The role of extreme temperature in cause-specific acute cardiovascular mortality in Switzerland: A case-crossover study

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HIGHLIGHTS
• Temperature related risk of cardiovascular mortality was highest on hot days.
• 2% of deaths were attributable to hot temperature and 5% to cold temperature.
• Older women with lower socio-economic position are more vulnerable to heat.
• Housing and air pollution, but not noise, modify vulnerability to temperature.
• Understanding effect modifiers is relevant for preventing temperature-related mortality.

ABSTRACT
Since the 2003 heatwave in Europe, evidence has been rapidly increasing on the association between extreme temperature and all-cause mortality. Little is known, however, about cause-specific cardiovascular mortality, effect modification by air pollution and aircraft noise, and which population groups are the most vulnerable to extreme temperature. We conducted a time-stratified case-crossover study in Zurich, Switzerland, including all adult cardiovascular deaths between 2000 and 2015 with precise individual exposure estimates at home location. We estimated the risk of 24,884 cardiovascular deaths associated with heat and cold using distributed non-linear lag models. We investigated potential effect modification of temperature-related mortality by fine particles, nitrogen dioxide, and night-time aircraft noise and performed stratified analyses across individual and social characteristics. We found increased risk of mortality for heat (odds ratio OR = 1.28 [95% confidence interval: 1.11–1.49] for 99th percentile of daily Tmean (24 °C) versus optimum temperature at 20 °C) and cold (OR = 1.15 [0.95–1.39], 5th percentile of daily Tmean (−3 °C) versus optimum temperature at 20 °C). Heat-related mortality was particularly strong for myocardial infarctions and hypertension related deaths, and among older women (>75 years). Analysis of effect modification also indicated that older women with lower socio-economic position and education are at higher risk for heat-related mortality. PM2.5 increased the risk of heat-related mortality for heart failure, but not all-cause cardiovascular mortality. This study provides useful information for preventing cause-specific cardiovascular temperature-related mortality in moderate climate zones comparable to Switzerland.
1. Introduction

There is well-established evidence of the association between heat and cold and mortality from a range of countries and climatic regions around the world (Gasparrini et al., 2015; Arbuthnott et al., 2020; Ryti et al., 2016; Breitner et al., 2014). In the context of a changing climate, the increased mortality observed during recent heatwaves has increasingly raised public health concern (Ragetti et al., 2017; Watts et al., 2020; Federal Office for the Environment, 2020). It is estimated that the heatwave of 2003 caused about 70,000 excess deaths in Europe (Robine et al., 2008). Since this notable episode, several further heatwaves have occurred across Europe leading to further deaths (Barriopedro et al., 2011; European Environment Agency, 2021). In Switzerland, the excess mortality was estimated around 1000 in 2003 (Grize et al., 2005), 800 in 2015 (Vicedo-Cabrera et al., 2016), 200 in 2018, and 500 in 2019 (Ragetti and Röösli, 2021). It is expected that most countries will experience more heatwave episodes in the future, especially in urban settings (Field et al., 2014). Cold temperatures are also important in terms of burden of disease, with some mainly northern countries reporting even higher attributable mortality than for heat (Oudin Astrom et al., 2018). The shape of the association between temperature and mortality, as well as optimum temperature, varies between areas (Gasparrini et al., 2015).

Cardiovascular diseases are among the leading causes of temperature-related mortality (Iniguez et al., 2020). Disparate exposure-response functions for cardiovascular diseases may be the consequence of different underlying physiological mechanisms; however, this is yet to be elucidated because few studies have systematically investigated the effects of temperature on cause-specific cardiovascular mortality. For instance, a recent longitudinal study reported a clear increased risk of cerebrovascular mortality in Lisbon for both warm (relative risk RR = 1.65 [1.37, 1.98] for the 99th percentile) and cold temperatures (RR = 2.09 [1.74, 2.51] for the 1st percentile) (Rodrigues et al., 2019).

