Effect of apparent temperature on mortality of persons with dementia

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Background

The current climate change is likely to increase the number of heat waves and hot weather, with the overall temperature distribution shifting away from the colder extremes (*O'Neill & Ebi, 2009*). Extreme weather conditions, such as heat waves or cold periods are expected to have effects on health and mortality. Extreme heat wave periods are the most common cause of severe weather fatalities in the United States (*Bobb et al., 2014*) and significantly affect death toll in Europe (*Robine et al., 2008*). Various studies have shown that admission rates related to specific causes, such as fluid and electrolyte disorders, renal failure, urinary tract infection, septicemia, heat stroke (*Bobb et al., 2014*), as well as unintentional injuries (*Otte Im Kampe et al., 2016*) are elevated during heat wave periods. A review by *Basu and Samet* (*2002*) has shown that mortality is increased during heat waves and that ambient heat exposures are positively associated with mortality. Likewise, cold-related morbidity and mortality is an important public health problem across Europe and should not be underestimated because of the recent focus on heat-wave episodes (*Analitis et al., 2008*). Cold temperatures are associated with an increase both in hospital admissions (*Myint et al., 2007*) and the number of total and cause-specific deaths, such as cardiovascular, respiratory, and cerebrovascular deaths (*Analitis et al., 2008; Laake & Sverre, 1996*). Especially elderly, infants and persons of low socio-economic status, as well as persons with impaired health or limited mobility suffer from increased risk of morbidity and death (*Balbus & Malina, 2009; O'Neill & Ebi, 2009*). Thus, people with cognitive constraints and dementia may be at particular risk. Very few studies explored the particular effect of weather conditions on morbidity and mortality of people with dementia. For instance, a study of *Salib and Sharp* (*1999*) found no statistically significant association between weather parameters and dementia admissions. *Page et al.* (*2012*) analyzed temperature-related deaths in England in people with mental illness, including psychosis, dementia and substance misuse, and found an increased risk of death during hot weather. Similarly, a study of *Hansen et al.* (*2008*) found a positive association between outdoor temperature and hospital admissions for as well as mortalities due to mental and behavioral disorders, respectively. Among other specific diseases, the risk of admission for dementia and dementia deaths increased during heat. The *Office for National Statistics* (*2013*) analyzed the excess winter mortality by underlying cause of death in England and Wales in 2011/12. Among those with dementia and Alzheimer's disease as cause of death, 29.4 percent more people died in the winter than in the non-winter months.

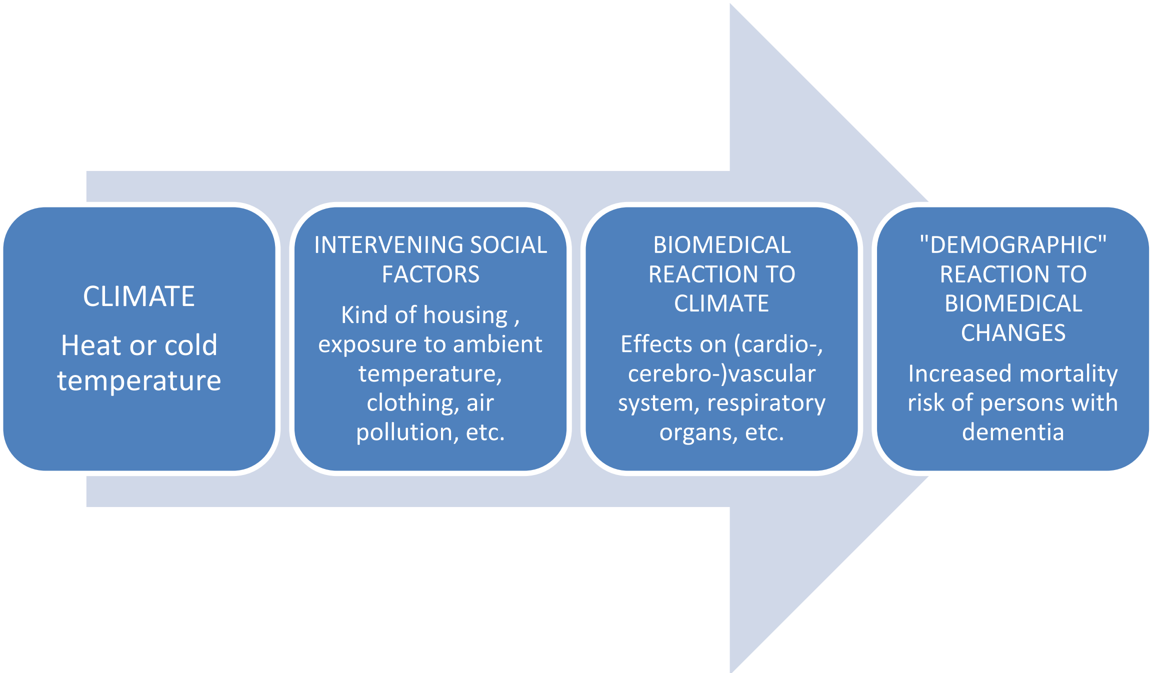
In general, the association of ambient temperature and mortality follows a V- or U-like distribution with lowest death rates during periods of 20 to 25°C and higher death rates below or above these temperatures (*Hajat et al., 2007; Hanna & Tait, 2015; Kunst et al., 1993*). Important determinants in this context are, among others, geographical patterns (*Bull & Morton, 1978; Donaldson & Keatinge, 1997; Lerchl, 1998; Mackenbach et al., 1997; Saez et al., 2000; The Eurowinter Group, 1997*), humidity (*Saez et al., 2000*), and age (*Collins, 1986*).

