Environmental Pollution 291 (2021) 118066

Contents lists available at ScienceDirect

Environmental Pollution

journal homepage: www.elsevier.com/locate/envpol

Mutual effects of fine particulate matter, nitrogen dioxide, and fireworks on cause-specific acute cardiovascular mortality: A case-crossover study in communities affected by aircraft noise☆

Apolline Saucy [a,b], Kees de Hoogh [a,b], Danielle Vienneau [a,b], Louise Tangermann [a,b], Beat Schäffer [c], Jean-Marc Wunderli [c], Nicole Probst-Hensch [a,b], Martin Röösli [a,b,*]

[a] Swiss Tropical and Public Health Institute (SwissTPH), Basel, Switzerland
[b] University of Basel, Basel, Switzerland
[c] Empa, Swiss Federal Laboratories for Materials Science and Technology, Dübendorf, Switzerland

ARTICLE INFO

Keywords:
Case-crossover
Nitrogen dioxide
Fine particulate matter
Cardiovascular mortality
Fireworks
Airport

ABSTRACT

Ambient air pollution is the leading cause of environmental mortality and morbidity worldwide. However, the individual contributions to acute mortality of traffic-related air pollutants such as nitrogen dioxide (NO_2) and fine particulate matter ($PM_{2.5}$) are still debated. We conducted a time-stratified case-crossover study for a population located around Zurich airport in Switzerland, including 24,886 adult cardiovascular deaths from the Swiss National Cohort. We estimated the risk of cause-specific cardiovascular mortality associated with daily NO_2 and $PM_{2.5}$ concentrations at home using distributed lag models up to 7 days preceding death, adjusted for daily temperature, precipitation, acute night-time aircraft noise, firework celebrations, and holidays. Cardiovascular mortality was associated with NO_2, whereas the association with $PM_{2.5}$ disappeared upon adjustment for NO_2. The strongest association was observed between NO_2 and ischemic stroke mortality (odds ratio = 1.55 per 10 μg/m^3, 95% confidence intervals = 1.20–2.00). Cause-specific mortality analyses showed differences in terms of delayed effect: odds ratios were highest at 1–3 days after exposure for most outcomes but at lags of 3–5 days for heart failure. Individual vulnerabilities to NO_2 associated cardiovascular mortality also varied by cause of death, possibly highlighting the role of different behaviours and risk factors in the most susceptible groups. The risk of cardiovascular mortality was also increased on firework days and after public holidays, independent from NO_2 and $PM_{2.5}$ concentrations. This study confirms the association between ambient NO_2, as a marker for primary emissions, and acute cardiovascular mortality in a specific setting around a major airport. Future research should clarify the role of additional air pollutants including ultra-fine particles on cardiovascular diseases to inform most efficient control measures.

The authors declare they have no actual or potential competing financial interests.

1. Introduction

Ambient air pollution is one of the leading causes of mortality and morbidity worldwide (World Health Organization, 2018). According to the Global Burden of Disease, approximately 4.5 million deaths were directly attributable to air pollution in 2015 (Cohen et al., 2017). Air pollution is typically assessed based on a range of individual pollutants, including particulate matter of various size fractions (e.g. diameter less than 10 μm [PM_{10}] and less than 2.5 μm [$PM_{2.5}$]), nitrogen dioxide (NO_2), ozone (O_3), carbon monoxide (CO) and others. Of these pollutants, the largest part of the estimated excess mortality was attributed to particulate matter and ozone (World Health Organization, 2018; Brook et al., 2010). Chronic exposure to air pollution can affect cardiorespiratory health and cause heart and vascular damage, even at low levels

☆ This paper has been recommended for acceptance by Payam Dadvand.
* Corresponding author. Socinstrasse 57, 4051, Basel, Switzerland.
E-mail address: martin.roosli@swisstph.ch (M. Röösli).

https://doi.org/10.1016/j.envpol.2021.118066
Received 15 April 2021; Received in revised form 19 August 2021; Accepted 27 August 2021
Available online 30 August 2021

(U.S. EPA, 2019; Schwartz et al., 2017; Bourdrel et al., 2017). Over time, such physiological damage and resulting chronic health conditions can set a susceptible ground for the development of cardiovascular health outcomes, which may be triggered by acute environmental conditions.

Besides chronic health effects, short-term exposure to ambient air pollution is associated with increased cardiovascular and respiratory mortality (Achilleos et al., 2017; Mustafic et al., 2012; Yang et al., 2015) and emergency visits and hospital admissions (Shah et al., 2013; Nawrot et al., 2011). The causal association between particulate matter and acute mortality has been established, even at levels below the regulatory limits (U.S. EPA, 2019; Schwartz et al., 2017). However, establishing causality for specific air pollutants, which are often correlated, is a challenge. So far, the importance of acute $PM_{2.5}$ exposure over other common air pollutants in relation to all-cause mortality and respiratory health outcomes has been assessed using various analytical approaches. These include the use of instrumental variables (Schwartz et al., 2017; Schwartz et al., 2015), the assessment of the stability of the initial effect estimates after adjusting for other pollutants, and the consistency of these results between seasons with varying correlation between the different pollutants (Sarnat et al., 2001). While such studies established the short-term and independent contribution of $PM_{2.5}$ over NO_2 for respiratory diseases (Yang et al., 2015; Orellano et al., 2020), the independent contribution of NO_2 is still widely debated with regard to acute cardiovascular health outcomes (Mustafic et al., 2012; Chiusolo et al., 2011).

Some studies point towards a possible association of short-term NO_2 exposure with cardiovascular health outcomes, including acute myocardial infarction, cerebrovascular diseases, heart failure and mortality. For example, Mustafic et al. conducted a systematic review, including studies worldwide published until 2011, on the contribution of air pollution on acute myocardial infarction and reported a risk increase of 11% (95% confidence intervals (CI) = 6–16) per 10 $\mu g/m^3$ increase in short-term exposure to NO_2 (Mustafic et al., 2012). However, as a result of insufficient studies focussing on the acute cardiovascular effects of NO_2, the US Environmental Protection Agency considered the evidence for premature mortality to be suggestive but insufficient to draw any causal pathway (U.S. EPA, 2016). Similarly, in their systematic review, Orellano and colleagues reported associations between $PM_{2.5}$ and acute all-cause, cardiovascular, respiratory, and cerebrovascular mortality, but due to a lack of epidemiological studies on cardiovascular disease, NO_2 was only reported to be associated with all-cause mortality (Orellano et al., 2020). More recently, studies have specifically investigated the joint effects of fine particulate matter and NO_2 on various health outcomes, including cardiovascular mortality, using multi-pollutant modelling approaches. While some report an independent effect of NO_2 on cardiovascular diseases (Costa et al., 2017; Chen et al., 2018; Linares et al., 2018; Tong et al., 2018), others support the overall importance of $PM_{2.5}$ and further gaseous pollutants over NO_2 (Qu et al., 2018; Liu et al., 2019). In a study conducted in Northern China, Liu et al. (2019) reported that NO_2 was more affected than $PM_{2.5}$ by mutual confounding in co-pollutant models. They also found a synergistic association between NO_2 and O_3, which may explain the absence of an independent effect observed for NO_2 in fully adjusted models.