Little is also known about effect modification of temperature-related cardiovascular mortality, since most papers on this topic have focussed on all-cause mortality. Son et al. (2019) conducted a meta-analysis on all-cause temperature-related mortality using evidence from around the world published before 2017, reporting increased relative risks of mortality for women with heat and for older individuals with both heat and cold. Their meta-analysis suggested limited evidence of effect modification by individual characteristics such as education, civil status and socio-economic position and weak evidence for effect modification by air pollution (ozone and PM10). More recently, several studies have investigated the role of age, gender and socio-economic position on temperature-related mortality. Marí-Dell’Olmo et al. (2019) observed a consistent increased risk of heat-related mortality among women and the older individuals in Spain. They also reported higher heat-related mortality among men with lower education, while women were similarly affected by heat across all education groups. In contrast, the role of air pollution in temperature-related mortality is less clear. Analitis et al. (2018) reported an increase in heat-related cardiovascular mortality with higher levels of ozone and PM10 in European cities, but only for some age groups and specific diagnoses. They did not find any evidence of effect modification by NO2 (Analitis et al., 2018). More research is needed to further understand the relationship between extreme temperature and cause-specific mortality, including a more detailed look at the associations within sub-groups of the population to identify groups that may be particularly vulnerable (Benmarhnia et al., 2015). A better understanding of the synergistic effects of temperature air pollution and noise among different groups is a key to promote equitable health in future local measures to combat heat in urban settings and future temperature-mortality mitigation efforts.

The aim of this study was to investigate the role of extreme temperature on cause-specific cardiovascular mortality using a case-crossover study design, and to identify the groups (in this study population of mortality cases) most vulnerable to heat and cold. Much of the research to date on temperature-related mortality uses time-series designs with one or several central temperature monitoring station(s) for exposure assessment, ignoring the spatial contrasts in temperature across the study area (Benmarhnia et al., 2015). The advantage of the case-crossover approach used in this study is that it exploits fine scale spatio-temporal temperature data, thus reducing the risk of exposure misclassification. By minimizing confounding from individual characteristics, the case-crossover design also strengthens effect modification analyses aimed to identify the most vulnerable groups of the population. This study specifically leveraged a large and precise environmental exposure database created for a previous study investigating the acute cardiovascular effects of aircraft noise around Zurich Airport in Switzerland based on the Swiss National Cohort (SNC) (Saucy et al., 2020a). The integrated database enabled the investigation of potential interaction of temperature with air pollution and, for the first time, acute noise exposure.

2. Methods

2.1. Study population

The SNC is a long-term cohort based on linkage of national census and mortality records for the whole Swiss population, containing personal information such as age, sex, socio-economic position, address history and mortality information (cause, date and time of death) (Spoerri et al., 2010). With a large range of individual information, including a Swiss-specific indicator for neighbourhood-based socio-economic position, the SNC provides longitudinal data suitable for investigating the health effects associated with differences in socio-economic profiles (Bopp et al., 2009). The selection of the study population was motivated by a previous study investigating the acute cardiovascular effects of aircraft noise in the vicinity of Zurich Airport which adjusted for air pollution and temperature effects. In leveraging this database, we now specifically focus on the short term effects of temperature in relation to mortality. Thus, we selected 24,886 cases of cardiovascular death occurring between 2000 and 2015 in adults >30 years, with available address at time of death and exposed to levels of aircraft noise above 47 dB during the day and/or 37 dB during the night (Schäffer et al., 2012) (Fig. A.1). This study area includes urban, peri-urban, and rural areas (Table 1). We considered the following primary causes of death: all cardiovascular diseases (CVD) (ICD-10: I00-I99), ischaemic heart diseases (ICD-10: I20-I25), myocardial infarction (ICD-10: I21-I22), stroke (ICD-10: I60-I64), heart failure (ICD-10: I50), hypertensive diseases (ICD-10: I10-I15), and arrhythmias (ICD-10: I14-I49).

2.2. Study design

We used a case-crossover study design to investigate the acute effects of heat and cold on cardiovascular mortality. The case-crossover study design, first described by Maclure in 1992, is a case-only approach, where each case event is matched with several control events for the same person at different times (Maclure, 1991). Each case was matched with up to four control events, selected within the same month and matched on day of the week, following a time-stratified sampling scheme (Navidi, 1998). As opposed to time-series where temperature is assigned from a central monitoring station, this design allowed us to use precise individual daily temperature estimates incorporating spatial contrasts in addition to the temporal.

