated the effect of air-conditioned patient rooms on the course of acute exacerbations in chronic lung disease (with a regulated room temperature of maximumally 23°C [set point]), we studied the effect of convection-free air conditioning on clinical variables. Furthermore, a study funded by the German Research Foundation (DFG) is in preparation, which will investigate the effect of environmental temperatures up to 36°C on patients' clinical course.

KEY MESSAGES

- Heat stress leads to an excess mortality risk of up to 43% in patients with chronic lung disease.
- The excess daily mortality risk in a temperature rise of as little as 1°C above the mean summer temperature is between 0.4% and 3.4%.
- Heat stress leads to an excess morbidity risk of 1–9%.
- Pathophysiologically, heat stress causes fluid loss and disruption of pulmonary perfusion, as well as—in combination with raised concentrations of noxious/toxic substances in the environmental air—to bronchial inflammation and lowering of the bronchoconstriction threshold.
- Preventive measures range from heat avoidance and adequate lifestyle of vulnerable patients to climate-adjusted medication therapy aiming to protect against exacerbations (dosage adjustment). Adaptive strategies include innovative patient management (for example, by telemonitoring) and the creation of air-conditioned hospitals and residences for older people. Studies to identify the population groups at risk during heat-waves should therefore be prioritized.

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Conflict of interest statement
Professor Witt has received lecture fees and honoraria for advisory board participation from TESA, GSK, Astra Zeneca, Pfizer, Berlin-Chemie, BMS, Roche, and MSD.

His co-authors declare that no conflict of interest exists.

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REFERENCES

1. Schuster C, Burkart K, Lakes T: Heat mortality in Berlin-Spatial variability at the neighborhood scale. Urban Climate 2014; 26: 34–147.
2. Gualdi S, Navarra A: Climate scenarios in the Mediterranean region. Forest 2005; 2: 19–30.
3. Alcamo J, Moreno J, Nováky B: Climate change 2007: impacts, adaptation and vulnerability. Contribution of working group II to the fourth assessment report of the intergovernmental panel on climate change. Cambridge University Press 2007; 541–80.
4. Pope CA, Thun MJ, Namboodiri MM, et al: Particulate air pollution as a predictor of mortality in a prospective study of U.S. adults. Am J Respir Crit Care Med 1995; 151: 669–74.
5. Dockery DW, Pope CA, Xu X, et al.: An association between air pollution and mortality in six U.S. cities. N Engl J Med 1993; 329: 1753–9.
6. Tebaldi C, Duffy PB: Increasing prevalence of extreme summer temperatures in the U.S. a letter. Climatic Change 2012; 111: 487–95.