It is thus still debated whether the association of short-term NO_2 exposure with acute cardiovascular health outcomes is independent of particulate matter exposure (Brook et al., 2007; Burnett et al., 2000). To date, few studies analysed the mutual confounding between $PM_{2.5}$ and NO_2 in Europe, despite the fact that particulate matter may differ in its composition across regions, time and seasons (Mills et al., 2016). For example, a stronger reduction in particulate matter than NO_2 was observed in recent years in Europe. Thus, NO_2 may have become an even stronger proxy for road traffic emissions including ultrafine particles (UFP) (Linares et al., 2018). In addition, the composition of air pollution mixtures including UFP around airports and their individual contribution on cardiovascular health remains unclear. Precise individual exposure estimates are therefore required to investigate mutual pollution confounding and reduce the potential bias from using central monitoring for exposure assessment as typically used in previous studies on acute health effects (Sarnat et al., 2001). Finally, epidemiological studies focussing on cause-specific cardiovascular mortality could help clarify the role of ambient air pollution on different cardiovascular diseases and their individual biological pathways.

The aim of this paper is to investigate the individual roles of NO_2 and $PM_{2.5}$ on cause-specific acute cardiovascular mortality in a population living in proximity to Zurich airport. We describe the mutual confounding between these two air pollutants, as well as with further environmental triggers of cardiovascular deaths, namely, temperature, precipitation, night-time aircraft noise, and planned fireworks.

2. Methods

2.1. Study population and design

We used data from the Swiss National Cohort (SNC), a longitudinal cohort based on linkage of national census data and complete mortality records for the Swiss population. The cohort contains mortality data (i.e. cause, date and time of death) as well as personal and housing information including age, sex, education, address history, building period and neighbourhood socio-economic position. We selected 24,886 adult cases of cardiovascular death (age >30) occurring between 2000 and 2015 with available address at time of death around Zurich airport, Switzerland. Zurich airport is a medium-sized airport with night curfew (ca. 270,000 flight movements each year between 2010 and 2016 (Zurich Airport, 2020)). The study extent was selected using the envelope of the calculation perimeters for the Zurich Aircraft Noise Index of the years 2000–2015 (Saucy et al., 2020a) for the highly annoyed and the highly sleep disturbed persons (Schäffer et al., 2012), which covers an area with distances of up to 50 km around the airport (Supplementary Figure 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: I44-I49).

We used a case-crossover study design to investigate the individual and combined short-term effects of NO_2 and $PM_{2.5}$ on acute cardiovascular mortality in Switzerland. Each case of death was matched with three to four control days selected on the same day of the week within the same month, following a time-stratified control sampling (Janes et al., 2005). While time-series analyses usually assign exposure data from a central monitoring station, the case-crossover design enables the use of precise individual daily air pollution estimates at the home location, taking advantage of the precise spatiotemporal estimates calculated in this study.

2.2. Exposure data

As ambient air pollution data sources, we used previously modelled daily NO_2 and $PM_{2.5}$ concentrations at 100 m × 100 m resolution for Switzerland, available for the years 2005–2016 and 2003–2013 respectively (de Hoogh et al., 2019; de Hoogh et al., 2017). The exposure estimates are based on a four-stage modelling strategy, combining daily monitored NO_2 and $PM_{2.5}$ data across Switzerland from the regulatory monitoring network NABEL (National Air Pollution Monitoring Network, 2001), satellite-based data from the Ozone Monitoring Instrument (OMI) at 13 km × 24 km resolution for NO_2 (OMINOA Team, 2016), Multi-Angle Implementation of Atmospheric Correction (MAIAC) spectral Aerosol Optical Depth (AOD) data derived from MODIS at 1 km × 1 km resolution for $PM_{2.5}$ (Lyapustin et al., 2011), and further spatial and temporal predictor data including traffic intensity, road density, land use, altitude, Normalized Difference Vegetation Index (NDVI), annual emissions, and daily meteorological data. An adapted modelling strategy was used to extend the exposure model of $PM_{2.5}$ at 100 m × 100

m resolution to the years 2014–2016 after the original time-series, needed for this study (Supplementary materials).

We used the 2-day average NO_2 and $PM_{2.5}$ at home locations for all case and control events. To include individual daily exposure estimates for the earliest years in the time series not covered by the original models (2000–2002 for $PM_{2.5}$ and 2000–2004 for NO_2), we applied the following two-stage modelling approach: first, we calibrated the spatial distribution of the annual average concentrations at home location for the first available modelled year with the daily values from routinely collected data at Dübendorf monitoring station (equation (1)). In a second step, the estimates calculated in (1) were refined using a random forest modelling approach calibrated with daily values from Dübendorf monitoring station, Julian day, and x and y coordinates (equation (2)).

$$P_{i,j} = P_{j,mean} - P_{D,mean} + P_{D,i} \quad (1)$$

- Where $P_{i,j}$ is the air pollution estimate calculated on day i and location j;
- $P_{j,\text{mean}}$ is the yearly average estimate at location j for the first available year of the 100 m × 100 m resolution model;
- $P_{\text{D, mean}}$ is the yearly average estimate from Dübendorf monitoring station for this same year;
- $P_{\text{D, }i}$ is the daily estimate monitored at Dübendorf station on day i.

$$P_{r,f} = f\left(P_{i,j},\ P_{D,I},\ x_j,\ y_j,\ jd_i\right) \quad (2)$$

- Where P_{rf} is the final pollution estimate calculated by random forest;
- $P_{i,j}$ is the exposure estimate on day i and location j as calculated in (1)
- $P_{\text{D},i}$ is the daily estimate monitored at Dübendorf station on day i;
- x_j and y_j the x and y coordinates from location j;
- jd_i is the Julian day on day i.

We used 2 km × 2 km meteorology data from MeteoSwiss (Grid-Data Products) and assigned daily outdoor mean temperature (T_{mean}) and precipitation at home location (MeteoSwiss, 2017; MeteoSwiss, 2016). Night-time aircraft noise exposure was calculated at home locations for the case and control nights by combining a list of all aircraft movements at Zurich airport between 2000 and 2015 with precise outdoor aircraft noise exposure calculations at 250 m × 250 m for specific aircraft types and air routes, as previously described in Saucy et al., 2020a. Building on our previous analysis of the acute noise effects on mortality (Saucy et al, 2020b), we used the average aircraft noise exposure (L_{Aeq}) during the night preceding daytime deaths and the average noise exposure within 2 h preceding night-time deaths. To make these comparable prior to confounding adjustment, we normalized the acute noise exposure values before aggregating the corresponding z-values into a single exposure measure.

