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Thermal Control, Weather, and Aging

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Abstract
Purpose of the Review The purpose of this review is to highlight the latest developments in the field of weather and health with a focus on the elderly. The current state of knowledge is summarized and open questions and emerging fields of research are discussed.
Recent Findings It is expected that climate change will lead to higher global average surface temperatures and more extreme climatic conditions. Previous studies have shown that non-optimal temperatures are associated with increased morbidity and mortality, specifically in elderly people. Future research fields comprise e.g., synergistic effects between meteorological variables and air pollution; long-term impacts of temperature changes; novel unraveling the underlying pathways using blood biomarkers; the association between temperature and mental health; and urban planning and adaptation processes.
Summary Understanding the health impacts associated with changes in thermal conditions requires multidisciplinary approaches. Adaptation processes, as well as improvements in urban planning and warning systems, can help reduce the predicted burden of climate change, especially in the elderly.

Keywords Aging · Weather · Climate · Heat · Cold · Health

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Introduction

The latest Intergovernmental Panel on Climate Change (IPCC) report reaffirms the increasing threat of climate change [1]. In the IPCC predictions, the global average surface temperature increase ranges between 1.4 and 5.8 °C by the end of 2100 depending on the assumed scenario [2]. Projections further suggest that climate change will lead to more persistent heat-waves indicated by a higher frequency and intensity, longer duration, and earlier timing within the year [3]. A previous Europe-wide heat wave resulted in nearly 45,000 deaths in August 2003 [4]. In addition, also cold spells [5] as well as increases or decreases in more moderate temperatures contribute to the observed temperature-related mortality and morbidity [6–8, 9••]. A recent study using data from 13 countries around the world estimated that 7.7% of the mortality was attributable to non-optimal temperatures [10••]. The majority of these deaths were due to moderately high and low temperatures, with cold being responsible for a higher proportion of deaths than heat.

Although cold episodes are expected to decrease in the near future under the changing climate, decreases in cold-related mortality may be small and not able to offset the potential increase in heat-related deaths if the adaptation to heat is not adequate [11, 12]. The health impacts of unexpected temperature changes may be more relevant than the absolute temperature level itself [13–15]. Moreover, the effect of summer temperatures on mortality has been found to be stronger in years characterized by low mortality in the previous winter as low-mortality winters may inflate the pool of the elderly susceptible population at risk for dying from high temperature the following summer [16].

The elderly (aged 65 years and older) are considered to be very vulnerable to temperature effects [8, 9••]. Due to natural aging processes, the regulation of body temperature deteriorates. This becomes particularly apparent when ambient temperatures remain high for several days. The decrease in the thermoregulatory ability can be ascribed to a combination of factors including changes in sweating, a reduced sense for dehydration, blood flow to the skin, and cardiovascular function [17].

Furthermore, pre-existing chronic conditions such as cardiovascular disease, diabetes, or mental disorders like dementia or Alzheimer disease can aggravate the vulnerability of older adults [18, 19]. Medication intake, e.g., diuretics during heat episodes, may exacerbate this risk [20, 21]. Also, respiratory mortality has been shown to be increased in the elderly when temperatures increase [4, 22]. Further, factors such as physical disability, individual behaviors, and the lack of family and/or social support could have impacts on temperature-related effects on the elderly [23•, 24].

As the age group 60 years and older is expected to comprise 21.1% of the population by 2050 [25], an aging population could substantially enhance the burden of temperature-related health risks in a warming climate [26, 27••].

Understanding the factors which link non-optimal temperatures and adverse health outcomes may help to prepare the population for the predicted challenges, and this way help to maintain a healthy life and aging process (including optimal physical and cognitive functioning, delaying the onset of chronic diseases as well as psychological and social wellbeing; [28]) for as many people as possible (Fig. 1).