7. Meehl GA, Tebaldi C: More intense, more frequent, and longer lasting heat waves in the 21st century. Science 2004; 305: 994–7.
8. Fouillet A, Rey G, Wagner V, et al.: Has the impact of heat waves on mortality changed in France since the European heat wave of summer 2003? A study of the 2006 heat wave. Int J Epidemiol 2008; 37: 309–17.
9. Karl TR, Knight RW: The 1995 Chicago heat wave: how likely is a recurrence? BMAS 1997; 78: 1107–19.
10. Coumou D, Rahmstorf S: A decade of weather extremes. Nature Clim Change 2012; 2: 491–6.
11. Robine JM, Cheung SL, Le Roy S, et al.: Death toll exceeded 70,000 in Europe during the summer of 2003. C R Biol 2008; 331: 171–8.
12. Ebi KL, Kovats RS, Menne B: An approach for assessing human health vulnerability and public health interventions to adapt to climate change. Environ Health Perspect 2006; 114: 1930–4.
13. Kovats RS, Hajat S: Heat stress and public health: a critical reviews, Annu Rev Public Health 2008; 29: 41–55.
14. Sardon JP: The 2003 heat wave. Euro Surveill 2007; 12: 226.
15. Dessai S: Heat stress and mortality in Lisbon Part II. An assessment of the potential impacts of climate change. Int J Biometeorol 2003; 48: 37–44.
16. Robinson PJ: On the definition of a heat wave. J Appl Meteorol 2001; 40: 762–75.
17. Chen K, Bi J, Chen J, Chen X, Huang L, Zhou L: Influence of heat wave definitions to the added effect of heat waves on daily mortality in Nanjing, China. Sci Total Environ 2015; 506–7: 18–25.
18. Gasparrini A, Armstrong B: The impact of heat waves on mortality Epidemiology 2011; 22: 68–73.
19. Kenny GP, Yardley J, Brown V, Sigal RJ, Jay O: Heat stress in older individuals and patients with common chronic diseases. CMAJ 2010; 182: 1053–60.
20. 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 U S A 2012; 109: 6608–13.
21. Semenza JC, Rubin CH, Falter KH, et al.: Heat-related deaths during the July 1995 heat wave Chicago. N Engl J Med 1996; 335: 84–90.
22. Barnett AG, Hajat S, Gasparrini A, Rocklöv J: Cold and heat waves in the United States. Environ Res 2012; 112: 218–24.
23. Gasparrini A, Guo Y, Hashizume M, et al.: Mortality risk attributable to high and low ambient temperature: a multicountry observational study. Lancet 2015; 386: 369–75.
24. Monteiro A, Cavalho V, Oliveira T, Sousa C: Excess mortality and morbidiy during the July 2006 heat wave in Porto, Portugal. Int J Biometeorol 2013; 57: 155–67.
25. Olivieri D, Scoditti E: Impact of environmental factors on lung defenses. Eur Respir Rev 2005; 14: 51–6.
26. Wang T, Chiang ET, Moreno-Vinasco L, et al.: Particulate matter disrupts human lung endothelial barrier integrity via ROS- and p38 MAPK-dependent pathways. Am J Respir Cell Mol Biol 2010; 42: 442–9.
27. Health Protection Agency: Public Health Adaptation Strategies to Extreme weather events (PHASE). www.hpa.org.uk/Topics/EmergencyResponse/ExtremeWeatherEventsAndNaturalDisasters/PHASE (last accessed on 14 April 2014).
28. Ni D, Gu Q, Hu HZ, Gao N, Zhu MX, Lee LY: Thermal sensitivity of isolated vagal pulmonary sensory neurons: role of transient receptor potential vanilloid receptors. Am J Physiol Regul Integr Comp Physiol 2006; 291: R541–50.
29. Ruan T, Gu Q, Kou YR, Lee LY: Hyperthermia increases sensitivity of pulmonary C-fibre afferents in rats. J Physiol 2005; 565: 295–308.
30. Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A: Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ 2015; 349: 7647.
31. Anderson GB, Dominici F, Wang Y, McCormack MC, Bell ML, Peng RD: Heat-related emergency hospitalizations for respiratory diseases in the medicare population. Am J Respir Crit Care Med 2013; 187: 1098–103.
32. Knowlton K, Rotkin-Ellman M, King G, et al.: The 2006 california heat wave: impacts on hospitalizations and emergency department visits. Environ Health Perspect 209; 117: 61–7.
33. Sheridan SC, Lin S: Assessing variability in the impacts of heat on health outcomes in New York City. Ecohealth 2014; 11: 512–25.
34. Miron IJ, Linares C, Montero JC, Criado-Alvarez JJ, Díaz J: Changes in cause-specific mortality during heat waves in central Spain. Int J Biometeorol 2015; 59: 1213–22.
35. Kovats RS, Hajat S, Wilkinson P: Contrasting patterns of mortality and hospital admissions during hot weather an heat waves in Greater London, UK. Occup Environ Med 2004; 61: 893–8.
36. Rocklöv J, Forsberg B: Comparing approaches for studying the effects of climate extremes – a case study. Glob Health Action 2009; 2.
37. Turner LR, Connell D, Tong S:The effect of heat waves on ambulance attendances in Brisbane, Australia. Prehosp Disaster Med 2013; 28: 482–7.
38. Zeng W, Lao X, Rutherford S, et al.: The effect of heat waves on mortality and effect modifiers in four communities of Guangdong Province, China. Sci Total Environ 2014; 482–483: 214–21.
39. Lim YH, Hong YC, Kim H: Effects of diurnal temperature range on cardiovascular and respiratory hospital admissions in Korea. Sci Total Environ 2012; 417–8: 55–60.

