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Association of ground-level ozone, meteorological factors and weather types with daily myocardial infarction frequencies in Augsburg, Southern Germany

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A B S T R A C T

The first part of the present study addresses meteorological and synoptic factors governing daily maximum 1-hour ozone (O_3) concentrations in the city of Augsburg in the months from March to September. In the second part statistical models are applied to assess the association between daily myocardial infarction (MI) frequencies and ozone exposure, under the additional consideration of climatic and synoptic factors. Daily maximum 1-hour ozone concentrations were increased with high air temperatures, low values of specific humidity and high ozone concentrations of the previous day. Besides, four weather types were connected with ozone, the weather type "U", which describes mainly low-flow conditions, being of particular importance. The daily maximum 1-hour ozone concentrations showed a notable non-linear relationship with MI frequencies in Augsburg. An enhanced MI risk occurred mainly at median to moderately high ozone concentrations. A piecewise linear regression up to the maximum relative risk at approximately the 75%-ozone percentile (116 μg/m^3) yielded a significant increase of 3.41% (95% confidence interval: [1.33%, 5.53%]) of the MI frequency per 10 μg/m^3 increase in ozone. At higher ozone concentrations a decrease of the MI risk occurred. Three weather types were selected as additional predictors in the statistical models. Most notable was the frequent weather type Anticyclonic (A), which is related to a reduction in MI frequencies.

1. Introduction

Tropospheric ozone (O_3) constitutes a secondary air substance, which is primarily built by photochemical reactions under solar radiation with the involvement of precursor gases including nitrogen oxides (NO_x), carbon monoxide, methane, and non-methane volatile organic compounds (VOCs). In urban areas where NO_x levels are high, nitric oxide (NO) contributes to O_3 depletion and O_3 formation depends on VOC availability. Ozone formation at rural sites is governed by levels of hydrocarbons, especially biogenic VOCs (BVOCs) emitted from vegetation and O_3 formation increases with increasing NO_x. Because of higher NO_x levels and lower BVOC emission, urban O_3 levels are usually lower than rural ones.

Observations and model studies indicate that tropospheric O_3 has significantly increased in the Northern Hemisphere extratropics during the course of the 20th century (Cooper et al., 2014; Young et al., 2013). Between 1950-1979 and 2000–2010 there was a significant trend in the surface O_3 concentrations of 1–5 ppbv/decade over the Northern Hemisphere, which corresponds to region-specific increases of 9%–55% since the 1970s (Cooper et al., 2014). With respect to Europe, Wilson et al. (2012) obtained for the period 1996–2005 significant positive trends mainly over Central Europe and north-western Europe, whereas the few negative trends were observed primarily over eastern and south-western Europe. Thus, Wilson et al. (2012) conclude that

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reductions in precursor emissions did not have a substantial effect on O_3 trends, probably due to meteorological variability, changes in background O_3 and shifts in source patterns. Furthermore, particularly background O_3 in cities shows increasing trends from 2000 onwards (Sicard et al., 2018). The increasing O_3 background levels in the cities are mainly attributed to a lower O_3 degradation by NO due to the reduction in local NO_x emissions.

In the northern mid-latitudes, peak surface O_3 concentrations occur in spring and summer, resulting from a stronger stratosphere-troposphere exchange and a high net photochemical production in these seasons (Pope et al., 2016). Surface O_3 concentrations are strongly governed by the meteorological conditions such as solar radiation fluxes, air temperature, humidity, wind speed and direction. In a study for the European area, Otero et al. (2016) found that daily maximum temperature is one of the main drivers of O_3. Furthermore, the inclusion of O_3 persistence (one-day lag of O_3) provided an added value for O_3 predictions. The synoptic weather situation is associated with significant changes in surface O_3 concentrations via transport and/or accumulation of O_3 and its precursor substances. Thus, Pope et al. (2016), in a study for the UK, connected specific weather situations like for instance anticyclonic conditions with an increased in situ O_3 production due to large-scale subsidence, clear skies, increased surface temperature and reduced horizontal and vertical mixing. Also easterly flows were connected with high O_3 concentrations due to the transport of O_3 and precursors from polluted regions in continental Europe, whereas clean maritime westerly flows reduced O_3 concentrations. For Spain Santurtún et al. (2015) found maximum O_3 concentrations at days with northern or eastern weather types, which were also associated with the transport of precursors into the target region.

Human health is directly related to the thermal and chemical conditions of the surrounding atmosphere. There are complex relationships with human health via specific weather events as well as physical and chemical effects. Thus, the exposure to ground-level O_3 can have significant health impacts. With respect to long-term ozone exposure, an effect was found on mortality, at least for respiratory or cardiorespiratory mortality, especially in people with potential predisposing conditions (WHO, 2013). Comprehensive information on health effects of short-term exposure to ozone on mortality and morbidity was provided for instance by the APHENA (Air pollution and health: a European and North American approach) study (Katsouyanni et al., 2009). In this study a 0.35 (0.12–0.58) per cent increase in cardiovascular mortality of those aged younger than 75 years (95% CI) per 10 $\mu g/m^3$ increase in daily maximum 1-hour ozone concentrations was found. While air temperature can modify ozone-mortality relationships (Pattenden et al., 2010), no confounding effects by particulate matter are found (Bell et al., 2004).