A person's ability to maintain and regulate a constant core temperature within an optimal range (36.8 °C +/- 0.5 °C) is defined as thermoregulation. The ability of thermoregulation depends on physiological and behavioral aspects and is reduced if one or both of these systems are impaired, leading to an increased sensitivity to heat exposure. The physiological part of thermoregulation allows the body to adjust the heat balance within a narrow range of environmental temperatures. The behavioral part depends on the individual's ability to percept the internal thermal environment and to modify that environment. Such modifying actions could be, e.g., finding a warmer or cooler space, appropriate clothing, or appropriate physical activity (*Hanna & Tait, 2015*). Similarly, exposure to extreme cold temperatures may lead to an unbalanced core body temperature if it is lost faster than it is reproduced. Cold temperatures increase the risk of cardiovascular and cerebrovascular diseases by narrowing of veins and arteries, increasing platelet and red cell counts, blood viscosity, as well as arterial pressure (*Keatinge et al., 1984; Neild et al., 1994; Seltenrich, 2015; The Eurowinter Group, 1997; Zhang et al., 2014*). The risk of respiratory diseases increases due to the survival of bacteria in droplets and due to a decrease of the immune system's resistance against respiratory infections at low temperatures (*Huynen et al., 2001; Keatinge et al., 2000; Rau, 2007; The Eurowinter Group, 1997*), subsequently leading to an increased risk of pulmonary diseases (*Huynen et al., 2001*). Exposure to cold also causes (accidental) hypothermia and is defined as an (unintentional) decrease in core body temperature below 35°C. Hypothermia occurs if the thermoregulation is impaired (*Kempainen & Brunette, 2004*). As mentioned before, impaired cognition (dementia, drug-induced, other encephalopathy), inadequate shelter and clothing (homelessness, poverty, wilderness exposure), or immobility (neuromuscular failures such as stroke, hip-fracture, or spinal cord-injury) impair behavioral responses to cold exposure (*Kempainen & Brunette, 2004*). However, hypothermia contributes only a small proportion to excess winter deaths (*Laake & Sverre, 1996; Rau, 2007*).

Among the elderly, dementia is one of the most common diseases. In 2013, an estimated 44.35 million people worldwide, and almost 11 million in Europe suffered from dementia (*Alzheimer's Disease International, 2013*). In Germany, about 1.4 million people currently suffer from dementia (*Schulz & Doblhammer, 2012*). Dementia and its consequences affect the life of patients and families, and is a challenge for the society as well as for the health care system. Apart from age and gender (*Doblhammer et al., 2012; Winblad et al., 2016*), well-known risk factors of dementia comprise cardiovascular (such as hypertension, diabetes, and obesity) (*Winblad et al., 2016*) and cerebrovascular diseases (such as stroke) (*Ivan et al., 2004; Pendelbury & Rothwell, 2009*), as well as psychosocial factors such as education, social engagements, and leisure activities (*Winblad et al., 2016*). Among the vascular risk factors, Type 2 diabetes increases the risk of cognitive impairment (*Fontbonne et al., 2001*), dementia (*Craft, 2009; Luchsinger et al., 2004*), and Alzheimer's disease (*Kopf & Frölich, 2009; Weuve et al., 2008*). Either a stroke itself causes dementia (*Pendelbury & Rothwell, 2009*) or a combination of degenerative and vascular pathologies may lead to the development of dementia after stroke (*Ivan et al., 2004*). Weight gain, high waist circumference (*Beydoun et al., 2008*) and hypertension increase the risk of dementia (*Khachaturian et al., 2006; Lindsay et al., 1997; Skoog, 2004; Skoog et al., 1996; Wu et al., 2003*). Hypertension, obesity as well as dyslipidemia and glucose intolerance are the features of the metabolic syndrome (*Levesque & Lamarche, 2008*) that is associated with an increased risk of cardiovascular disease, type 2 diabetes mellitus, all-cause mortality (*Kaur, 2014*), Alzheimer's disease (*Vanhanen et al., 2006*), and vascular dementia (*Solfrizzi et al., 2010*). This brief overview points out that elderly in general and dementia patients in particular often suffer from diseases that are aggravated during periods with extreme ambient temperatures. Furthermore, dementia increases the mortality and thus lowers life expectancy (*Dewey & Saz, 2001; Doblhammer et al., 2015; Jagger et al., 2000; Tom et al., 2015*).