2.3. Statistical analyses

We investigated the acute and delayed (up to seven days) effects of daily NO_2 and $PM_{2.5}$ concentrations on cardiovascular mortality using a distributed lag modelling approach (DLM). We modelled lag-specific association between acute ambient air pollution and cause-specific cardiovascular mortality using the 'dlnm' package (Gasparrini, 2011). We specified the lag function as a natural spline with two equally spaced knots on the logarithmic scale. We estimated the lag-specific and cumulative (over 7-days lag) odds of mortality per 10 μg/m^3 increase in NO_2 and $PM_{2.5}$ separately. Both DLM models were adjusted for the other pollutant, as well as for 3-day average temperature ($T_{\text{mean}} + (T_{\text{mean}})^2$), daily precipitation (linear relation), night-time normalized aircraft noise, national holidays (lags 0 and 1) and national firework days (August 1st and December 31st, lags 0 and 1). We investigated mutual confounding of NO_2 and $PM_{2.5}$ plus the two other short-term environmental exposures (night-time aircraft noise and temperature) by removing each covariate in turn, thus reporting the cumulative odds ratio (OR) for NO_2 and $PM_{2.5}$ with and without adjustment for each covariate. Finally, we evaluated and opted for a simplified model after successfully proving the equivalence of risk estimates. We used the average of lags 0–4 for NO_2 and $PM_{2.5}$, identified as meaningful from the DLM and validated using Akaike's criterion (AIC). This simplified multiple exposures model enabled us to investigate effect modification between air pollution and cardiovascular mortality by individual characteristics (e.g. age, sex, socio-economic position, education, marital status) by introducing, in turn, each individual interaction term (Supplementary Equation S.1). To support the findings from individual interaction analyses, sensitivity analysis was performed by creating additional models combining several interaction terms including age, education, and socio-economic position. All analyses were performed using conditional logistic regression in R version 4.0.2, 'survival' package (Therneau, 2021).

3. Results

We identified 24,886 cases of adult (age >30 years) deaths from cardiovascular cause from the SNC between 2000 and 2015. Median NO_2 and $PM_{2.5}$ were 23 and 16 μg/m^3, respectively. Both NO_2 and $PM_{2.5}$ levels were higher in the lower socio-economic groups and in urban and peri-urban settings (Kruskal-Wallis test, $p < 0.01$). The two pollutants did not differ between the other population subgroups presented in Table 1. Pearson correlation coefficient between daily NO_2 and $PM_{2.5}$ levels was 60% (Supplementary Figure 2 shows a detailed correlation matrix for all lags and exposure variables).

The associations between ambient air pollutants and cause-specific cardiovascular mortality from the distributed lag models are presented in Tables 2 and 3. In the mutually adjusted models (main models), only NO_2 was significantly associated with an increase in the odds of cardiovascular mortality, showing a 5% increase in the odds of mortality for each increase in 10 μg/m^3 (OR NO_2 = 1.05 [1.01–1.10]; OR $PM_{2.5}$ = 0.90 [0.95–1.02]). The risk estimates from the NO_2 single-pollutant models remained stable with and without adjustment for $PM_{2.5}$ (Main Model vs. Model 2 in Table 2). The strongest association with NO_2 was observed for ischaemic stroke (OR NO_2 = 1.55 [1.20–2.00]). Suggestive associations were also observed for ischaemic heart diseases, myocardial infarction, heart failure and haemorrhagic stroke in relation to NO_2 concentrations; no association for deaths due to hypertensive diseases and arrhythmia were found. For most diagnoses, the strongest association with NO_2 was observed for lag days 1–3. The shape of the lag-mortality response was distinct for heart failure, with reduced OR for lag day 1 and increased OR for lag days 3–5 (Fig. 1). In contrast, the effect estimates for $PM_{2.5}$ moved towards OR = 1 when adjusting for NO_2, and none of the cause specific associations with $PM_{2.5}$ were significant in the multi-pollutant models (Main Model in Table 3).

The OR coefficients of all exposures included in the multi-pollutant models remained stable through adjustment by the covariates aircraft noise and temperature (Models S2 and S3 in Tables 2 and 3). Similar, the risk estimates remained stable with and without adjustment for precipitation, firework days and national holidays. Overall, except two significant risk estimates for $PM_{2.5}$ disappearing after co-adjustment by NO_2 (Model 2 in Table 2), there was only limited mutual confounding between the different short-term exposures (acute night-time aircraft noise, NO_2, $PM_{2.5}$, firework days and national holidays) in association with acute cardiovascular mortality (Supplementary Table S1).

Based on the results from the distributed lag models (Tables 2 and 3), we created a multi-pollutant model using air pollution levels (NO_2 and $PM_{2.5}$) averaged over lags 0 to 4 for all cardiovascular deaths (Table 4, Overall Model). Correlation between daily NO_2 and $PM_{2.5}$ was 60%, but the variation inflation factor (VIF) remained below 3 for all variables. From this model, the OR for cardiovascular mortality was 1.04 (95% CI = 1.00–1.08) for NO_2 and 0.98 (95% CI = 0.95–1.02) for $PM_{2.5}$, which closely corresponds to the values of the Main Models in Tables 2 and 3.

Table 1
Summary statistics of the characteristics of all deaths included in the study with respect to the NO_2 and $PM_{2.5}$ distribution on the day of death and control days.

	N (%)	NO_2			$PM_{2.5}$		
Percentiles		25th	50th	75th	25th	50th	75th
Cause of death							
All cardiovascular deaths	24,886 (100)	14.1	22.6	33.0	11.1	16.2	23.6
Ischaemic heart diseases	10,521 (41)	14.3	22.6	33.0	11.4	16.5	24.0
Myocardial infarction	3248 (13)	13.7	22.3	33.1	11.2	16.3	24.2
Stroke	3750 (15)	14.3	23.2	34.1	11.3	16.6	24.1
Heart failure	1753 (7)	13.7	22.0	32.7	11.0	15.9	24.0
Hypertensive diseases	2728 (11)	14.2	22.7	33.1	10.7	15.6	22.8
Arrhythmias	1392 (6)	13.4	22.0	32.9	11.1	16.0	22.7
Sex							
Female	13,269 (53)	14.2	22.9	33.4	11.2	16.3	23.7
Male	11,617 (47)	13.9	22.2	32.6	11.1	16.1	23.6
Age groups							
<75	5632 (23)	13.7	22.3	32.8	11.3	16.4	24.0
75-85	8324 (33)	14.4	22.7	33.0	11.1	16.3	24.0
>85	10,930 (44)	14.0	22.6	33.2	11.1	16.2	23.1
Neighbourhood SEP[a]							
Q1	2512 (10)	18.2	27.5	38.4	12.2	17.2	24.9
Q2	3685 (15)	15.2	24.2	34.6	11.9	17.1	24.8
Q3	4470 (18)	14.4	22.5	33.5	11.2	16.5	23.9
Q4	6263 (25)	13.8	22.0	32.1	11.0	16.1	23.5
Q5	6572 (26)	12.2	20.4	30.3	10.3	15.2	22.1
Unknown	1384 (6)	13.9	22.4	33.1	12.2	17.5	25.0
Education (lowest to highest)							
Compulsory or less	8830 (35)	14.2	22.6	33.2	11.4	16.6	23.9
Upper secondary level	12,353 (50)	14.3	22.9	33.4	11.1	16.2	23.7
Tertiary level	3150 (13)	13.1	21.2	31.1	10.6	15.3	22.8
Unknown	553 (2)	13.8	22.8	33.4	10.5	15.4	23.1
Civil status							
Married	9286 (37)	13.7	21.8	32.3	11.2	16.2	23.5
Non married	15,600 (63)	14.3	23.1	33.5	11.1	16.3	23.7
Urbanisation							
Urban	9108 (36)	19.6	29.1	39.0	12.1	17.4	25.1
Peri-urban	14,347 (58)	12.5	20.0	29.2	10.8	15.8	22.9
Rural	1431 (6)	8.6	14.4	21.6	9.4	13.9	20.7
Building period							
Before 1970	14,957 (60)	14.7	23.5	33.9	11.5	16.8	24.3
1970–1990	7082 (28)	13.4	21.7	31.8	11.0	16.0	23.0
After 1990	2372 (10)	13.0	21.2	31.1	10.1	15.0	22.0
Unknown	475 (2)	10.6	18.3	28.4	9.0	13.3	20.3