High O3 concentrations reduce various pulmonary function parameters, can cause inflammatory response in the lung and can increase asthma attacks (WHO, 2013). Besides such pulmonary effects, there is evidence that O_3 also impacts on the cardiovascular system. Possible mechanisms of the impact of air pollution on myocardial infarction (MI) comprise inflammation, abnormal regulation of the cardiac autonomic system, an increase in blood viscosity, and an increase of vasoconstrictors (Mustafić et al., 2012; Srebot et al., 2009). However, the findings regarding O_3 differ compared with findings for other air pollutants, and positive, no, or even negative O_3-MI relationships are reported in the literature (Mustafić et al., 2012). Recent studies have shed more light on the mechanisms how O_3 impacts on MI. For instance, Hampel et al. (2012) observed immediate O_3 effects on heart rate and repolarization, which were stronger in individuals with metabolic disorders. Zhang et al. (2018) found that short-term exposure to fine particular matter and O_3 has acute effects on atrioventricular conduction and ventricular depolarization and repolarization, which could potentially mediate the associations of air pollution with cardiac arrhythmias and cardiovascular mortality. However, there still exists considerable uncertainties on the specific relationships between O_3 and MI, because O_3-health associations are difficult to estimate and O_3 is a highly reactive photochemical component with complex mechanisms of formation and destruction.

The present study analyses meteorological and synoptic factors of daily maximum 1-hour ozone concentrations. The impact of ozone on health is exemplified for daily myocardial infarction frequencies. Thus, in the first part of the present study meteorological and synoptic factors governing ozone concentrations in the city of Augsburg, southern Germany, are investigated. Based on larger-scale atmospheric temperature and humidity information and using a weather type classification the local daily maximum 1-hour ozone concentrations are analysed and statistically modelled. The second part of the present study involves the question whether there is a relationship between the daily maximum 1-hour ozone concentrations and the frequency of daily myocardial infarction events. In this regard, the prevailing weather situation as well as the local meteorological conditions are also considered. In summary, the present contribution aims to add to the understanding of air substances-health relationships by analysing the large-scale atmospheric circulation and meteorology, which are connected to health-relevant local O_3 concentrations, as well as by investigating the effects of short-term exposure to local O_3, climate and atmospheric circulation on daily MI frequencies.

2. Data and methods

2.1. Data

Station-based ozone data were provided by the Bavarian Environment Agency (Bayerisches Landesamt für Umwelt, 2019). The station Augsburg LfU (Landesamt für Umwelt) was used which represents urban background conditions for the region of Augsburg. From the hourly data the daily maximum 1-hour ozone concentration was derived. Preliminary analyses using the daily maximum 8-hour average O_3 concentration or the daily mean O_3 concentration provided a lower performance in the regression models. Thus, the daily maximum 1-hour ozone concentration was chosen.

Daily mean sea level pressure data for the weather types classification as well as other larger-scale predictor variables were taken in a $1^\circ \times 1^\circ$ resolution from the European Centre for Medium-Range Weather Forecasts (ECMWF) reanalysis (ERA-Interim, Dee et al., 2011). Mean sea level pressure data was derived for the domain 30°N-60°N, 20°W-40°E. For the other potential predictors (mean and maximum air temperature, specific and relative humidity, all in the 850 hPa level) the mean of the 9 grid boxes 49°N-47°N, $10^\circ E - 12^\circ E$, covering the area over and around the city of Augsburg (48.4°N, 10.9°E) was used.

Daily MI frequencies come from the KORA Augsburg myocardial infarction registry (KORA: Cooperative Health Research in the Augsburg Region, Helmholtz Zentrum München, 2019). In this study, non-fatal infarctions and coronary deaths in the city of Augsburg for the age group 25 years–74 years were considered. Data for the surrounding districts were excluded, since preliminary analyses showed clearer O_3-MI-associations using the city data only.

Daily 2 m mean and maximum air temperature and daily mean relative humidity from the station Augsburg-Mühlhausen of the German Weather Service (Deutscher Wetterdienst, 2019) were also extracted.

The years from 2000 to 2016 were selected, because this period is continuously covered by all variables. Since higher O_3 concentrations occur in Augsburg primarily in spring and summer and previous studies found the largest impact on health at elevated levels of O_3 (Srebot et al., 2009), all analyses comprise the months from March to September.

3. Methods

3.1. Synoptic classification

The daily mean sea level pressure fields were classified according to the Jenkinson-Collison (JC) classification (Jenkinson and Collison, 1977; Jones et al., 2013). The classification method, which was originally developed for the British Isles, is one of the most prominent weather types classification schemes applied in the European area for many different purposes (in the context of ozone see for instance Otero et al., 2016). A set of airflow indices associated with the direction, speed and vorticity of the airflow characterizes the daily circulation. This results in 27 types- eight types giving the direction of flow, two types describing the rotation, 16 combined weather types as well as an "unclassified" type, which describes mainly weak or chaotic flow conditions. As central point for the calculation of the indices 48°N/11°E, focusing the target location Augsburg, was chosen.

3.1.1. Statistical model for daily maximum 1-hour ozone

The impact of weather types and air mass characteristics on daily maximum 1-hour O_3 concentrations was analysed using lasso regression (lasso: least absolute shrinkage and selection, Tibshirani, 1996; Tibshirani, 2012). Lasso regression is specifically suitable to optimize prediction accuracy and interpretability of the statistical models, in particular if multicollinearity of predictors is present. Thus, lasso tries to enhance prediction accuracy by shrinking or setting to 0 some coefficients and determines a subset of variables with the strongest effects. Within lasso a 10-fold cross validation is used to decide on the value of the tuning parameter t, with t controlling the amount of shrinkage that is applied to the estimates. The package glmnet within the free software environment for statistical computing R was used to perform lasso regression.