Theoretical approaches of causality for seasonal effects in mortality have been outlined by, among others, *Rau* (*2007*) and *Kovats and Hajat* (*2008*). While the first explained how cold temperatures affect biomedical reactions in the body, subsequently leading to mortality, the latter described a very similar model for hot temperatures. Similarly, the models include mediating factors that may affect exposure to heat or cold, or the sensitivity to a given temperature exposure. Following these causal chain models, Figure 1 shows a theoretical approach to describe the increased mortality of persons with dementia as the effect of biomedical reactions on extreme outdoor temperatures.

Figure 1: Causal chain model for effects of ambient temperature in dementia mortality



Source: Own presentation, following (*Kovats & Hajat, 2008; Rau, 2007*)

The aim of this study was to explore seasonal effects on mortality of persons with and without dementia in Germany. In particular, we look how exposure to apparent hot and cold temperatures affects the risk to die among persons with dementia and whether this risk differs among persons without dementia. Positive findings in terms of increased mortality risks during extreme temperatures would have health, social, and political implications.

Data and Methods

We merged claims data of the Allgemeine Ortskrankenkasse (AOK), the largest German health insurer, and daily historical meteorological information obtained from the German Meteorological Service (DWD).

Claims data contained information on medical diagnoses coded by International Classification of Diseases (ICD-10) of the inpatient and outpatient sectors. An age-stratified sample of 250,000 persons aged 50+ was drawn based on all insured persons in the first quarter of 2004. Longitudinal observation took place from 2004–2010. The years 2004 and 2005 were used to verify dementia diagnoses by means of multiple diagnoses by different specialists or over time. From the baseline year 2006 all individuals aged 65+ were followed until death, a change of the insurance company, or through the end of 2010, whichever occurs first. Dementia was defined using ICD codes: G30, G31.0, G31.82, G23.1, F00, F01, F02, F03, and F05.1.

Daily historical meteorological data between 1 January 2004 and 31 December 2010 were obtained from the Deutscher Wetterdienst (DWD), which is part of the Federal Ministry of Transport and Digital Infrastructure (more details via http://www.dwd.de/). Meteorological data contained information on daily mean air temperature, relative humidity, wind velocity, and other weather indicators from 80 weather stations across Germany. The location of the weather stations was assigned to the according 2-digit postal code region. We computed mean values within each postal code region with more than one weather station. Missing values on a specific date in a specific postal code region occurred, if no station exists or a station exists but no values could be recorded on that day in that region. Missing values were then replaced by computing mean values of the according indicator in the surrounding regions. We used two measures to indicate apparent temperature: The Heat Index for temperatures above 20°C (*Rothfusz, 1990; Steadman, 1979*) and the Wind Chill Temperature Index for temperatures below 10°C (*OFCM, 2003*). Both Heat Index and Wind Chill Temperature were then used to compute an indicator to define whether a specific day had especially high (≥27°C), low (≤0°C), or normal apparent temperatures.

Since the health claims data were on a quarterly basis we had to expand them to a daily basis to link the dataset to the daily meteorological data. As a result, information from the claims data was now constant over the according quarter. Finally, we linked the claims data and the meteorological data via date and postal code region.

Methods of Event-History analysis were conducted to study the mortality risk in persons with dementia, depending on apparent temperature. Cox proportional hazard models were performed to explore the effect of apparent temperature on mortality, controlling for dementia, residency (nursing home yes/no), care level, urban living, climate regions within Germany, as well as for vascular and other comorbidities, which were also coded according to ICD-10. Demographic information contained gender and age.