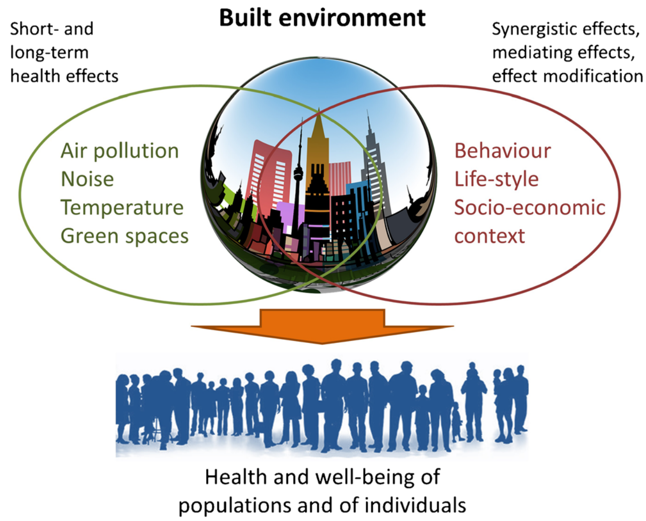

Fig. 1 The interplay between environmental, behavioral, lifestyle-related and socioeconomic factors on human health and well-being

Thermal Control/Thermoregulation

Thermoregulation is the ability of an organism to maintain an optimum temperature for the chemical reactions within the body even if the surrounding temperatures vary. For this, the thermoregulatory system has a range of physiological mechanisms at its disposal, mainly a combination of dry heat exchange and evaporative heat loss [17]. Hyperthermia or hypothermia will occur if the body is exposed to high or low temperatures, respectively, for too long.

Recent studies on heat waves have shown an increase in cardiorespiratory [29–31] mortality and morbidity [7, 21, 32] during periods of prolonged increases in ambient temperatures. Causes of heat-related cardiovascular mortality comprise e.g., myocardial infarction, heart failure, and stroke. Heat-related morbidity measured as emergency room visits and hospital admissions has been reported for e.g., renal disease, stroke, inflammatory bowel disease, infectious gastroenteritis and respiratory disease [21].

Several pathophysiological mechanisms which connect heat stress and cardiovascular morbidity and mortality have been suggested:

1. Increased surface blood circulation and sweating, followed by dehydration and salt depletion leading to

   (a) Increased cardiac work load as a compensational reaction of the circulation to maintain the heart minute volume [20, 33] and falling blood pressure. For example, higher temperature levels (per 10.4 °C) were associated with reductions in both systolic and diastolic blood pressure in a panel of cardiac rehabilitation patients [34].

   (b) Hemoconcentration and a "thrombosis promoting" state due to the release of platelets into the circulation and increases in red and white cell counts, elevated blood viscosity, and plasma cholesterol [35–37]. Further, among patients undergoing treatment for heart failure, Wilker et al. (2012) [38] observed positive associations between temperature and both B-type natriuretic peptide and C-reactive protein–predictors of heart failure prognosis and severity. It is hypothesized that most of the heat-related sudden deaths are due to congestive heart failure, which has been identified as a major prognostic factor in patients with heatstroke [39] and as a strong determinant of in-hospital mortality during hot days [40].
2. It has been shown that heat stress induces the release of interleukins like interleukin-1 and interleukin-6 which modulate local and systemic inflammatory responses [41] and can result in damage and hyperactivation of endothelial cells.

For respiratory morbidity and mortality, the underlying mechanisms are less clear and occur often in combination with the cardiovascular effects described above. Mostly people with pre-existing respiratory diseases seem affected, and chronic obstructive pulmonary disease (COPD) is one of the most common reasons for hospital admissions for respiratory causes in association with heat in the elderly population [42, 43]. Michelozzi et al. [43] speculate that during an extreme heat event, subjects with COPD may hyperventilate [20], thus increasing the possibility of dynamic hyperinflation, leading to dyspnea and to mechanical and cardiovascular effects. Additionally, changes in blood towards a more coagulant state might increase their risk of developing pulmonary vascular resistance [20]. Moreover, these vascular changes may trigger a respiratory distress syndrome through the activation of the complement system [43, 44].

However, also low ambient temperatures can lead to adverse health effects and mortality. While heat effects have been shown to be more immediate in most studies [35, 45], cold effects are usually found with a delay of several days or even weeks [35, 46]. It is, therefore, reasonable to assume that mechanisms for heat and cold effects differ. This interpretation is reinforced by the fact that this particular temporal pattern was not only seen in humans but also observed in dairy cattle [47].