In the present study lasso regression was used for predictor selection and to establish robust relationships of local O_3 with larger-scale weather types and meteorology. As explanatory variables for daily maximum 1-hour O_3 concentrations in Augsburg the time series of the weather types (coded as binary time series with 1: occurrence, 0: no occurrence), air temperature and humidity of the 850 hPa pressure level (each as mean over 9 grid boxes, see section 2.1) as well as O_3 persistence (i.e. maximum 1-hour O_3 concentration of the previous day) and seasonality (defined by sin (2πd/365) and cos (2πd/365)) were considered. The selection of significant predictors was based on a bootstrap procedure with 100,000 samples. Within each sample two third of the data was used for calibrating the model, the remaining one third of the data for validation of the model. Predictors, which were chosen in at least 95% of the 100,000 lasso regressions, built the final predictor set. The overall model performance in calibration and validation was evaluated using the correlation coefficient between observed and modelled O_3 as well as the Mean Squared Error Skill Score (MSESS, Wilks, 2006). The mean squared error is a common accuracy measure for continuous forecasts. The corresponding MSESS relates the averaged squared difference between modelled O_3 and observed O_3 to the difference resulting from the use of a reference. In the present study, long-term climatology was used as reference. MSESS < 0 indicates no skill, whereas MSESS $= 100\%$ implies a perfect model.

3.1.2. Statistical models of the ozone-infarction relationships

Relationships between daily maximum 1-hour O_3 concentrations and daily MI in the region of Augsburg were assessed using quasi-Poisson generalized additive models (GAM, Wood, 2017). GAM is a generalized linear model involving a sum of smooth functions of covariates for the linear predictor. Within GAM nonlinear as well as linear relationships can be modelled. Thus, the model can be written for example as

$$g(\mu_i) = A_i\theta + f_1(x_{1i}) + f_2(x_{2i}) + f_3(x_{3i}) + x_{4i} + x_{5i} + \cdots$$

where $\mu_i \equiv E(Y_i)$ and $Y_i\ EF(\mu_i, \varnothing)$. Y_i is a response variable, $EF(\mu_i, \varnothing)$ is an exponential family distribution with mean μ_i and scale parameter $\varnothing$, A_i is a row of the model matrix for any strictly parametric model components, θ is the corresponding parameter vector, and the f_i are smooth functions of the covariates x_k. In the present work, penalized thin plate regression splines were used for estimating the smooth functions. Thin plate regression splines avoid the problem of knot placement, can be constructed for smooths of multiple predictor variables, and are relatively computationally efficient (Wood, 2017).

The response variable daily MI frequencies was investigated, with daily maximum 1-hour O_3 concentrations representing the exposure. A linear (x_1) as well as a non-linear ($f(x_1)$) characterization of the MI-O_3 relationship was tested. Even though previous studies have shown no delayed effects for O_3 (e.g. von Klot et al., 2005), in addition to simultaneous relationships, O_3 lags up to 5 days were checked ($x_{1(i-1)}$, $x_{1(i-2)}$, ... or $f(x_{1(i-1)})$, $f(x_{1(i-2)})$, ...). As further explanatory variables the station-based local mean or maximum 2 m air temperature and mean relative humidity using splines ($f(x_2)$, $f(x_3)$) as well as the time series of the weather types using linear relationships ($x_4 + x_5 + ...$) were considered. Other than O_3, no further air pollutants like NO_x or particulate matter were used in the models. To control for systematic variation over time, a day-of-week indicator, seasonality (defined by sin (2πd/365) and cos (2πd/365)), and long-term trend (as monotonic function) using penalized splines were taken into account. The statistical analyses of the MI-O_3 relationships were performed using the R packages mgcv and dlnm.

Performance of the models was evaluated using the p-values of the model coefficients, the adjusted R^2 of the model, the partial autocorrelation function of the residuals, and the generalized cross validation score (GCV) which can be written

$$v_g = \frac{n\sum_{i=1}^{n}(y_i - \hat{f}_i)^2}{[n - tr(A)]^2}$$

where $\hat{f}$ is the estimate from fitting to all the data, and A is the corresponding influence matrix (Wood, 2017).

Furthermore, a bootstrap procedure was used, again, in order to test the suitability of each weather type as additional predictor for infarction frequencies. Based on 10,000 random samples statistical models were built using one weather type at a time. A weather type, which was selected in at least 50% of the 10,000 models, entered the final predictor set. The final predictor set was subsequently used to assess the relationships between daily maximum 1-hour O_3 concentrations and daily MI frequencies.

To illustrate the relationships between O_3-relevant weather types and those daily maximum 1-hour O_3 concentrations, which are connected to significantly enhanced MI frequencies, the following probabilities P were calculated:

P(MI-O_3): Marginal probability of finding daily maximum O_3 concentration, which is associated with enhanced MI frequency.
P(MI-O_3|W): Conditional probability of MI-relevant O_3 concentration given that a day is governed by a certain weather type.
P(W|MI-O_3): Conditional probability of the appearance of a certain weather type given a day with MI-relevant O_3 concentration.