[a] Neighbourhood socio-economic position (SEP) index ranging from lowest (0) to highest (100), displayed as quantiles (Q1 to Q5) (Panczak et al., 2012).

Table 2
OR of cardiovascular mortality for all and cause-specific cardiovascular deaths per 10 μg/m^3 increase in NO_2, cumulative over 0–7 lag days. Statistically significant results (α = 5%) are marked in bold.

Cause of death	NO_2 Model 1[a]	NO_2 Model 2[b]	NO_2 Model 3[c]	NO_2 Model 4[d]
All cardiovascular diseases	**1.05 (1.01–1.10)**	**1.03 (1.00–1.07)**	**1.05 (1.01–1.10)**	**1.04 (1.00–1.09)**
Ischaemic heart diseases	1.05 (0.99–1.13)	1.03 (0.98–1.08)	1.05 (0.99–1.13)	1.04 (0.97–1.11)
Myocardial infarction	1.08 (0.95–1.22)	1.02 (0.93–1.12)	1.08 (0.95–1.22)	1.06 (0.94–1.20)
Stroke	**1.13 (1.01–1.26)**	**1.14 (1.05–1.23)**	**1.13 (1.01–1.26)**	**1.13 (1.02–1.26)**
Haemorrhagic stroke	1.03 (0.81–1.31)	1.11 (0.93–1.32)	1.03 (0.81–1.31)	1.06 (0.84–1.34)
Ischaemic stroke	**1.55 (1.20–2.00)**	**1.41 (1.17–1.71)**	**1.55 (1.2–02.00)**	**1.46 (1.14–1.87)**
Hypertensive	0.97 (0.82–1.13)	0.97 (0.86–1.10)	0.96 (0.82–1.13)	0.97 (0.83–1.14)
Heart failure	1.09 (0.95–1.24)	1.04 (0.94–1.15)	1.09 (0.95–1.24)	1.07 (0.94–1.22)
Arrhythmias	0.90 (0.75–1.09)	0.95 (0.82–1.09)	0.90 (0.74–1.08)	0.90 (0.75–1.08)

[a] Model 1 (Main Model) is adjusted for $PM_{2.5}$, temperature, precipitation, night-time aircraft noise, holidays and firework days.
[b] Model 2: Main Model without adjustment for $PM_{2.5}$
[c] Model 3: Main Model without adjustment for aircraft noise.
[d] Model 4: Main Model without adjustment for temperature.

Table 3
OR of cardiovascular mortality for all and cause-specific cardiovascular deaths per 10 μg/m^3 increase in $PM_{2.5}$, cumulative over 0–7 lag days. Statistically significant results (α = 5%) are marked in bold.

Cause of death	$PM_{2.5}$ Model 1[a]	$PM_{2.5}$ Model 2[b]	$PM_{2.5}$ Model 3[c]	$PM_{2.5}$ Model 4[d]
All cardiovascular diseases	0.99 (0.95–1.02)	1.01 (0.99–1.04)	0.99 (0.95–1.02)	1.00 (0.97–1.03)
Ischaemic heart diseases	0.98 (0.92–1.03)	1.01 (0.97–1.06)	0.98 (0.92–1.03)	1.00 (0.95–1.05)
Myocardial infarction	0.96 (0.87–1.07)	1.01 (0.93–1.09)	0.96 (0.87–1.07)	0.98 (0.89–1.08)
Stroke	1.01 (0.92–1.11)	**1.08 (1.01–1.15)**	1.01 (0.92–1.11)	1.01 (0.93–1.09)
Haemorrhagic stroke	0.94 (0.78–1.14)	1.01 (0.88–1.17)	0.94 (0.78–1.14)	0.89 (0.75–1.07)
Ischaemic stroke	1.02 (0.81–1.27)	**1.21 (1.03–1.43)**	1.02 (0.81–1.27)	1.12 (0.91–1.37)
Hypertensive	1.02 (0.89–1.16)	0.98 (0.89–1.08)	1.02 (0.89–1.16)	1.01 (0.89–1.14)
Heart failure	0.94 (0.84–1.05)	0.97 (0.90–1.06)	0.95 (0.85–1.06)	0.97 (0.88–1.08)
Arrhythmias	1.02 (0.87–1.20)	0.95 (0.84–1.07)	1.02 (0.87–1.20)	1.03 (0.89–1.19)

[a] Model 1 (Main Model) is adjusted for NO_2, temperature, precipitation, night-time aircraft noise, holidays and firework days.
[b] Model 2: Main Model without adjustment for NO_2
[c] Model 3: Main Model without adjustment for aircraft noise.
[d] Model 4: Main Model without adjustment for temperature.

Since only NO_2 was associated with an increased risk of mortality in the fully adjusted model, interaction analysis was performed for this pollutant only. An increased OR was also observed for all cardiovascular deaths in relation to national firework days (August 1st and December 31st) (OR = 1.29 [1.08–1.54]) and national public holidays with lagged effect for the day after (OR_{lag0} = 0.98 [0.89–1.08]; OR_{lag1} = 1.08 [0.99–1.18]).