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Supplementary material to:

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eREFERENCES

e1. Analitis A, Michelozzi P, D'Ippoliti D, et al.: Effects of heat waves on mortality: effect modification and confounding by air pollutants. Epidemiology 2014; 25: 15–22.

e2. Revich B, Shaposhnikov D: Excess mortality during heat waves and cold spells in Moscow, Russia. Occup Environ Med 2008; 65: 691–6.

e3. Fouillet A, Rey G, Laurent F, Pavillon G, Bellec S, Guihenneuc-Jouyaux C: Excess mortality related to the August 2003 heat wave in France. Int Arch Occup Environ Health 2006; 80: 16–24.

e4. Conti S, Masocco M, Meli P, et al.: General and specific mortality among the elderly during the 2003 heat wave in Genoa (Italy). Environ Res 2007; 103: 267–74.

e5. Gronlund CJ, Zanobetti A, Schwartz JD, Wellenius GA, O'Neill MS: Heat, heat waves, and hospital admissions among the elderly in the United States 1992–2006. Environ Health Perspect 2014; 122: 1187–92.

e6. Sun X, Sun Q, Zhou X, et al.: Heat wave impact on mortality in Pudong New Area, China in 2013. Sci Total Environ 2014; 493: 789–94.

e7. Michelozzi P, Accetta G, De Sario M, et al.: High temperature and hospitalizations for cardiovascular and respiratory causes in 12 European cities. Am J Respir Crit Care Med 2009; 179: 383–9.

e8. Michelozzi P, Kirchmayer U, Katsouyanni K: Assessment and prevention of acute health effects of weather conditions in Europe, the PHEWE project: background, objectives, design. Enviro Health 2007; 6: 12.

e9. Ma W, Xu X, Peng L, Kan H: Impact of extreme temperature on hospital admission in Shanghai, China. Sci Total Environ 2011; 409: 3634–7.

e10. Son JY, Bell ML, Lee JT: The impact of heat, cold, and heat waves on hospital admissions in eight cities in Korea. Int J Biometeorol 2014, 58:1893–903.

e11. Yang J, Liu HZ, Ou CQ, et al.: Impact of heat wave in 2005 on mortality in Guangzhou, China. Biomed Environ Sci 2013; 26: 647–54.

e12. Huynen MM, Martens P, Schram D, Weijenberg MP, Kunst AE: The impact of heat waves and cold spells on mortality rates in the Dutch population. Environ Health Perspect 2001; 109: 463–70.

e13. D'Ippoliti D, Michelozzi P, Marino C, et al.:The impact of heat waves on mortality in 9 European cities: results from the EuroHEAT project. Environ Health 2010; 9: 37.

e14. Mastrangelo G, Fedeli U, Visentin C, Milan G, Fadda E, Spolaore P: Pattern and determinants of hospitalization during heat waves: an ecologic study. BMC Public Health 2007; 7: 200.

e15. Hertel S, Le Tertre A, Jockelll KH, Hoffmann B: Quantification of the heat wave effect on cause-specific mortality in Essen, Germany. Eur J Epidemiol 2009; 24; 407–14.

e16. Ma W, Zeng W, Zhou M, et al.: The short-term effect of heat waves on mortality and its modifiers in China: An analysis from 66 communities. Environ Int 2015; 75: 103–9.

e17. Lin H, Zhang Y, Xu Y, et al.: Temperature changes between neighboring days and mortality in summer: a distributed lag non-linear time series analysis. PLoS One 2013; 8: e66403.

e18. Baccini M, Biggeri A, Accetta G, et al.: Heat effects on mortality in 15 European cities. Epidemiology 2008; 19: 711–9.

e19. Stafoggia M, Forastiere F, Agostini D, et al.: Vulnerability to heat-related mortality: a multicity, population-based, case-crossover analysis. Epidemiology 2006; 17: 315–23.

e20. Huang W, Kan H, Kovats S: The impact of the 2003 heat wave on mortality in Shanghai, China. Sci Total Environ 2010; 408: 2418–20.

e21. Peng RD, Bobb JF, Tebaldi C, McDaniel L, Bell ML, Dominici F: Toward a quantitative estimate of future heat wave mortality under global climate change. Environ Health Perspect 2011; 119: 701–6.

e22. Wu J, Zhou Y, Gao Y, et al.: The time trend temperature-mortality as a factor of uncertainty analysis of impacts of future heat waves: Wu et al. respond. Environ Health Perspect 2014; 122: A118–9.

e23. O'Neill MS, Ebi KL: Temperature extremes and health: impacts of climate variability and change in the United States. J Occup Environ Med 2009; 51: 13–25.

e24. Hoshiko S, English P, Smith D, Trent R: A simple method for estimating excess mortality due to heat waves, as applied to the 2006 California heat wave. Int J Public Health 2010; 55: 133–7.

e25. Pinkerton KE, Rom WN, Akpinar-Elci M, et al.: An official American Thoracic Society workshop report: climate change and human health. Proc Am Thorac Soc 2012; 9: 3–8.