Furthermore, for the specific weather types, which govern daily maximum O_3 concentrations as well as for the weather types, which were selected in the MI-O_3 models as additional predictors, the probability of the appearance of a certain weather type was calculated as well as mean O_3, temperature and humidity characteristics were analysed.

4. Results

4.1. Characterisation of ozone concentrations in Augsburg

Highest O_3 concentrations occur primarily in the afternoon hours in spring and summer due to the dependence of photochemical O_3 production from the intensity of solar radiation income. In the period 2000–2016 the mean 1-hour O_3 concentrations reached in general

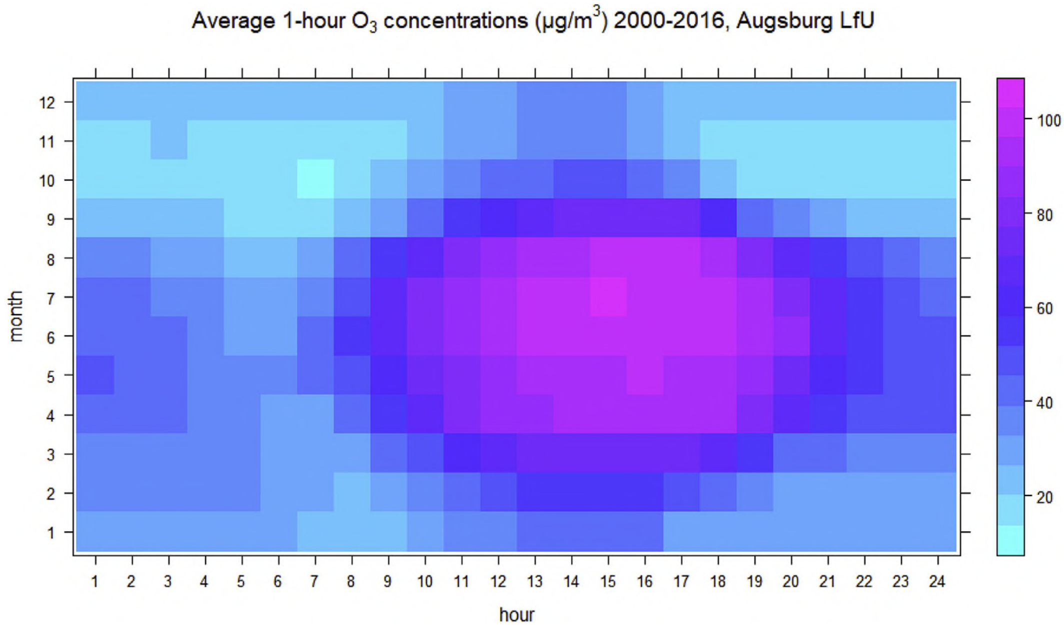

Fig. 1. Annual and diurnal cycle of 1-hour ozone concentrations in Augsburg (observational data in the period 2000–2016).

values above 70 µg/m^3 during the day in the months from March to September, in June and July above 100 µg/m^3 (Fig. 1). Daily maximum 1-hour O_3 concentrations were observed in the range from 18 µg/m^3 to 205 µg/m^3. The individual values were often considerably high and exceeded the information threshold of 180 µg/m^3 according to the 39th regulation of the Federal Immission Control Act (BImSchG). In contrast to other air substances like particulate matter and nitrogen oxide, no decreasing trend of mean O_3 concentrations was observed in the period 2000–2016 (Bayerisches Landesamt für Umwelt, 2018).

4.2. *Impact of weather types and air-mass characteristics on daily maximum ozone concentrations*

The dependencies of daily maximum 1-hour O_3 from weather types and air-mass characteristics were analysed using lasso regressions. The binary time series of the weather types as well as the standardized time series of the other predictor variables temperature and relative humidity of the 850 hPa level, O_3 persistence, and seasonality entered the statistical models as predictors. Standardisation prior to regression analysis was done, because the penalty method within lasso regression uses the magnitude of the coefficients associated to each variable, as well as to ease interpretability of the regression coefficients. The correlation coefficient between observed and modelled O_3, averaged across the 100,000 statistical models, corresponded to 0.84, the MSESS amounts to 70% in calibration as well as in validation.

It became apparent, that seasonality, O_3 persistence (max. 1-hour O_3 concentration of the previous day), daily 850 hPa-level temperature maximum and relative humidity are of high importance within the assessment of daily maximum 1-hour O_3 in Augsburg. Thus, these variables served as predictors in all 100,000 models. In addition, there are specific weather types, which were selected in all/almost all regressions. This applies to the weather type "unclassified" (U), a weather type which is mainly associated with low flow conditions (weak pressure gradients, and thus, neither flow direction nor vorticity can be identified), and to the weather types South (S), Anticyclonic Northwest (ANW), and Northwest (NW). Table 1 shows the predictors, which were selected in at least 95% of all regression models as independent variables for daily maximum 1-hour O_3 concentrations.

The standardised regression coefficients in Table 1 can be used to induce strength and direction of the relationships. Thus, maximum temperature as well as O_3 persistence show a strong positive relationship with the daily 1-hour O_3 maximum. This implies that high O_3 concentrations of the previous day and high air temperatures at the target day cause high O_3 concentrations. In contrast, relative humidity has a strong negative relationship with O_3, implying that high values of specific humidity inhibit ozone formation.