We did not observe any effect modification for the association between 4-day average NO_2 and all cardiovascular deaths by sex,

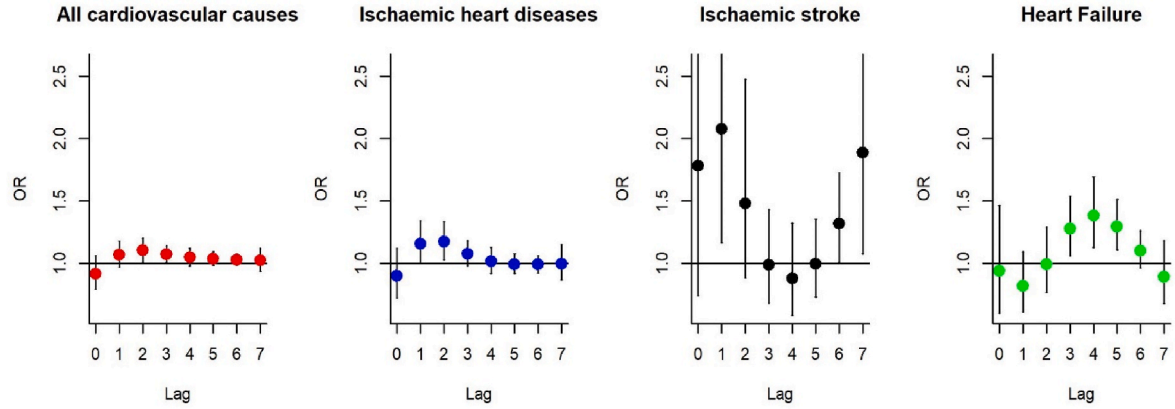

Fig. 1. Odds ratios (ORs) of mortality associated with daily NO_2 (lag days 0–7) for all cardiovascular deaths and for specific causes of death (ischaemic heart disease, ischaemic stroke, and heart failure). DLM models adjusted for $PM_{2.5}$, temperature, precipitation, night-time aircraft noise, holidays and firework days.

Table 4
OR of mortality associated per 10 μg/m^3 increase in 4-day average NO_2 concentrations at home location for different groups of the population and causes of death. Models adjusted for $PM_{2.5}$, temperature, precipitation, night-time aircraft noise, holidays and firework days. Statistically significant results (α = 5%) are marked in bold. Interaction terms for continuous variables (e.g. age, socio-economic position) were introduced as linear interaction variables, and ORs are reported for different levels within the range of the interaction variable.

Groups	All CVD (N = 24,886)	p-int*	Myocardial infarction (N = 3,248)	p-int*	Heart failure (N = 2,728)	p-int*	Ischaemic stroke (N = 627)	p-int*
Overall Model	1.04 (1.00–1.08)		1.08 (0.97–1.20)		1.05 (0.94–1.19)		**1.35 (1.07–1.69)**	
Sex		0.64		0.95		0.33		0.33
Males	**1.05 (1.00–1.10)**		1.08 (0.95–1.22)		1.00 (0.85–1.17)		**1.48 (1.10–1.99)**	
Females	1.04 (0.99–1.09)		1.09 (0.94–1.25)		1.09 (0.95–1.24)		1.28 (0.99–1.64)	
Age		**0.04**		0.64		**0.04**		**0.03**
60	**1.10 (1.04–1.17)**		1.04 (0.88–1.19)		**1.28 (1.06–1.50)**		**1.96 (1.55–2.36)**	
75	**1.06 (1.02–1.10)**		1.07 (0.96–1.19)		**1.14 (1.00–1.27)**		**1.52 (1.26–1.77)**	
90	1.02 (0.98–1.07)		1.12 (0.98–1.25)		1.00 (0.88–1.13)		1.17 (0.91–1.43)	
Building period*								
before 1970	**1.05 (1.00–1.09)**	0.34	1.09 (0.97–1.24)	0.93	1.06 (0.92–1.21)	0.45	1.23 (0.96–1.58)	0.16
1970–1990	1.04 (0.98–1.10)		1.08 (0.92–1.27)		1.07 (0.90–1.27)		**1.84 (1.29–2.63)**	
after 1990	1.07 (0.98–1.10)		1.00 (0.76–1.32)		1.11 (0.83–1.48)		1.16 (0.62–2.17)	
Neighbourhood SEP**		0.93		0.25		0.54		0.27
10	1.05 (0.89–1.21)		1.40 (0.93–1.86)		1.23 (0.73–1.73)		**2.26 (1.33–3.20)**	
50	1.04 (0.98–1.11)		1.16 (0.99–1.34)		1.10 (0.92–1.29)		**1.58 (1.22–1.94)**	
90	1.04 (0.96–1.11)		0.97 (0.76–1.18)		0.99 (0.76–1.23)		1.10 (0.67–1.54)	
Education								
Compulsory or less	1.02 (0.97–1.08)	0.74	1.01 (0.86–1.18)	0.60	1.00 (0.85–1.16)	0.59	1.08 (0.79–1.48)	0.18
Upper secondary	**1.05 (1.00–1.10)**		**1.13 (1.00–1.29)**		1.08 (0.93–1.24)		**1.46 (1.12–1.90)**	
Tertiary	1.06 (0.98–1.15)		1.05 (0.85–1.29)		1.20 (0.91–1.57)		**1.72 (1.08–2.75)**	
Civil status		**0.05**		0.53		0.64		0.38
Married	**1.08 (1.03–1.14)**		1.11 (0.97–1.27)		1.02 (0.86–1.22)		**1.45 (1.09–1.94)**	
Non-married	1.02 (0.98–1.07)		1.06 (0.93–1.20)		1.07 (0.94–1.21)		1.27 (0.98–1.65)	

*P-value from the interaction term with NO_2 (p-int).
**Neighbourhood socio-economic position (SEP) index ranging from lowest (0) to highest (100) (Panczak et al., 2012).

education, or socio-economic position. The OR of cardiovascular mortality was increased for younger age and for the civil status married (Table 4). Though the interaction terms did not significantly indicate effect modification, the OR of ischaemic stroke mortality was increased for males, lower neighbourhood socio-economic position, and higher education groups. In contrast, the OR of mortality from myocardial infarction was highest for older age.

4. Discussion

4.1. Summary and main findings

The aim of this study was to assess the mutual independent associations of short-term NO_2 and $PM_{2.5}$ with cause-specific cardiovascular mortality in Switzerland while adjusting for the acute effect of other environmental exposures with adverse cardiovascular health effects. In single pollutant models NO_2, and to a lesser extent $PM_{2.5}$, was associated with all cardiovascular deaths or specific causes of death for a cumulative exposure lag-period of 7 days preceding death. However, two-pollutant models point to an association with NO_2 but not $PM_{2.5}$. The largest point estimate was observed between NO_2 and ischemic stroke mortality (Table 2).

4.2. Confounding in the multiple exposures models

The distributed lag model was useful to identify the most relevant exposure period for each health outcome and inform the multi-pollutant model. The two approaches were equivalent and yielded similar risk estimates (OR NO_2 = 1.04 [1.00–1.08] for the multi-pollutant model based on 4-day average air pollution levels and OR NO_2 = 1.05 [1.01–1.10] for the distributed lag model). Overall, most of the observed increase in cardiovascular mortality could be attributed to NO_2. On the

other hand, the association between $PM_{2.5}$ and cardiovascular mortality was strongly reduced when adjusting for NO_2, leaving only little individual effect of $PM_{2.5}$ in this study. The models did not show much autocorrelation (VIF) between these two variables, supporting the relevance of NO_2 for acute cardiovascular mortality.