Several pathophysiological mechanisms which connect low air temperatures and cardiorespiratory morbidity and mortality have been suggested:

1. When ambient temperatures decrease below a certain level,

   (a) Cold receptors in the skin are stimulated, and the skin vessels constrict to reduce heat loss regulated by the sympathetic nervous system via catecholamines [46, 48]. Heart rate and blood pressure increase, which leads to an increase of the blood volume per beat and, therefore, a rising need for oxygen [33]. Due to the increased blood pressure, up to 1 l of blood plasma is shifted from the skin and legs to central body parts and then either removed by urine or shifted to extracellular spaces. The shift of blood plasma leads to hemoconcentration, similar to the effects of high temperatures. The increased blood pressure may also lead to oxygen deficiency in the cardiac muscle possibly inducing myocardial ischemia or arrhythmias. If the increase in blood pressure is too sudden, there is the potential for vascular spasm and rupture of an atherosclerotic plaque potentially followed by thrombus formation [33, 36, 37, 46].

   (b) Changes in the blood can increase the possibility of adverse events. Significant increases in fibrinogen and factor VII—both important risk factors for cardiovascular diseases [49]—have been shown in association with cold temperatures in older people [50–52].
2. Moreover, infections in the winter could lead to an acute phase response, which can induce an increase in the mentioned blood markers and, therefore, lead to a higher risk of ischemic heart diseases.

New Ideas for Future Research

Despite the increasing number of publications on the effects of high and low temperatures on health, a number of open questions and potential research questions remain:

Synergistic Effects and Effect Modifiers

Climate change not only affects air temperature, but also other meteorological variables which might be as important to human health as temperature changes. This includes, for example, humidity, barometric pressure, and precipitation. However so far, not much clear evidence for associated health effects exists and more research is definitely needed.

Moreover, the interplay with air pollution (e.g., particulate matter and ozone) is complex.

It is well-known that greenhouse gas emissions increase climate change but climate change might also affect outdoor air pollution (e.g. particulate matter and ozone) by regional weather conditions [2, 53]. Therefore, it is essential to look at the interplay of these factors and their joint effect on health. However, previous studies mainly investigated isolated effects of air pollutants or temperature as an indicator for weather.

While air temperature was usually included as a confounder variable in assessing short-term air pollutant effects, only a few studies considered air pollutants in assessing short-term temperature effects [35]. Several studies investigated effect modification or interacting effects of air pollutants and temperature/weather on mortality or hospital admissions (e.g., [35, 54–61]), but only some of them reported interactive effects/effect modification on health with higher adverse air pollution effects for warmer days (e.g. [35, 54, 58, 60, 62•, 63]). Evidence on effect modification or interacting effects of air pollutants and temperature/weather on outcomes such as heart rate variability, blood pressure or marker of endothelial function is scarce (e.g. [64–66]).

In addition, several other air contaminants like pollen, molds, and smoke from wildfires but also factors of the built environment like noise, urban heat islands (defined as built-up areas that are hotter than nearby rural areas), and green spaces interfere with climate change and need to be considered as well, especially in urban areas [62•, 67].

Therefore, studies with a comprehensive assessment of these environmental factors and carefully designed multicenter studies including different climatic conditions as well as sophisticated multi-pollutant approaches are needed to tackle those challenges [62•]. For informing stakeholders and policy-makers, there is the need to project future ambient levels of temperature as well as air pollutants and compute the associated health impacts with consideration of uncertainties from interaction between temperature and air pollution, variation of mortality risk over time, population adaptation, and demographic changes [27••]. The identification of the potential effect modifiers of population's vulnerability to temperature/air pollution will help to account for future adaptation.

Long-Term Impacts

So far, mostly short-term air temperature fluctuations are used as one of the main markers for analyzing the association between meteorology and mortality or morbidity. These studies are often used to draw conclusions about climate effects. A weak point in assessing the effects of climate change is therefore the lack of real long-term temperature (and relative humidity) studies in association with health outcomes. More research needs to be done on the evaluation of long-term variations in temperature effects as this could be used as a reflection of how well a population can adapt to temperature changes over a certain time span [68]. For example, the assessment of summer temperature variability showed an association with mortality especially in the elderly with underlying chronic diseases [67]. Studies on long-term effects combining weather and air pollution are particularly scarce [14, 69, 70]. Only two studies have investigated the two exposures in parallel [71, 72] both reporting higher effects of particulate matter <2.5 μm on mortality for higher temperatures.