The four O_3-relevant weather types, which are characterized in Table 2 and illustrated in Fig. 2, show a positive relationship for the weather type "U", whereas the occurrence of the weather types "S", "ANW", and "NW" leads to a decrease of daily maximum 1-hour O_3 concentrations. The weather type "U", occurring at almost 19% of all days in the study period, is characterized by a weak pressure gradient over the target region, accompanied with low wind, very high O_3 and air temperature and reduced relative humidity values. The weather type "S" is associated with a high-pressure system with centre over eastern Europe and a low-pressure centre west of the British Isles. Consequently, a southerly flow results into the target region and relatively warm and dry conditions prevail. The weather type appears predominantly in spring and in September. In spring, it is connected with reduced daily maximum 1-hour O_3 concentrations, causing the negative regression coefficient with O_3. The weather types "NW" and "ANW" are characterized by a low-pressure centre over Scandinavia and a high-pressure system over the North Atlantic and western Europe, leading to a (anticyclonic) north-westerly flow and below average O_3 and temperature in Augsburg.

4.3. *Relationships of daily maximum ozone concentrations and myocardial infarction frequencies*

Generalized additive models were used to analyse relationships between daily maximum 1-hour O_3 concentrations and daily MI frequencies in Augsburg. During the "ozone season" on average 1.24 MI cases per day occurred with a range between no case up to five (June, July, September) and no case up to six (March to May, August). The total number of MI cases in the considered period was 4320, ranging from 539 cases (June) up to 675 cases (March).

Table 3 shows descriptive statistics and the correlation coefficients of ozone and the local climate variables used within the GAMs. The best final model configuration was achieved using a non-linear function of O_3 (penalized thin plate regression spline with approx. 2 empirical

Table 1
Frequency (%) and regression coefficients of the predictors seasonality (sin_sc, cos_sc), ozone persistence (O3_persist), 850 hPa temperature maximum (maxT), 850 hPa relative humidity (RH), and the weather types “unclassified” (U, corresponds to low flow conditions), South (S), Anticyclonic Northwest (ANW), and Northwest (NW). Shown are only predictors, which were selected in at least 95% of 100,000 models.

Predictor	sin_sc	cos_sc	O3_persist	maxT	RH	U	S	ANW	NW
Frequency	100	100	100	100	100	100	99.99	99.82	98.85
Regression coeff.	4.5	1.6	10.1	11.9	−7.5	4.0	−7.8	−3.9	−3.3

Table 2
Probability of appearance of the O_3-relevant weather types “unclassified” (U, associated with low flow conditions), South (S), Northwest (NW), and Anticyclonic Northwest (ANW) in % and as absolute number of days as well as the weather type-specific mean daily maximum 1-hour O_3 concentration, local daily maximum temperature and relative humidity in Augsburg for March–September 2000–2016.

Weather type	Probability (%)	Number of days	Max. O_3 (μg/m^3)	Max. temp. (°C)	Rel. humidity (%)
U	18.8	684	114.3	22.4	75.3
S	1.8	65	95.2	20.0	72.2
NW	1.5	55	79.9	14.2	79.7
ANW	1.5	55	86.3	16.1	76.0

degrees of freedom), seasonality (defined by sin (2πd/365)), trend, and day of the week. All non-linear terms were significant on the 99%-significance level. The incorporation of local atmospheric temperature and local relative humidity as well as the individual consideration of time lags from one up to five days did not impact on the results. In this regard, the insignificance of temperature and humidity in the GAMs may be explained by the already indirect inclusion of this information via the O_3 time series.

Besides, three weather types were selected in at least 50% of the 10,000 GAM models: the weather type Anticyclonic (A, selected in 81% of all models) as well as the weather types Cyclonic North (CN, selected in 56% of all models) and Cyclonic (C, selected in 51% of all models). The occurrence of the weather type “A” is related with a reduction of the MI frequency, whereas the weather types “CN” and “C” are connected with an increase in MI frequencies. Table 4 and Fig. 3 show specifications of the HI-relevant weather types “A”, “CN” and “C”, which were selected in the GAMs as predictors. The weather type “A” is characterized by a strong high-pressure system over the target region, going along with slightly above average maximum O_3, above average maximum temperature and below average relative humidity. It occurs at about 25% of all days in the study period. The weather type “C”, occurring at approx. 9% of all days, reflects low-pressure conditions over the target region itself. In case of the rarely occurring weather type “CN” the low-pressure centre is located eastwards, leading to a cyclonic northerly flow at the western side of the low. Both weather types are associated with below average O_3 and temperature and above average humidity, but much more pronounced for the weather type “CN”.

Fig. 4 shows the cumulative exposure-response association of daily maximum 1-hour O_3 concentrations and MI frequencies. The observed