2.3. Exposure assessment

We assigned daily outdoor temperature values at the home location for each of the case and control event days. We used 2 km resolution historical meteorological exposure maps from MeteoSwiss (Grid-Data...
All-cause cardiovascular 24,886 (100) −2.76 19.37 24.59 −5.68 14.17 17.72 −0.28 25.79 32.81
Ischaemic heart diseases 10,521 (41) −2.97 19.53 24.61 −5.81 14.22 17.67 −0.26 26.04 32.96
Myocardial infarction 3248 (13) −2.83 19.23 24.95 −5.80 14.21 17.80 −0.25 25.66 32.99
Stroke 3750 (15) −2.44 19.23 24.45 −5.54 14.06 17.72 −0.07 25.66 32.66
Heart failure 1753 (7) −3.04 18.92 25.16 −6.02 13.89 18.02 −0.49 25.22 32.85
Hypertensive diseases 2728 (11) −2.56 19.27 24.52 −5.59 14.06 17.75 −0.30 25.55 32.67
Arthritis 1392 (6) −2.84 19.50 24.56 −5.44 14.26 17.65 −0.51 26.07 32.80
Gender Female 13,269 (53) −2.74 19.29 24.45 −5.65 14.15 17.67 −0.28 25.70 32.62
Male 11,617 (47) −2.79 19.44 24.80 −5.68 14.21 17.77 −0.28 25.93 32.94
Age groups ≤75 5632 (23) −2.96 19.26 24.83 −5.98 14.20 17.75 −0.48 25.72 32.93
75–85 8324 (33) −2.45 19.56 24.72 −5.32 14.22 17.70 −0.14 26.03 33.14
>85 10,930 (44) −2.71 18.90 24.50 −5.62 14.12 17.70 −0.19 25.70 32.56
Socio-economic positiona
1 2512 (10) −2.70 19.59 24.78 −5.67 14.24 17.64 −0.26 26.03 32.97
2 3685 (15) −2.89 19.17 24.53 −5.85 14.02 17.76 −0.39 25.49 32.95
3 4470 (18) −2.87 19.31 24.80 −5.83 14.15 17.68 −0.40 25.66 32.91
4 6263 (25) −2.73 19.52 24.54 −5.60 14.16 17.72 −0.26 26.09 32.62
5 6572 (26) −2.64 19.26 24.87 −5.53 14.27 17.78 −0.15 25.68 32.95
Unknown 1364 (6) −2.83 19.15 24.08 −5.53 14.14 17.61 −0.68 25.52 31.47
Education Compulsory or less 8830 (35) −2.94 19.32 24.52 −5.70 14.16 17.76 −0.49 25.84 32.60
Upper secondary level 12,353 (50) −2.71 19.38 24.62 −5.63 14.16 17.69 −0.25 25.83 32.86
Tertiary level 3150 (13) −2.74 19.50 24.61 −5.77 14.30 17.71 −0.28 25.80 32.94
Unknown 553 (2) −2.06 18.64 24.61 −5.46 13.41 18.04 0.42 24.86 32.57
Urbanisation Urban 9108 (36) −2.74 19.51 24.44 −5.80 14.27 17.81 −0.31 25.89 32.46
Peri-urban 14,347 (58) −2.80 19.34 24.68 −5.56 14.16 17.67 −0.25 25.78 33.01
Rural 1431 (6) −2.70 18.73 24.43 −5.48 13.72 17.45 −0.27 25.10 32.50
Building period Before 1970 9478 −2.67 19.36 24.59 −5.55 14.19 17.67 −0.07 25.79 32.78
1970–1990 8631 −2.93 19.29 24.45 −5.79 14.11 17.59 −0.48 25.87 33.70
After 1990 6302 −2.63 19.42 24.85 −6.61 14.20 18.11 −0.22 25.81 32.92
Unknown 475 (2) −3.57 19.27 24.07 −6.66 14.14 18.25 −1.44 25.16 32.95
Civil status Married 9286 (37) −2.54 19.61 24.64 −5.56 14.34 17.78 −0.01 26.14 33.03
Non married 15,600 (63) −2.85 19.20 24.55 −5.70 14.06 17.69 −0.44 25.55 32.71

a Socio-economic position index ranging from lowest (0) to highest (5) quantiles (Panczak et al., 2012).