Air pollution mixtures and the composition of fine particulate matter are subject to large variations across regions and may depend on the major types of pollution sources. Few studies have systematically assessed the mutual confounding between NO_2 and $PM_{2.5}$ in Europe or in regions exposed to air traffic related pollution. Our study thus contributes to a better understanding of the short-term effects of combined particulate matter and NO_2 on cardiovascular mortality in populations living near a major airport, where an increased contribution of UFP can be expected (Rivas et al., 2020). In this context, NO_2 may thus be a proxy measure of other, unmeasured vehicle emissions such as air-traffic related UFP or volatile organic compounds (Brook et al., 2007). This may explain our somewhat different results with previous studies, mostly observing associations of $PM_{2.5}$ with acute cardiovascular mortality (Schwartz et al., 2015; Orellano et al., 2020; Liu et al., 2019; Lee et al., 2014). Nevertheless, the causal role of NO_2 for acute cardiovascular mortality may be supported by its gaseous nature and quick passage into the bloodstream (U.S. EPA, 2016). Generally, increased knowledge on the physiological action of NO_2, UFP, and particulate composition on the cardiovascular system is needed to interpret and disentangle the underlying origins of cause-specific cardiovascular mortality.

Compared to previous studies, air pollution concentrations in our study population were rather low, and exposure was specifically modelled for the place of residence using spatiotemporal models, yielding more precise individual estimates as opposed to the more simple approach to use central monitors (Chiusolo et al., 2011; Samoli et al., 2006). With this spatial resolution, NO_2 may be an important primary air pollution indicator for traffic including UFP from the airport or for secondary pollutants like O_3, not included in this study. For instance, Luo and colleagues reported greater health effects in association with NO_2 in highly populated areas and increased civil air traffic than in rural areas (Luo et al., 2016). Peters and colleagues observed an association between time spent in traffic and acute myocardial infarction (Peters et al., 2004). UFP, a pollutant easily crossing the alveoli-capillary barrier, may therefore be more relevant than $PM_{2.5}$ with regards to acute cardiovascular mortality. In Switzerland, $PM_{2.5}$ is predominantly an indicator of background air pollution resulting to a large extent from long range air transport (FOEN, 2013). With urban population and air traffic density expected to increase (Güneralp et al., 2017), it is especially important to further disentangle the individual contributions of NO_2, $PM_{2.5}$, and UFP as well as particle composition on cardiovascular health to inform future health policies.

To the best of our knowledge, this is the first study to adjust for acute aircraft noise in air pollution studies. For long-term exposure, Héritier et al. provided evidence that the association between NO_2 and particulate matter in Switzerland was confounded by transportation noise (Héritier et al., 2018). In this study, we did not find an indication of confounding of the association between short-term air pollution and cardiovascular mortality by short-term night-time aircraft noise. Further, no confounding is to be expected from long-term environmental exposures due to the individual matching in this case-crossover study. We found that for acute cardiovascular mortality, the different environmental exposures investigated here were rather stable, showing no sign of mutual confounding. This confirms that at least on the short term, the cardiovascular effects of NO_2, night-time aircraft noise, temperature and precipitation are independent from each other.

The risk of cardiovascular mortality was increased by 29% on 'firework' days (August 1st and December 31st), independent from NO_2 and $PM_{2.5}$ concentrations, which is in line with Greven and colleagues (Greven et al., 2019). Fireworks on national day and New Year's eve are known to affect ambient air quality (Godri et al., 2010; Seidel and Birnbaum, 2015), but this observed excess mortality may also be the consequence of specific behaviours (e.g. excess consumption of food and alcohol, lack of sleep) or firework associated noise exposure, which may be the reason for the different lag structure compared to air pollution.

4.3. Cause-specific cardiovascular mortality in relation to ambient air pollution

While ischaemic and haemorrhagic strokes are often considered as a single group of diseases in epidemiological studies, they may be caused by different underlying physiological mechanisms, resulting in differential association with air pollution (Bourdrel et al., 2017; Wichmann and Voyi, 2012). In this study, we observed a strong risk increase for ischaemic but not haemorrhagic stroke in association with ambient NO_2, supporting the differential action of environmental exposures on these two disease groups. Despite a relatively small sample size, the association between NO_2 and ischaemic stroke was strongly significant due to a large effect size, but reduced power may explain the inconclusive results observed for arrhythmias. More generally, the risk of mortality was increased for all disease groups involving some type of ischaemia (i.e. ischaemic heart diseases, myocardial infarctions and ischaemic strokes), coherent with the suspected physiological response described for NO_2, including acute inflammation, and increased coagulation. However, the cardiorespiratory physiological changes in response to NO_2 exposure need to be further studied and described, as specific knowledge is currently limited (U.S. EPA, 2016).

Unlike a previous study, which reported an increased risk of heart failure associated with same-day NO_2 and $PM_{2.5}$ levels (Shah et al., 2013), we found that the risk of heart failure in association with NO_2 was highest 3–5 days after exposure, following an initial risk reduction. The physiology of heart failure is different from the ischaemic events. Patients with heart failure have already been described to be at higher risk of cardiovascular mortality in association with air pollution, mainly due to subsequent increased heart rate and diastolic blood pressure (Buteau et al., 2018; Goldberg et al., 2015; Goldberg et al., 2011). In a previous study, we demonstrated that the association between heat and mortality from heart failure was modified by the presence of ambient air pollution (Saucy et al., 2021). A generalized vasodilatation and volume depletion as a response to a heat event may explain the initial risk decrease in our study population, followed by increased mortality in relation to the combined stress event.

Air pollution levels were associated with the same acute cardiovascular diagnoses as previously observed for short-term night-time aircraft noise (Saucy et al., 2020b), highlighting some common pathophysiological mechanisms as a response to short-term air pollution and aircraft noise, both suspected to be involved in vascular oxidative stress reactions (Bourdrel et al., 2017; Münzel et al., 2020). However, aircraft noise exposure in the night preceding death events did not affect the risk of NO_2 associated cardiovascular mortality.

4.4. Effect modification and vulnerability groups

The distribution of $PM_{2.5}$ and NO_2 was uneven with respect to socio-economic position, with higher pollution levels in locations with lower socio-economic position, showing that social inequity related to air quality reported in previous studies (Fairburn et al., 2019) was also present in our study population. Individual vulnerabilities to NO_2 related mortality varied across the specific causes of death, highlighting potential variations of risk factors in relation to these different pathologies. For example, social determinants of health such as sex, education and socio-economic position did not modify the short-term association between NO_2 and all cardiovascular deaths. Despite a higher susceptibility to cardiovascular mortality with older age (mean age was 80 years old in our study population), the relative acute risks were lower in the oldest age groups. This observation was consistent for heart failure and ischaemic stroke, but not for myocardial infarction, where the OR

(non-significantly) increased with older age. In these three groups of diseases, increased susceptibility was observed for people with lower socio-economic position, who were also exposed to increased levels air pollution and were therefore more vulnerable to air pollution overall. In contrast, increased OR was only observed with increasing education for ischaemic stroke, possibly in relation with specific behaviours and risk factors in this group of the population. Sensitivity analysis including multiple interactions suggest that the described effect modification by education and socio-economic status is not influenced by differential age and sex in these groups.