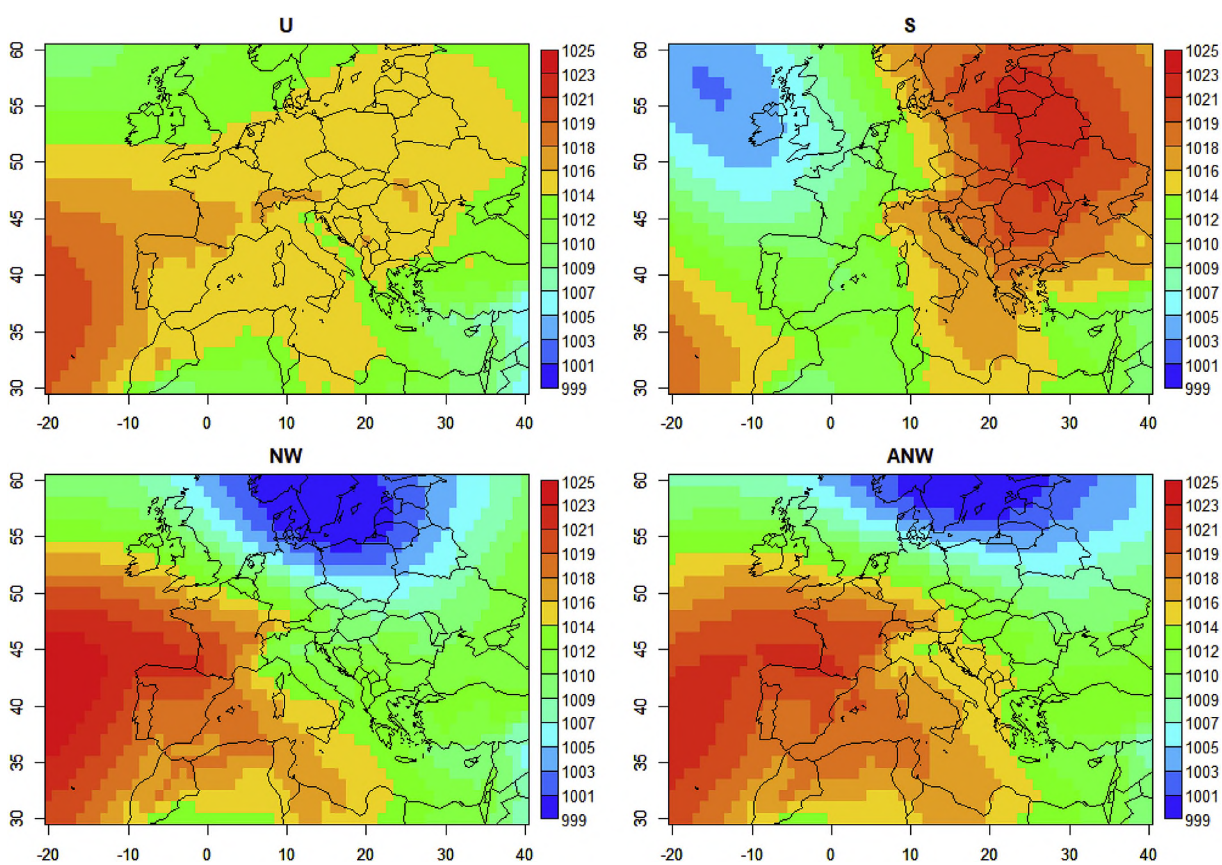

Fig. 2. Mean sea level pressure (in hPa) of the weather types, which are related with daily maximum 1-hour O_3 concentrations in Augsburg. U: “unclassified” (low flow conditions), S: South, NW: Northwest, ANW: Anticyclonic Northwest.

Table 3
Descriptive statistics and Spearman correlation coefficients for daily maximum 1-hour ozone concentrations, local mean and maximum temperature and relative humidity in Augsburg for the months March–September 2000–2016.

	Mean (Min/Max)	Correlation coefficient			
		Daily maximum 1- hour ozone	Daily mean temperature	Daily maximum temperature	Daily mean relative humidity
Daily maximum 1- hour ozone (μg/m^3)	98.8 (18/205)	1	0.55	0.67	−0.66
Daily mean temperature (°C)	13.2 (−14.9/26.9)		1	0.95	−0.31
Daily maximum temperature (°C)	18.5 (−4.7/35.7)			1	−0.45
Daily mean relative humidity (%)	76.1 (37.5/99.9)				1

Table 4
Probability of appearance of the MI-relevant weather types Anticyclonic (A), Cyclonic North (CN) and Cyclonic (C) in % and as absolute number of days as well as the weather type-specific mean daily maximum 1-hour O_3 concentration, local daily maximum temperature and relative humidity in Augsburg for March–September 2000–2016.

Weather type	Probability (%)	Number of days	Max. 1-hour O_3 (μg/m^3)	Daily max. temp. (°C)	Daily mean rel. humidity (%)
A	25.8	939	99.6	19.7	74.0
CN	0.5	18	79.1	14.3	88.7
C	9.3	338	92.6	16.7	81.7