Products), including daily maximum (Tmax), minimum (Tmin) and mean (Tmean) temperature and precipitation. Temperature estimates in these maps were calculated at 2 m above ground level, using near-surface air temperature measurements following a deterministic analysis method specifically designed for temperature interpolation in mountainous areas (MeteoSwiss, 2017; MeteoSwiss, 2016).

We used 4-day average air pollution exposure, assessed at the home location. Daily fine particulate matter (PM2.5) and nitrogen dioxide (NO2) data were available at 100 m resolution for Switzerland, from 2003 to 2013 and from 2005 to 2015 respectively (de Hoogh et al., 2019; de Hoogh et al., 2017). To obtain individual PM2.5 data for the years 2014 and 2015, we extended the existing models following the 4-stage modelling approach described by de Hoogh et al. (2017). To extend the time series back in time to year 2000, we simply estimated daily PM2.5 and NO2 exposure at the residence using the annual average for the first available modelled year calibrated by the daily values from a single routine monitor. We used the Dübendorf site located in the centre of the study area for this purpose (Fig. A2).

Acute aircraft noise was calculated at home locations by combining a list of all aircraft movements at Zurich airport between 2000 and 2015 with outdoor aircraft noise exposure calculations at 250 m resolution, specific for aircraft type, air route, time, and year as previously described in detail (Saucy et al., 2020b). We used the average noise exposure during the night preceding daytime deaths and the average noise exposure within 2 h preceding the night-time deaths. To make these comparable, we normalized the two types of noise exposure values before aggregating the corresponding z-values into a single exposure measure. Other sources of transportation noise (e.g. road traffic and railway noise) were not considered in this analysis. Noise from road traffic and railways typically show little day-to-day variability and are therefore already adjusted by the individual matching in the case-crossover study design. This is the first study to investigate whether aircraft noise, which has a high day-to-day variation, is a confounder in the short-term association between temperature and cardiovascular mortality.

2.4. Statistical analyses

We investigated the association between cardiovascular mortality and temperature using a distributed lag non-linear model (DLNM) approach, as described by Gasparini (2014). The DLNM approach relies on the definition of a “cross-basis” function, allowing for non-linear and delayed effects of temperature (Goldberg et al., 2011). We modelled the relationship between daily average temperature (Tmean) and mortality using a lag structure up to 14 days before death. The lag function was specified as a natural spline with two equally spaced knots on the logarithmic scale, and Tmean was specified as a b-spline with three knots placed at the 10th, 75th and 90th percentiles of the annual temperature distribution. The choice of the temperature knots was defined a-priori as described in other studies (Gasparini et al., 2015; Inguez...
et al., 2020) and validated using Akaike’s criterion (AIC). For air pollution adjustment, 2 to 5 days were tested and the 4-day average selected by minimizing the AIC. We conducted conditional logistic regression adjusted for 2-day average precipitation, 4-day average NO₂ and/or PM₂.₅, normalized aircraft noise prior to deaths, and national holidays. We estimated the odds ratio (OR) of mortality as the deviation from the empirically derived optimum temperature (20 °C) to the 99th percentile of the daily Tmean distribution for heat and from the optimum temperature to the 5th percentile for cold as described by Gasparri and Leone (2014). The reference value at 20 °C was derived from an estimate of the optimum temperature previously calculated for Switzerland (Vicedo-Cabrera et al., 2018) and approximately corresponds to the 90th percentile of the daily Tmean distribution in our data. As heat-related health effects usually last up to a week (Ragetti et al., 2017), and to account for potential short-term harvesting, we reported cumulative OR over lags 0–7 for heat-related mortality. For cold-related mortality, cumulative OR included lags 0–14 to consider the longer delay for cold related mortality. We ran sensitivity analyses with 21–days lag to account for potential harvesting effect for cold temperatures, as well as separate analyses using Tmin and Tmax instead of Tmean as main exposure metrics. To investigate the effect modification by non-varying individual characteristics, we conducted stratified analyses by sex, age, building period, socio-economic position, education, and marital status.

The fraction of mortality cases attributable to heat and cold was estimated by combining the temperature-mortality function derived for Tmin and Tmax with the distribution of observed temperature (in 5 °C temperature classes) and the observed average number of deaths per day.