Results

The 182,384 persons contributed 1,084,111 person-years and 49,040 cases of death during the period 2006 to 2010 (Table 1). The overall mortality rate (MR), displayed as death cases per 100 person-years, was 4.52 (95% confidence interval CI=4.48-4.56). With regard to apparent temperature, mortality rate was highest on days with extreme cold temperatures (MR=4.90, CI=4.82-4.99), compared to days with normal temperatures (MR=4.39, CI=4.40-4.43) and high temperatures (MR=4.56, CI=4.34-4.80). The mortality rate for persons with dementia was 19.21 (CI=18.95-19.48) and exceeded the rate for persons without dementia (MR=2.90, CI=2.87-2.94).

Table 1: Mortality rates by key variables

Variable	Value	Person-years	Cases	Mortality rate*100	LCI	UCI
Apparent temperature	normal	772598.93	33884	4.39	4.34	4.43
	cold	277431.48	13601	4.90	4.82	4.99
	heat	34080.65	1555	4.56	4.34	4.80
Dementia	no	976448.74	28356	2.90	2.87	2.94
	yes	107662.32	20684	19.21	18.95	19.48
Total		1084111.10	49040	4.52	4.48	4.56

Data source: Claims data AOK 2006-2010, own calculations

Hazard ratios estimated by multivariate Cox proportional hazard models are presented in Table 2. All models adjusted for age, gender, nursing home, care level, comorbidities, urban living, and climate zones. Exposure to extreme cold temperatures increased the risk of dying by 13 per cent (HR=1.13, p<0.001), while high apparent temperature (HR=1.00, p=0.893) seem to have no significant effect. The risk of dying was more than fivefold for persons with dementia (HR=5.34, p<0.001). Model 2 included the interaction effect of dementia and apparent temperature. While hot temperature did not have a significant main effect, the statistically significant interaction effect above one (HR=1.10, p=0.058) for those with dementia and exposure to hot temperature implies a comparatively higher risk of dying for those with dementia compared to persons without dementia. There was no significant interaction effect between dementia and cold temperature.

Table 2: Hazard ratios of mortality

		Model 1		Model 2	
Variable (reference)	Value	HR	p	HR	p
Apparent temperature (normal temperature)	cold	1.13	0.000	1.12	0.000
	heat	1.00	0.893	0.96	0.253
Dementia (no)	demented	5.34	0.000	5.30	0.000
Apparent temperature*	cold*demented			1.01	0.513
Dementia	heat*demented			1.10	0.058

Data source: Claims data AOK 2006-2010, own calculations; adjusted for age, gender, nursing home, care level, comorbidities, urban living, climate zones

Conclusion

Apparent temperature significantly affects the risk of dying in the elderly population. While exposure to cold temperature increases the risk of all persons, exposure to hot temperatures particularly increases the risk of people with dementia. The results are in line with a number of studies analyzing seasonal effects in mortality. Increased mortality risks in winter season and due to low temperatures have been found in other studies (e.g. (*Analitis et al., 2008; Healy, 2003; Rau, 2007; The Eurowinter Group, 1997*)). Heat wave events have been found to increase mortality in the general population (see overview in (*Kovats & Hajat, 2008*)) as well as in specific populations such as persons with mental and behavioral disorders (*Hansen et al., 2008*).

Dementia itself is known to be associated with increased mortality and decreased life expectancy (*Dewey & Saz, 2001; Doblhammer et al., 2015; Jagger et al., 2000; Tom et al., 2015*). The current findings confirm earlier research results. More interesting is the question whether a person with dementia is more vulnerable to extreme temperatures compared to persons without dementia. And indeed, there is evidence for a significant interaction between dementia and apparent temperature, particularly for high temperatures. Other studies found acute effects of heat waves and hot temperatures on morbidity and mortality among people with mental disorders. *Hansen et al.* (*2008*) analyzed the effect of heat waves on mental health in Adelaide, a temperate Australian city. They found an increased number of dementia deaths in the 15- to 64-year age group only, indicating the susceptibility of persons with early-onset dementia. However, the authors themselves raise concern with regard to small sample sizes. *Page et al.* (*2012*) explored temperature-related deaths in people with dementia and other mental illnesses in a database on four million primary care patients living in the UK. They found an elevated risk to die of 4.9% (95% CI 2.0–7.8) per 1°C increase in temperature above the 93rd percentile of the annual temperature distribution.