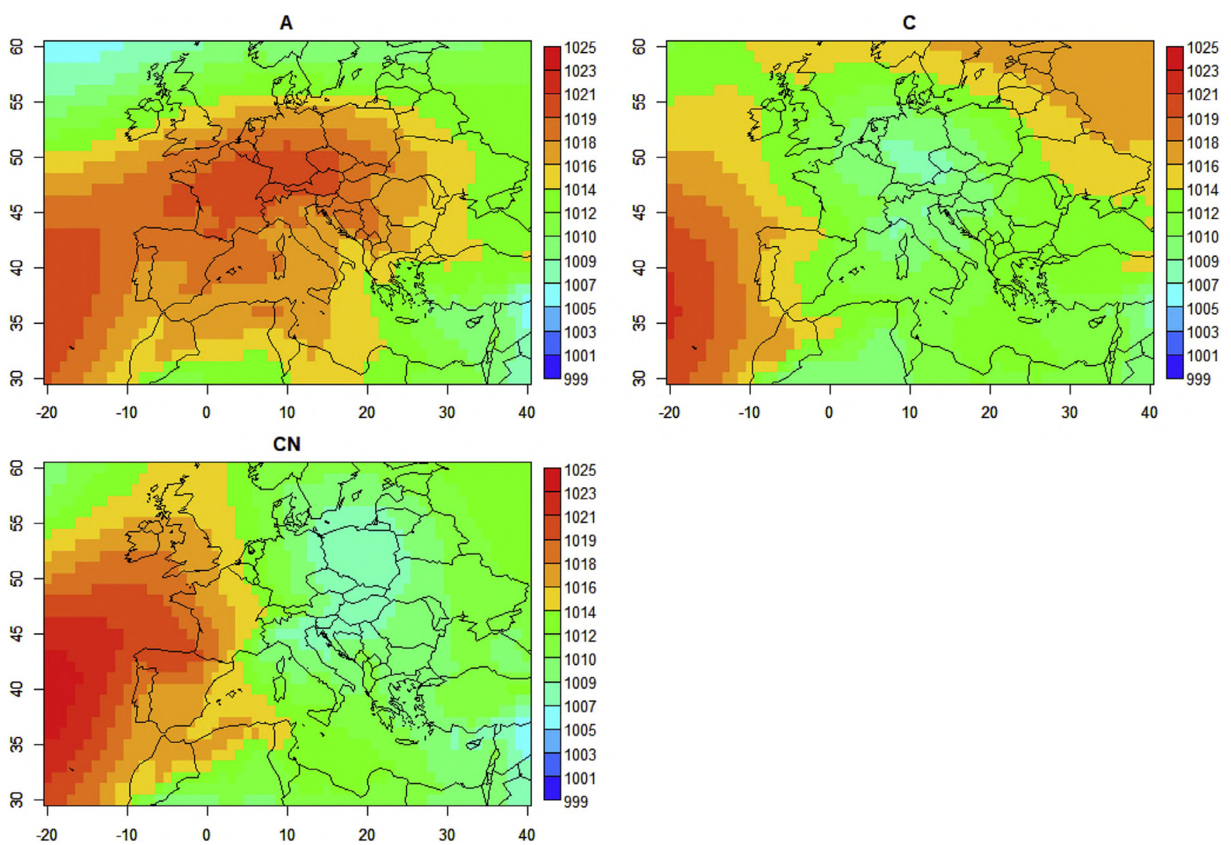

Fig. 3. Mean sea level pressure (in hPa) of the weather types, which are related to MI frequencies in Augsburg. A: Anticyclonic, C: Cyclonic, CN: Cyclonic North.

O_3 minimum of the time series (18 μg/m^3) was set as reference value for the calculation of the exposure-response curve. From Fig. 4 it becomes apparent that there is in general no linear relationship between O_3 concentrations and MI frequencies, but that significantly enhanced MI frequencies (95% significance level) occur at mean to moderately high values of the daily O_3 maximum in the range between 96 μg/m^3 and 138 μg/m^3. In this regard, MI frequencies show an almost linear increase until the maximum relative risk (RR) at an O_3 concentration of 117 μg/m^3, whereas afterwards RR is decreasing with further increases of O_3. Thus, the range of significant RR values ranges approximately between the median (96 μg/m^3) and the 90%- percentile (135 μg/m^3), with maximum RR close to the 75%- percentile (116 μg/m^3). These values are subsequently used as threshold values for further analyses.

Since the MI-O_3 relationships appear to be almost linear until the maximum RR, a piecewise linear regression for all O_3 concentrations up to the 75%- percentile (116 μg/m^3) was fitted using the same predictors as for the non-linear setup. It results in a significant increase of 3.41% (95% confidence interval (CI): [1.33%, 5.53%]) of the myocardial

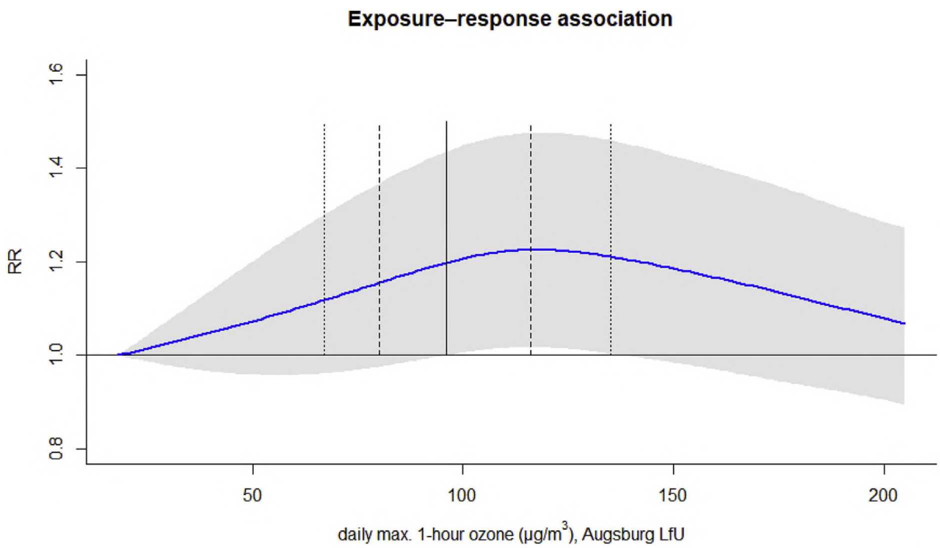

Fig. 4. Cumulative exposure-response association of daily maximum 1-hour O_3 concentrations and MI frequencies in Augsburg. Reference value: 18 µg/m^3, Grey signature: 95%- confidence interval. Vertical lines: 50%- (solid), 25%-, 75%- (dashed) and 10%-, 90%- (dotted) percentiles of daily maximum 1-hour O_3 concentrations.

infarction frequency per 10 µg/m^3 increase in O_3 until the cut-off at the 75%- percentile. A linear fit above this cut-off point yields a non-significant decrease of the risk (−3.11%, 95% CI: [-6.60%, 0.52%]).