Furthermore, also for the abovementioned interactions of long-term temperature exposure with urban heat islands, or distance to green spaces as well as with selected candidate genes or epigenetic markers [73•], long-term study designs are inevitable.

Blood Biomarkers

Low-grade systemic inflammation seems to play an essential role in the initiation, progression, and the final pathophysiological steps of atherosclerosis, plaque erosion, and eventually plaque rupture [74]. It also participates in the development of obesity, insulin resistance, and hypertension [75–77]. With regard to pathophysiologic mechanisms of the weather-health relationship, it is necessary to look deeper into metabolic disease development, e.g., by investigating effects of temperature on metabolites, kynurenine metabolism (which offers a very novel link between psychiatric, metabolic, and aging related mechanisms), or blood lipids. Also, other health outcomes such as kidney function or immune regulation have rarely been investigated in association with weather and climate changes to date. Bunker et al. (2016) [9••] found an increased risk for heat-induced diabetes, renal, and infectious disease morbidity all of which are likely to increase further with climate change and global aging. Furthermore, more large panel studies are needed that investigate conventional blood biomarkers (e.g., C-reactive protein, interleukin-6) in combination with more disease-specific blood markers. Examples are endothelin-1, troponin I and T or N-terminal pro-brain natriuretic peptide–biomarkers for heart failure, as this life-limiting condition is reported to affect 6–10% of people older than 65 years in industrialized countries [78]. As early as 2004, Ebi et al. [79] detected a higher number of hospital admissions due to heart failure in association with a decrease in the 7-day average of maximum temperature and precipitation in three regions in California, USA. Also, parameters such as blood viscosity, differential cell counting, cystatin C (e.g., representing kidney function), circadian variation in cortisol level (e.g., representing stress reactions), heat shock proteins (related to the inflammatory response; [80]) as well as methylation patterns [81] should be more deeply investigated in relation to thermal conditions.

Vascular Function

Impaired function of the vascular endothelium is one hypothesized pathway linking changes in ambient temperature to adverse cardiovascular events, however only few studies have examined this relationship so far with inconsistent results [82–84]. Lanzinger et al. [64] observed immediate and delayed decreases in flow-mediated dilatation in association with a decrease in temperature in a panel of diabetic patients. These effects were more pronounced in association with higher concentrations of $PM_{2.5}$ and ozone, highlighting once more the importance of considering interactive effects of temperature and air pollutants in future analyses.

Thermogenesis

Thermogenesis and its impairment have so far only rarely been assessed in human observational studies. Recent discoveries highlight e.g., the role of brown fat tissue and impaired thermogenesis for the development of type 2 diabetes based on animal experiments [85]. So far, there is not much understanding of the joint effects of genetic predisposition and environmental exposures. For example, within the brown adipose tissue, *uncoupling protein 1* gene (*UCP1*) increases the combustion of free fatty acids but is also involved in responses to temperature [86].

Mental Health and Cognitive Function

With an aging population mental health and cognitive function, in particular, is an emerging field of concern. In studies assessing health in old age, cognitive function and subjective assessments of health, well-being and health-related quality of life are gaining steadily importance [87, 88]. Environmental stressors surely play an important role in this. Also, outcomes of physical disability and its progression as well as frailty (e.g., grip strength, walking speed, and bone density) need more attention in association with temperature variability. In addition, effect modifiers such as medication intake or (psychological) stress are under-investigated so far.

Geographic Regions

While there seems to be an ever-increasing quantity of studies in Europe and the USA, temperature risks for elderly populations in Africa, Middle East, Asia, and South America are under-represented in literature reviews so far [9••], as evidence there is still scarce and more research is needed.