We controlled for a series of information that are known to be associated with mortality in general and temperature-related mortality in particular: Institutionalization (*Fouillet et al., 2006; Hajat et al., 2007; Heudorf & Meyer, 2005; Holstein et al., 2005*); care level (*Belmin et al., 2007; Foroni et al., 2007*); comorbidities (*G.B.D. 2013 Mortality and Causes of Death Collaborators, 2015; Piirtola et al., 2008; Tiainen et al., 2013*); urban living (*Applegate et al., 1981; Hajat et al., 2007; Jones et al., 1982; Kovats & Hajat, 2008; Kravchenko et al., 2013*); and climate zones (*Mercer, 2003; The Eurowinter Group, 1997*). Although we controlled for such information that may explain increased mortality, there remained an effect of apparent temperature on mortality and mortality with dementia. The theoretical approaches of *Rau* (*2007*) as well as *Kovats and Hajat* (*2008*) on the causal association of temperature on mortality took into account mediating social factors such as housing conditions or exposure to outdoor temperature. Literature reveals several aspects that may have an intervening effect within that causal chain. However, we were not able to take into account all of these aspects due to the character of the health claims data as a secondary data source. On a macro level, air pollution and poor air quality affect health and mortality and aggravate the health effects of low (see overview by *Rau* (*2007*)) and high temperatures (see (*Basu & Samet, 2002; Kravchenko et al., 2013*)). On the micro level, living alone or not leaving home daily is associated with increased mortality during heat periods (*Fouillet et al., 2006; Kravchenko et al., 2013; Naughton et al., 2002*). Persons of lower socio-economic status suffering deprivations are affected by heat-related (*Basu & Samet, 2002; Hajat et al., 2007*) and cold-related mortality (*Mercer, 2003*). Mortality related to temperature is associated with poor housing standards and adverse indoor climate. During heat waves, access to air-conditioning in the home decreased the mortality risk (*Basu & Samet, 2002*). During cold periods, mortality increased in populations with cooler homes (*The Eurowinter Group, 1997*). The latter often depends on the medical status of the person and its ability to react appropriately on adverse temperatures (*Mercer, 2003*).

A pattern that is often discussed in studies of seasonal variation in mortality is “mortality displacement” or also referred to as “harvesting”. Mortality displacement describes the effect that death rates are increased during periods of extreme temperatures and are lower than expected shortly after these periods (*Revich & Shaposhnikov, 2008*). Mortality displacement depends on the population at risk with its baseline health status and socio-demographic characteristics (*Qiao et al., 2015*) and may occur among people whose health status is already compromised and who will die shortly thereafter even in the absence of exposure to extreme temperatures (*Hajat et al., 2005*). Research on this topic reveals that mortality displacement is pronounced in heat periods, although these findings are inconclusive. While some studies revealed evidence for mortality displacement as explaining factor in heat-related deaths (*Hajat et al., 2005; Medina-Ramon & Schwartz, 2007; Revich & Shaposhnikov, 2008*), other studies found any or only little evidence (*Davis et al., 2004; Kysely & Kim, 2009; Le Tertre et al., 2006; Tong et al., 2012*). Studies on the role of mortality displacement in excess mortality during cold spells did not find such a pattern (*Braga et al., 2002; Huynen et al., 2001; Revich & Shaposhnikov, 2008*). With regard to the increased heat-related mortality among people with dementia our findings fit into that pattern. People with dementia have a higher vulnerability that may lead to an increased mortality during heat periods, and possibly to decreased mortality rates thereafter. Thus it is not clear whether the findings actually describe an effect of excess mortality or a timing effect and further studies are needed to clarify this pattern.

The use of health claims data offers some shortcomings. Health claims data are primarily relevant for cost reimbursement and cost calculation, which leads to two issues. First, only those diagnoses leading to treatment are relevant for the purposes of cost calculation. Thus, a patient's cognitive impairment might not be documented if no further treatment is given. This could be particularly true for mild cases of dementia and cognitive impairment. Second, many important aspects with regard to dementia and dementia mortality are not relevant for cost reimbursement and are thus not collected. As mentioned before, this includes information such as family status, education and socio-economic status, housing standards, or behavioral habits. The strength of this study is the large longitudinal sample with more than 180,000 persons including the institutionalized. There is no bias in the results due to self-selection, selection by the health care provider, or the study design. Using medical diagnoses also prevents recall bias by the patient.

In combination with meteorological data, the health claims data offer the possibility to explore seasonal variation in mortality outcomes. The increased mortality during cold temperatures is interesting per se and confirms findings of earlier studies. Together with the increase in the risk of death for elderly persons with dementia due to hot temperatures the results prove the need of improved protection of vulnerable persons, increased public spending on health care, and improved socioeconomic conditions to reduce morbidity and mortality.

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