A number of additional models were conducted. We assessed the potential effect modification of heat-related cardiovascular mortality with short-term ambient air pollution and aircraft noise—other acute triggers of cardiovascular mortality—by introducing an interaction term. As heat effects are found to last up to 3 to 5 days (Ragetti et al., 2017; Analitis et al., 2018), we investigated the effect modification by 4-day average air pollution levels on the association between heat (Tmean averaged for lags 0–3) and cardiovascular mortality. We modelled Tmean as a second-degree polynomial term and introduced interaction terms with NO₂, PM₂.₅ and normalized aircraft noise. We created separate models for each pollutant and specific cause of death. All models were fully adjusted for all other exposures (Eq. A.1). We report the change in the OR of heat and cold related mortality for increasing levels of 4-day average air pollution and aircraft noise in the night preceding death respectively.

3. Results

Tmean ranged between −14 and +28 °C (mean = 9 °C) within the study population. Tmean was highly correlated with Tmin (0.84) and with Tmax (0.95, Pearson correlation coefficient). The temperature distribution was homogeneous between the different groups of the population presented in Table 1. More cases of death from cardiovascular origin were observed during the summer than winter (Fig. A.3). The OR of cardiovascular mortality associated with Tmean are represented in Fig. 1. For heat effects, the OR of the 99th percentile of the annual temperature distribution (24 °C) compared to the 90th percentile (20 °C) was 1.28 [1.11–1.49], and the corresponding OR for the 5th percentile (−3 °C) was 1.15 [0.95–1.39] for cold effects (Table 2). The shape of the association between annual temperature and cardiovascular morality was similar across all temperature metrics (Tmin, Tmean, Tmax), with an increase in the OR of mortality observed from 15 °C for Tmin and 27 °C for Tmax (Fig. A.4). The increased OR for mortality lasted up to 5 days for heat and over 14 days for cold (Fig. 1). Sensitivity analyses extending the lag period to 21 days to account for potential harvesting effect did not affect these findings. The estimated mortality fraction attributable to higher temperatures (above the optimum temperature at 20 °C) was 2% and to colder temperatures (below the optimum temperature) 5%.

With respect to heat related mortality, the strongest associations were found for hypertension related deaths and myocardial infarction (Table 2), and the risk of mortality was higher for women than men (41% increase in OR of cardiovascular mortality for women versus 14% for men). We also observed increased risk of mortality for older individuals and for those with less education, living in older buildings, and who were not married. In general, cold temperatures were not significantly associated with mortality, although significantly increased ORs were observed individuals with low socio-economic position, low education and not married.

In general, heat-related effects were stronger in women with lower socio-economic position and lower education (Table A.1). In men, the stronger heat-related effects were in those with higher socio-economic position, which has driven the corresponding result in the full sample (Table 2).

We did not observe strong indications of effect modification from PM₂.₅ and NO₂ in relation to heat or cold for all cause cardiovascular mortality (Fig. 2). However, heat-related heart failure mortality increased with increasing PM₂.₅ (p-value of interaction term = 0.03). The same tendency was observed for NO₂, although not significant (p-interaction = 0.86). The OR of cold-related mortality for myocardial infarction was slightly increased at higher levels of NO₂ without reaching significance (p-interaction = 0.50) (Fig. 2). We found no evidence of an interaction with acute aircraft noise.

4. Discussion

This is one of the first studies investigating the temperature-related mortality for cause-specific cardiovascular mortality. We found increased odds of mortality mainly for heat but also in tendency for cold in our study population. The strongest associations with heat were found for ischaemic heart diseases, myocardial infarction, and hypertension-related causes of deaths. Further, our analysis suggests that older women with lower socio-economic position and lower education are at higher risk for heat-related mortality. We did not find a strong interaction between air pollutants and temperature-related mortality, except for heat-related heart failure and PM₂.₅.

The shape of the association between temperature and mortality in the Zurich region is similar to observations in cities like Stockholm or Toronto with similar optimum temperature around 20 °C (Gasparri et al., 2015). While the OR of mortality steadily increases with maximum temperature, the increase in risk with cold temperature was modest with little evidence for a risk increase in the most extreme cold temperature range. The lowest temperatures observed in this study are likely to be in the more rural areas and at higher altitude which are colder over the whole year. We expect this population is either better equipped (e.g. efficient insulation and heating system) or adapted for cold weather, possibly explaining this pattern. It may also be that the design using a one week interval between case and control events may be less suitable for cold compared to heat, specifically given that the effects of very cold temperatures are known to last over a longer period (Gasparri et al., 2015).