Personal Exposure

Yet not resolved is also the issue of personal exposure to meteorological factors. It is, for example, unclear why indoor temperature changes show on average little effect on health while outdoor temperature changes show consistent (adverse) effects across all geographical regions despite the fact that adults and especially the elderly spend most of their time indoors.

Urban Planning

It is well-known that cities have on average higher ambient temperature and air pollution levels than rural areas. The majority of Europeans live in cities and urbanization is continuing. The role of urban areas and the "built environment" on health, especially in the elderly, has been recognized [67]. A high density of buildings and roads can for example cause urban heat islands [89]. These urban heat islands contributed significantly to the negative health impact of the heat wave in Paris in 2003 [90]. The study of the health impact of green spaces is still an emerging field [91]. A large prospective study in Canada was able to link green spaces within a 500 m buffer to reduced non-accidental mortality [92]. Gill et al. [93] estimated that a 10% reduction of the green cover in cities will increase urban temperatures by 8.2 °C over the next 70 years. However, literature is still scarce on the effects of environmental exposures such as temperature, air pollution or noise and e.g., the mediating effect of urban green spaces on health and well-being in the urban population—although this topic becomes even more important with an aging and probably more multi-morbid population with a diminished capacity to respond to external stimuli. Moreover, the temperature–mortality/morbidity relationship varies greatly by geographic, climatic, social, and demographic characteristics [94].

Conclusion and Future Perspectives

Adaptation to Climate Change

The magnitude of temperature-related health effects might vary considerably in both space and time. Generally, it is expected that the additional deaths during hotter months will overwhelm the reductions during colder months [95•]. One key issue for forecasting the health impacts of climate change is the extent to which populations will be able to adapt to increasing and also more variable temperatures in the future [53]. Previous studies projecting mortality under a changing climate generally assume that the relationship between temperature and mortality will stay constant over time [96]. Projecting future mortality effects of climate change without consideration of heat adaptation may lead to substantial overestimates [10••, 97, 98•]. This attenuation in risk can be—dependent on the geographical location—more pronounced for less extreme temperature or stronger for more extreme heat [10••]. The evaluation of effect modifiers of the current association between temperature and health might give us hints which parameters might change in the future making the population better adapted to a changed climate. Moreover, Wanka et al. (2014) [99•] pointed out that the impact of social inequalities on environmental stressors and aging is not clear yet and so it remains open which of the existing heat/cold adaptation strategies older adults will deploy and to what extent they will really mediate temperature stress.

Improving the Built Environment

The percentage of the European population living in urban areas is projected to increase from about 75 to 80% by 2020 [100]. Air pollution, noise, urban heat islands, the absence of green space, but also social inequality are likely to negatively affect health and quality of life; however, no comprehensive assessments of the "built environment" have been conducted yet [67]. While urbanization facilitated the access to education, employment, and health care for a greater part of the population, it also altered their living conditions and lifestyles, as well as the overall environmental conditions. Therefore, comprehensive city-planning having the increasing elderly population in mind will gain more and more importance when "preparing" cities for the climate change as there is clearly potential for improving human health and well-being by improving the built environment.

Heat Warning Systems

It should be mentioned that many countries and cities already have implemented heat warning systems. So far, the weight of the evidence suggests that heat warning systems are effective in reducing mortality and, potentially, morbidity. However, their effectiveness may be mediated by cognitive, emotive and sociodemographic characteristics. More research is urgently required regarding the cost-effectiveness of heat warning systems' measures and improving the utilization of the services [101, 102••]. In 2015, the World Meteorological Organization (WMO) and the World Health Organization (WHO) have developed a guide for warning system development [103]. Here, ongoing evaluation of the effectiveness of the warning systems and their adaptation to aging populations and changing societies seems to be mandated.

Summary

Especially in the elderly population understanding health impacts associated with changes in thermal conditions requires multidisciplinary approaches that derive from climate and air pollution sciences, exposure assessment, human biology, and environmental epidemiology. Adaptation processes as well as improvements in urban planning and heat warning systems can help to reduce the predicted burden of climate change.

Compliance with Ethical Standards

Conflict of Interest Alexandra Schneider, Regina Rückerl, Susanne Breitner, Kathrin Wolf, and Annette Peters declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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