4.5. Strengths and limitations

While time-series analyses rely on centralized data from monitoring stations, the case-crossover design enables the use of individual exposure data, considering spatial fluctuations at different locations on a daily basis, which is an asset of this study. The NO_2 and $PM_{2.5}$ exposure data used in this study were extracted at home location from longitudinal nationwide air pollution models with high spatial and temporal resolution, thus minimizing potential exposure misclassification. Due to the individual matching between case and control events within a short period of one month, all analyses were adjusted by design for individual characteristics such as age, sex, and socio-economic position. Combined with distributed lag models, this approach enabled us to investigate the delayed cause-specific exposure-response between ambient air pollution and cardiovascular mortality with minimum bias. Potential confounders that also vary over a short time, such as meteorological conditions, were similarly included from high resolution models designed for Switzerland. This study additionally adjusts for acute environmental (specifically aircraft) noise, which is rarely considered in air pollution studies, but has been described as a potential confounder on the association between long-term air pollution exposure and cardiovascular mortality.

A limitation of this study is that we did not include ozone, ultra-fine particles and relative humidity, as they were not available in our study area at a similar spatial resolution. Our study population was selected around Zurich airport (up to 50 km distance), which is an interesting setting from an air pollution emission perspective with possible specific air pollution mixtures in relation to air traffic. While this choice may limit the generalization of our results to other neighbourhoods, not exposed to air traffic, it offers unique information for future discussion of health outcomes in various exposure settings. Finally, a larger range of urbanization levels, language regions, and socio-economic positions would also be necessary for the generalization of our results to the broader Swiss population. Similar studies focussing on populations exposed to intense air traffic should help support our findings and the role of unmeasured traffic-related pollutants for cardiovascular mortality.

5. Conclusion

Based on precise individual exposure estimates and a robust study design, this study confirms the association between short-term ambient NO_2 and acute cardiovascular mortality in a specific setting around a major airport. The association between $PM_{2.5}$ and cardiovascular mortality was strongly reduced when adjusting for NO_2, leaving only little individual effect of $PM_{2.5}$. Future research should further investigate the role of different air pollutants such as UFP emitted by the air traffic as well as particles composition in relation to acute cardiovascular diseases to inform most efficient control measures.

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 and the Swiss National Cohort Study group for providing the mortality and population data. Calculations were performed at sciCORE scientific computing centre at the University of Basel. We thank the Swiss Federal Statistical Office for providing mortality and census data and for the support which made the Swiss National Cohort and this study possible. 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). Finally, we thank Meltem Kutlar, responsible for the LUDOK database (funded by Swiss Federal Office for the Environment) for her support during the literature review.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envpol.2021.118066.

Credit author statement

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

References

Achilleos, S., et al., 2017. Acute effects of fine particulate matter constituents on mortality: a systematic review and meta-regression analysis. Environ. Int. 109, 89–100.

Bourdrel, T., et al., 2017. Cardiovascular effects of air pollution. Arch Cardiovasc Dis 110 (11), 634–642.

Brook, J.R., et al., 2007. Further interpretation of the acute effect of nitrogen dioxide observed in Canadian time-series studies. J. Expo. Sci. Environ. Epidemiol. 17 (2), S36–S44.

Brook, R.D., et al., 2010. Particulate matter air pollution and cardiovascular disease: an update to the scientific statement from the American Heart Association. Circulation 121 (21), 2331–2378.

Burnett, R.T., et al., 2000. Association between particulate- and gas-phase components of urban air pollution and daily mortality in eight Canadian cities. Inhal. Toxicol. 12 (4), 15–39.

Buteau, S., et al., 2018. Associations between ambient air pollution and daily mortality in a cohort of congestive heart failure: case-crossover and nested case-control analyses using a distributed lag nonlinear model. Environ. Int. 113, 313–324.

Chen, R., et al., 2018. Associations between ambient nitrogen dioxide and daily cause-specific mortality: evidence from 272 Chinese cities. Epidemiology 29 (4), 482–489.

Chiusolo, M., et al., 2011. *Short-term Effects of nitrogen Dioxide on Mortality and susceptibility Factors in 10 Italian cities: the EpiAir study.* Environ health perspect, 119 (9), 1233–1238.

Cohen, A.J., et al., 2017. *Estimates and 25-year trends of the global burden of disease attributable to ambient air pollution: an analysis of data from the Global Burden of Diseases Study 2015.* The Lancet, 389 (10082), 1907–1918.

Costa, A.F., et al., 2017. *Effects of NO2 exposure on daily mortality in Sao Paulo, Brazil.* Environ Res, 159, 539–544.

de Hoogh, K., et al., 2017. Modelling daily PM2.5 concentrations at high spatio-temporal resolution across Switzerland. Environ. Pollut. 233, 1147–1154.

de Hoogh, K., et al., 2019. Predicting fine-scale daily NO2 for 2005-2016 incorporating OMI satellite data across Switzerland. Environ. Sci. Technol. 53, 17, 10279–10287.

Fairburn, J., et al., 2019. Social inequalities in exposure to ambient air pollution: a systematic review in the WHO European Region. Int. J. Environ. Res. Publ. Health 16 (17), 3127.

FOEN, 2013. PM10 and PM2.5 Ambient Concentrations in Switzerland, Modelling Results for 2005, 2010, 2020. Federal Office for the Environment (FOEN). Available from: https://www.bafu.admin.ch/bafu/en/home/topics/air/publications-studies/publications/pm10-and-pm2-5-ambient-concentrations-in-switzerland.html.