Having modest odds ratios for moderate to cold temperature does not necessarily mean that attributable fraction is also small. In many cities around the world, moderate cold temperatures are common and, similar to our study, the highest temperature-related mortality burden has been attributed to the contribution of moderate cold (Gasparri et al., 2015; Fu et al., 2018).

We found that heat-related mortality was especially driven by ischaemic heart disease including myocardial infarction (1.67 [1.09–2.55]) and by hypertensive diseases (1.91 [1.20–3.06]). In addition to respiratory diseases, Gasparri et al. (2012) also reported increased mortality for myocardial infarctions, arrhythmias and pulmonary heart diseases. Contrary to previous research in Lisbon, we did not find evidence of
cold-related mortality for cerebrovascular diseases (Rodrigues et al., 2019). Increased heart rate and organ oxygen demand resulting from general vasodilatation required for body temperature regulation during heat events can explain the occurrence of ischaemic events. Heat-related heart failure seems to occur in combination with fine particles, possibly as a sign of cardiac exhaustion after combined stress events. While the increase in hypertension-related mortality may seem contradictory as a response to heat, our results are coherent with recent research also showing an increased risk of mortality for people diagnosed with hypertension. In parallel, they observed a reduction in the number of hospitalization due to acute hypertensive disease during heatwaves (Ragettli et al., 2020). These two opposite effects were attributed to a possible interaction between heat and anti-hypertensive medication, which may explain our similar findings. For cold temperature, the increased cardiovascular mortality was driven by heart failure and hypertension related deaths. Even though this was not significant in our sample, it is compatible with the physiological response to cold temperatures through general vasoconstriction and increased peripheral resistance.

For cardiovascular deaths specifically, studies to date mainly report that ozone and PM_{2.5} modify the association between temperature and mortality, and only few studies included interaction with NO_{2} (Analitis et al., 2018). We found that fine particles modified the association between heat and mortality due to heart failure, but not other cardiovascular deaths. NO_{2} did not interact with temperature-related mortality. We did not find clear evidence for an interaction between heat and aircraft noise, as could be expected due to more frequent open windows during warm nights.

Our effect modification analysis showed that less privileged groups of the population were at higher risk for temperature-related mortality. Namely, the odds of mortality were higher for people living in older building, likely to be less insulated, consistently through warm and cold temperatures. Women and people from older age groups were also at higher risk of heat-related cardiovascular mortality. Interestingly, we found gender-differential effect modification by education, especially relevant for women. These results are in line with previous studies reporting gender-differential effects of education level (Mari-Dell’Olmo et al., 2019) and age (Ragettli et al., 2017) on heat-related mortality. Previous research also reported higher heat-related mortality for women and for those with low education level in some age groups during the 2003 heatwave in Barcelona (Borrell et al., 2006), but no effect modification by indicators of socio-economic position in London (Murage et al., 2020). While women lived longer than men in our study population (mean age at death = 84 vs. 74 years old), the age difference at death is unlikely to explain the full gender differential on mortality; stratified analyses also showed effect modification by age within women (Table A.1). The observed increase in heat-related cardiovascular mortality for women with older age may also be related to post-menopausal status (Dratva et al., 2007), although the number of younger women (1.5% of all women...
were under 55 years old) was too limited in our study population to confirm this hypothesis. While the increased risk of heat-related mortality for men with higher socio-economic position cannot be fully explained, it may be related to differences in behaviour and lifestyle. Specifically behaviour such as drinking or reduced physical activity may explain some of the effect modification observed in our study (e.g. gender, marital status). Lower education may also be associated with more heat exposure at work, lower health literacy, potentially higher prevalence of pre-existing conditions and lower adherence to behavioural adaptations during heat events.