e26. Bernstein AS, Rice MB: Lungs in a warming world: climate change and respiratory health. Chest 2013; 143: 1455–9.

e27. Cadot E, Rodwin VG, Spira A: In the heat of the summer: lessons from the heat waves in Paris. J Urban Health 2007; 84: 466–8.

e28. Forsberg B, Bråbäck L, Keune H, et al.: An expert assessment on climate change and health – with a European focus on lungs and allergies. Environ Health 2012; 11: 4.

e29. Wu J, Zhou Y, Gao Y, et al.: Estimation and uncertainty analysis of impacts of future heat waves on mortality in the eastern United States. Environ Health Perspect 2014; 122: 10–6.

e30. Montero JC, Mirón IJ, Criado JJ, Linares C, Díaz J: Comparison between two methods of defining heat waves: a retrospective study in Castile-La Mancha Spain. Sci Total Environ 2010; 408: 1544–50.

e31. Saha MV, Davis RE, Hondula DM: Mortality displacement as a function of heat event strength in 7 US cities. Am J Epidemiol 2014; 179: 467–74.

e32. Armstrong B, Gasparrini A, Hajat S: Estimating mortality displacement during and after heat waves. Am J Epidemiol 2014; 179: 1405–6.

e33. Pascal M, Laaidi K, Wagner V, et al.: How to use near real-time health indicators to support decision-making during a heat wave: the example of the French heat wave warning system. PLoS Curr 2012; 4: e4f83ebf72317d.

e34. O'Neill MS, Jackman DK, Wyman M, et al.: US local action on heat and health: are we prepared for climate change? Int J Public Health 2010; 55: 105–12.

e35. Zhang K, Chen YH, Schwartz JD, Rood RB, O'Neill MS.: Using forecast and observed weather data to assess performance of forecast products in identifying heat waves and estimating heat wave effects on mortality. Environ Health Perspect 2014; 122: 912–8.

e36. O'Neill MS, Carter R, Kish JK, Gronlund CJ, Jalonn L: Preventing heat-related morbidity and mortality: New approaches. NIH Public Access 2009; 64: 98–103.

e37. Tessier F, Plante C, Kosatsky T: The validation of a new population surveillance system that analyzes the daily mortality rates in Montreal. Can J Public Health 2009; 100: 153–6.

e38. Josseran L, Caillère N, Brun-Ney D, et al.: Syndromic surveillance and heat wave morbidity: a pilot study based on emergency departments in France. BMC Med Inform Decis Mak 2009; 20: 9–14.

e39. Michelozzi P, de' Donato FK, Bargagli AM: Surveillance of summer mortality and preparedness to reduce the health impact of heat waves in Italy. Int J Environ Res Public Health 2010; 7: 2256–73.

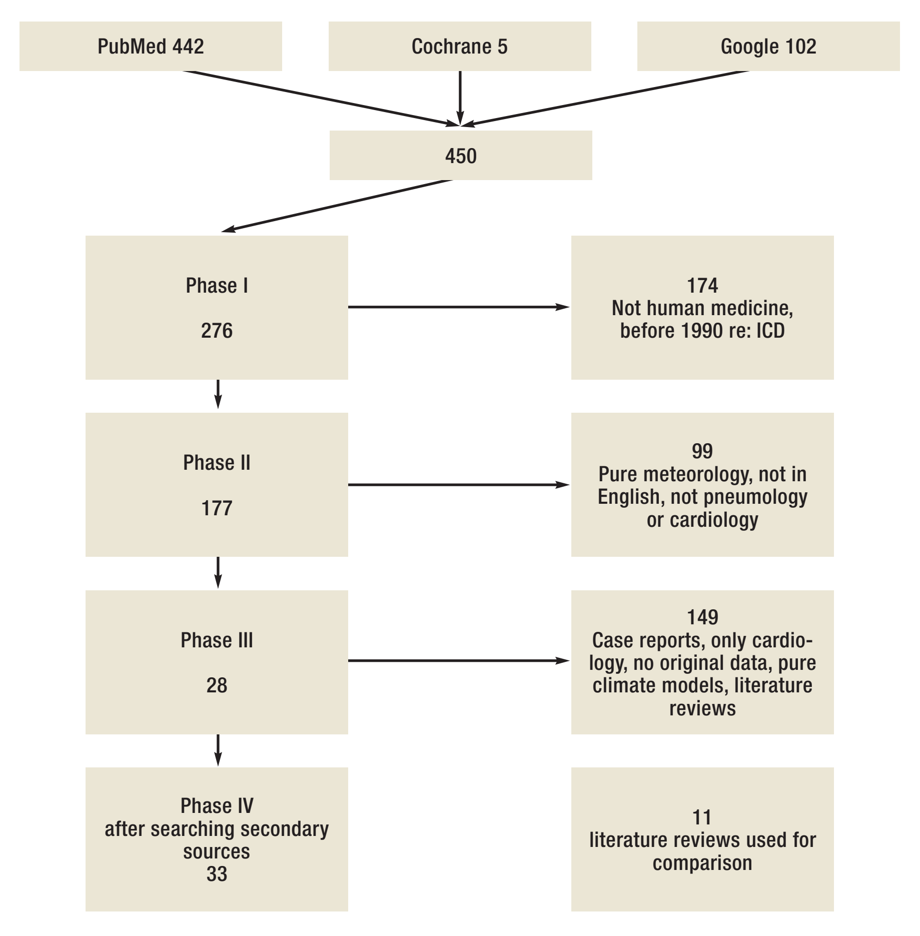
e40. Toutant S, Gosselin P, Bélanger D, Bustinza R, Rivest S: An open source web application for the surveillance and prevention of the impacts on public health of extreme meteorological events: the SUPREME system. Int J Health Geogr 2011; 10: 39.