Gasparrini, A., 2011. Distributed lag linear and non-linear models in R: the package dlnm. J. Stat. Software 43 (8), 1–20.
Godri, K.J., et al., 2010. Particulate oxidative burden associated with firework activity. Environ. Sci. Technol. 44 (21), 8295–8301.
Goldberg, M.S., et al., 2011. The short-term influence of temperature on daily mortality in the temperate climate of Montreal, Canada. Environ. Res. 111 (6), 853–860.
Goldberg, M.S., et al., 2015. Physiological and perceived health effects from daily changes in air pollution and weather among persons with heart failure: a panel study. J. Expo. Sci. Environ. Epidemiol. 25 (2), 187–199.
Greven, F.E., et al., 2019. Air pollution during New Year's fireworks and daily mortality in the Netherlands. Scientific reports 9 (1), 1–8.
Güneralp, B., et al., 2017. Global scenarios of urban density and its impacts on building energy use through 2050. Proc. Natl. Acad. Sci. U. S. A. 114 (34), 8945–8950.
Héritier, H., et al., 2018. A systematic analysis of mutual effects of transportation noise and air pollution exposure on myocardial infarction mortality: a nationwide cohort study in Switzerland. Eur. Hear. J. 40 (7), 598–603.
Janes, H., Sheppard, L., Lumley, T., 2005. Case-crossover analyses of air pollution exposure data: referent selection strategies and their implications for bias. Epidemiology 16 (6), 717–726.
Lee, B.J., Kim, B., Lee, K., 2014. Air pollution exposure and cardiovascular disease. Toxicol Res 30 (2), 71–75.
Linares, C., et al., 2018. An approach estimating the short-term effect of NO2 on daily mortality in Spanish cities. Environ. Int. 116, 18–28.
Liu, M., et al., 2019. Population susceptibility differences and effects of air pollution on cardiovascular mortality: epidemiological evidence from a time-series study. Environ. Sci. Pollut. Res. Int. 26 (16), 15943–15952.
Luo, K., et al., 2016. Acute effects of nitrogen dioxide on cardiovascular mortality in Beijing: an exploration of spatial heterogeneity and the district-specific predictors. Sci. Rep. 6, 38328.
Lyapustin, A., et al., 2011. Multiangle Implementation of Atmospheric Correction (MAIAC): 2. Aerosol Algorithm. J. Geophys. Res.: Atmos. 116, D3.
MeteoSwiss, 2016. Daily Precipitation 2016. Available from: https://www.meteoschweiz.admin.ch/content/dam/meteoswiss/de/service-und-publikationen/produkt/raeumliche-daten-niederschlag/doc/ProdDoc_RhiresD.pdf.
MeteoSwiss, 2017. Daily Mean, Minimum and Maximum Temperature. MeteoSwiss. Available from: https://www.meteoschweiz.admin.ch/content/dam/meteoswiss/de/service-und-publikationen/produkt/raeumliche-daten-temperatur/doc/ProdDoc_TabsD.pdf.
Mills, I.C., et al., 2016. Distinguishing the associations between daily mortality and hospital admissions and nitrogen dioxide from those of particulate matter: a systematic review and meta-analysis. BMJ Open 6 (7), e010751.
Münzel, T., Steven, S., Hahad, O., Daiber, A., 2020. Noise and cardiovascular risk: nighttime aircraft noise acutely triggers cardiovascular death. Eur. Heart J. 42 (8), 844–846.
Mustafic, H., et al., 2012. Main air pollutants and myocardial infarction: a systematic review and meta-analysis. Jama 307 (7), 713–721.
National Air Pollution Monitoring Network, 2001. Swiss Agency for the Environment, Forests and Landscape (SAEFL): Bern, Switzerland. NABEL.
Nawrot, T.S., et al., 2011. Public health importance of triggers of myocardial infarction: a comparative risk assessment. Lancet 377 (9767), 732–740.
OMINOA Team, 2016. OMNO2 README Document, Data Product Version 3.0, Document Version 7.0. NASA.
Orellano, P., et al., 2020. Short-term exposure to particulate matter (PM10 and PM2.5), nitrogen dioxide (NO2), and ozone (O3) and all-cause and cause-specific mortality: systematic review and meta-analysis. Environ. Int. 142, 105876.
Panczak, R., et al., 2012. A Swiss neighbourhood index of socioeconomic position: development and association with mortality. J. Epidemiol. Community Health 66 (12), 1129–1136.
Peters, A., et al., 2004. Exposure to traffic and the onset of myocardial infarction. N. Engl. J. Med. 351 (17), 1721–1730.
Qu, Y., et al., 2018. Short-term effects of fine particulate matter on non-accidental and circulatory diseases mortality: a time series study among the elder in Changchun. PLoS One 13 (12), e0209793.
Rivas, I., et al., 2020. Source apportionment of particle number size distribution in urban background and traffic stations in four European cities. Environ. Int. 135, 105345.
Samoli, E., et al., 2006. Short-term effects of nitrogen dioxide on mortality: an analysis within the APHEA project. Eur. Respir. J. 27 (6), 1129–1138.
Sarnat, J.A., et al., 2001. Gaseous pollutants in particulate matter epidemiology: confounders or surrogates? Environ. Health Perspect. 109 (10), 1053–1061.
Saucy, A., et al., 2020a. Individual aircraft noise exposure assessment for a case-crossover study in Switzerland. Int. J. Environ. Res. Publ. Health 17 (9), 3011.
Saucy, A., et al., 2020b. Does night-time aircraft noise trigger mortality? A case-crossover study on 24 886 cardiovascular deaths. Eur. Heart J. 42 (8), 835–843.
Saucy, A., et al., 2021. The role of extreme temperatures in cause-specific acute cardiovascular mortality in Switzerland: a case-crossover study. Sci. Total Environ. 790, 147958.
Schäffer, B., et al., 2012. Zurich aircraft noise index: an index for the assessment and analysis of the effects of aircraft noise on the population. Acta Acustica united Acustica 98 (3), 505–519.
Schwartz, J., et al., 2015. Estimating causal associations of fine particles with daily deaths in Boston. Am. J. Epidemiol. 182 (7), 644–650.
Schwartz, J., Bind, M.A., Koutrakis, P., 2017. Estimating causal effects of local air pollution on daily deaths: effect of low levels. Environ. Health Perspect. 125 (1), 23–29.
Seidel, D.J., Birnbaum, A.N., 2015. Effects of Independence Day fireworks on atmospheric concentrations of fine particulate matter in the United States. Atmos. Environ. 115, 192–198.
Shah, A.S.V., et al., 2013. Global association of air pollution and heart failure: a systematic review and meta-analysis. Lancet (London, England) 382 (9897), 1039–1048.
Therneau, T.M., 2021. A Package for Survival Analysis in R.
Tong, Y., et al., 2018. Association between multi-pollutant mixtures pollution and daily cardiovascular mortality: an exploration of exposure-response relationship. Atmos. Environ. 186, 136–143.
U.S. EPA, 2016. Integrated Science Assessment for Oxides of Nitrogen–Health Criteria (Final Report, Jan 2016), EPA/600/R-15/068. U.S. Environmental Protection Agency (Washington, DC).
U.S. EPA, 2019. Integrated Science Assessment (ISA) for Particulate (Final Report, Dec 2019), EPA/600/R-19/188. U.S. Environmental Protection Agency (Washington, DC).
Wichmann, J., Voyi, K., 2012. Ambient air pollution exposure and respiratory, cardiovascular and cerebrovascular mortality in Cape Town, South Africa: 2001–2006. Int. J. Environ. Res. Publ. Health 9 (11), 3978–4016.
World Health Organization, 2018. Ambient (outdoor) air pollution. Available from: https://www.who.int/news-room/fact-sheets/detail/ambient-(outdoor)-air-quality-and-health.
Yang, Y., et al., 2015. Multi-site time series analysis of acute effects of multiple air pollutants on respiratory mortality: a population-based study in Beijing, China. Sci. Total Environ. 508, 178–187.
Zurich Airport, 2020. Facts and Figures 2019. Zurich Airport, 2020 [cited 2021; Available from: file:///C:/Users/saucap/AppData/Local/Temp/Facts_and_Figures_2019_en.pdf.