A particular strength of this study is the combination of precise spatial and temporal individual exposures. While the case-crossover design is being increasingly used to investigate temperature and air pollution related health effects, many studies still use centrally monitored temperature data, similar to a time-series analysis (Buteau et al., 2018; Guo et al., 2011), or exposure data at coarser spatial resolution (Fu et al., 2018). We used individual daily temperature and precipitation data at 2 km resolution, and daily air pollution exposure data at 100 m resolution, which reduces the risk of exposure misclassification. A further strength of the study is the adjustment for aircraft noise, which minimizes potential bias as temperature and air pollution may each be correlated with aircraft noise. Case and control events are selected within the same month and following a time-stratified sampling scheme, limiting the risk of potential seasonal bias and adjusting by design. Specifically, individual characteristics which are stable over the short study time, such as age, socio-economic position, and long-term exposure to environmental pollutants are controlled. Combined with distributed lag linear models, this approach thus enables the investigation of the acute effects of temperature with minimum bias. Our findings generally agree with the existing literature, and offer additional understanding of the vulnerable groups for temperature-related mortality, including exposure to cold temperatures which have not yet been extensively studied in Switzerland. A potential limitation, however, is that our study population has been selected in Zurich, with higher proportions of those with high socio-economic position compared to the whole country. To confirm our results and extrapolate the findings to the general population, a larger proportion of individuals living in rural areas and other cultural and language regions should be conducted. As the strength of the association for cold-related mortality was weaker than for heat-related mortality, stratification and corresponding loss of power made it more difficult to identify potential effect modifiers for cold. Finally, we did not have the data to additionally investigate the interaction between heat and ozone in this study.

5. Conclusion

Our study shows that heat related mortality is more pronounced than cold related mortality, and that temperature-related mortality varies depending on individual differences likely to be related to housing, social, physiological, and behavioural characteristics. Differences in environmental co-exposures also play a role in modifying the effects. Women of older age and with lower education and socio-economic position were found to be at highest risk for heat related cardiovascular mortality. Identification of the most vulnerable population groups under different exposure circumstances is essential to refine prevention campaigns in order to efficiently reduce temperature-related mortality. Climate shifts toward warmer temperatures may further increase the burden of heat-related mortality in many countries. Thus, effective public health measures are crucial to ensure heat-related mortality does not become an even larger problem in the future.

CRediT authorship contribution statement

Conceptualization; M.Rö. and A.S.; Formal analysis: A.S.; Funding acquisition: M.Rö.; Methodology: A.S., M.Rö.; Resources: M.Ra., B.S., J.-M.W., D.V., K.dH.; Supervision: M.Rö. and N.P-H.; Original draft: A.S.; Review & editing: M.Rö., M.Ra., N.P-H., J.-M.W., B.S., D.V., I.T, K.dH. All authors have read and approved the current version of this manuscript.

Funding

This research was funded by the Swiss National Fund (SNF) [grant number 324730_173330].

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

We acknowledge the Swiss Federal Statistical Office for providing the mortality and population data. Meteorological information was obtained from MeteoSwiss. Calculations were performed at sciCORE scientific computing centre at the University of Basel. We thank Martin Bissegger of Zurich Airport for the permission to use the lists of movements and aircraft noise exposure data, and Christian Schindler for his insights on statistical methods. We also acknowledge the members of the Swiss National Cohort Study Group: Matthias Egger (Chairman of the Executive Board), Adrian Spoerri and Marcel Zwahlen (all Bern), Milo Puhan (Chairman of the Scientific Board), Matthias Bopp (both Zurich), Martin Röösli (Basel), Murielle Bochud (Lausanne) and Michel Oris (Geneva).

Appendix A. Supplementary materials

Supplementary materials to this article can be found online at https://doi.org/10.1016/j.scitotenv.2021.147958.
Fig. 2. Odds ratio (OR) of temperature-related cardiovascular mortality associated with increasing NO2 and PM2.5 levels based on the interaction models. The left panes (A and C) present heat-related mortality (90th to 99th percentile of the annual distribution of Tmean averaged over lags 0–3). The right panes (B and D) present cold-related mortality (90th to 5th percentile of the annual distribution of Tmean averaged over lags 0–3). The ORs are displayed for all cardiovascular diseases (CVD), ischemic heart diseases (IHD), myocardial infarction (MI), stroke (STR), hypertensive diseases (BP), and heart failure (HF).

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