e41. Gabriel KM, Endlicher WR: Urban and rural mortality rates during heat waves in Berlin and Brandenburg, Germany. Environmental Pollut 2011; 159: 2044–50.

e42. Witt C, Burger M, Hüther M: ACATECH-Empfehlungen zur Klimapolitik. Springer Verlag 2012: 23–5.

e43. Chen D, Wang X, Thatcher M, Barnett G, Kachenko A, Prince R: Urban vegetation for reducing heat related mortality. Environ Pollut 2014; 192: 275–84.

eFIGURE



Study exclusion

eBOX

Additional information on the inclusion process of the literature search

In order to identify suitable studies, we conducted a systematic search in PubMed, the Cochrane Library, and Google (to cover more recent articles on platforms that were not included) on 12 January 2015. Our search terms were "heat wave AND mortality" or "heat wave AND morbidity" in PubMed and the same search terms in the advanced search for Cochrane and Google. In accordance with the PRISMA guidelines, we conceived a flow diagram on the exclusion process and documented this in a file. Our initial search yielded 442 studies from PubMed, 5 Cochrane hits, and 102 Google results (2014–2015, in order to check a sample of the most recent studies for completeness). Six studies from Google were included and 2 from the Cochrane Library, which were consistent with the topic and were not identified in the initial PubMed search. Furthermore, we searched the reference lists of the remaining publications for potential hits.

- **Selection phase I**

In the initial search, we used the word combination "heat wave AND mortality" or "heat wave AND morbidity" for PubMed and in the advanced search in the Cochrane Library. The advanced Google search for heat wave and mortality and heat wave and morbidity was restricted to 2014 and 2015 and yielded 102 hits; 6 of these (on the subject of heat waves; no duplicate hits) were included in the primary pool. PubMed yielded 442 hits and Cochrane 5, of which 3 were immediately excluded as they were on different subjects. At the conclusion of phase I, the primary pool included 450 articles.

- **Selection phase II**

174 articles were excluded, which had been published before 1990 (the threshold for the comparability of respiratory codes in the ICD) or which did not focus on human medicine topics. At the end of phase II, 276 articles remained in the pool.

- **Selection phase III**

99 articles were excluded because they consisted of purely meteorological considerations, were not written in English, did not have a cardiological approach (search term: "cardiology AND respiratory") or respiratory and cardiological (search term "cardiology AND respiratory") approaches (for example neurology [search term "heat stroke"], hyperthermia, psychiatry). 177 articles remained in the pool.

- **Selection phase IV**

149 publications were excluded. Exclusion criteria were: pure case reports, only cardiology, pure climate modeling/erection of warning systems, no free full text access, mere reviews without their own raw data/reviews of secondary data, no data that could have been potentially recalculated as RR.
We used the cumulative excess risk (CER) (with source code) and recalculated it as RR. Mere percentages of daily mortality and morbidity increases were recalculated into rate ratios (RR) in the 1.00 format.

For the comparison discussion with other reviews, 11 reviews were retained after selection phase IV. The 28 publications that were left after exclusion were increased to 33 by selective searches of the references of the primary articles (17, 20, 22, 24, 31–39, e1–e20).