In the context of analysing the influence of weather types on MI frequencies, it can be differentiated between direct relationships of weather types with MI frequencies, as they became apparent in the GAMs, and an indirect influence of weather types on MI frequencies via their association with O_3 concentrations, as was manifested in the lasso regressions. Thus, besides the information for the MI-relevant weather types "A","CN" and "C" (Table 4, Fig. 3) and the O_3-relevant weather types "U", "S","NW" and "ANW" (Table 2, Fig. 2), specific probabilities were calculated for the O_3-relevant weather types "U", "S","NW" and "ANW". The probabilities detail the weather type-specific relationships of the MI-relevant O_3 concentrations (defined as the daily 1-hour O_3 maximum in the range between the median and the 90%- percentile) and are shown in Table 5. From Tables 2 and 4 it can be inferred that the occurrences of two weather types "A" and "U" clearly dominate in the months from March to September and sum up to about 45% of all days. With respect to their effect on MI frequencies the occurrence of the Anticyclonic weather type is related to low MI values, probably due to high-pressure conditions associated with air temperatures and humidity conducive to human comfort and health. In contrast, the occurrence of the weather type "U" is in general associated with low flow conditions, high O_3 concentrations and high air temperatures, leading to discomfort due to little ventilation, high O_3 pollution and thermal load. The MI-relevance of the weather type "U" is further highlighted by the high probability of MI-relevant O_3 concentrations of over 40% when this weather type occurs and its large share of over 20% in days with MI-relevant O_3 concentrations (Table 5). The occurrences of the O_3-relevant weather types "S", "NW", and "ANW" are in general associated with a decrease in daily maximum O_3 (Table 1). Nevertheless, with respect to MI-relevant O_3 concentrations, at about 40% of the days with occurrence of the weather type "S" and at about 20% of the days with occurrence of the weather type "ANW" MI-relevant O_3 concentrations can be observed (Table 5). However, due to their relatively rare occurrence (1.8% and 1.5%, respectively, Table 2), their total share in days with MI-relevant O_3 concentrations is quite low (2.1% and 0.9%, respectively, Table 5).

Table 5
Relationships between MI-relevant daily maximum O_3 concentrations in the range between the median (96 µg/m^3) and the 90%-percentile (135 µg/m^3) and O_3-relevant weather types. P(MI-O_3): Marginal probability of finding daily maximum O_3 concentration, which is associated with enhanced MI frequency. P (MI-O_3|W): Conditional probability of MI-relevant O_3 concentration given that a day is governed by a certain weather type. P(W|MI-O_3): Conditional probability of the appearance of a certain weather type given a day with MI-relevant O_3 concentration.

	O_3	U	S	NW	ANW
P(MI-O_3) %	35.2	–	–	–	–
P(MI-O_3|W) %	–	42.6	39.7	5.4	21.1
P(W|MI-O_3) %	–	22.7	2.1	0.2	0.9

5. Discussion

The statistical models of the relationships of daily maximum 1-hour O_3 concentrations in Augsburg with larger-scale weather types and meteorological variables illustrate the well-known correlations of enhanced O_3 formation at high air temperatures and low humidity (e.g. Monks et al., 2015; Otero et al., 2016; Demuzere and van Lipzig, 2010). The daily temperature maximum can in general be regarded as a proxy variable for solar radiation. Since ground-level O_3 is photochemically built, a positive correlation between O_3 maximum and air temperature maximum becomes apparent. Furthermore, at high temperatures there is an enhanced generation of volatile organic compounds, hydroxyl-radicals and nitrogen dioxide, which have an important function as precursors for O_3 formation. In contrast, high values of relative humidity point in general to enhanced cloudiness, reduced incoming solar radiation, and thus imply reduced O_3 concentrations. Furthermore, high atmospheric humidity plays a role by the formation of secondary organic aerosols and by reducing the chemical reactivity of the system, particularly under low NO_x conditions. The O_3 concentration of the previous day also plays an important role, in particular in cases of stagnant or inversion-type weather situations.

The analysis of the relationships between specific weather types and O_3 concentrations was based on the widely used Jenkinson-Collison classification. In order to provide detailed and demonstrative information, the relationships were depicted using all 27 original weather types, without reducing information to the associated air flow indices (e.g. Otero et al., 2016) or by classifying hybrid types as purely directional (e.g. Santurtún et al., 2015). Four different weather types were selected in the lasso regression models as relevant predictors for maximum daily 1-hour O_3 concentrations. The "unclassified" weather type "U", which mainly comprises low flow conditions, is associated with high O_3 concentrations. The appearance of this weather type is connected with air mass stagnation, i.e. there are long residence times of the air masses, which favour a strong O_3 formation and accumulation. The relatively high air temperatures and low relative humidity values associated with this weather type also support O_3 formation. Due to the strong contribution of the weather type "U" to the occurrence of MI-relevant O_3 concentrations in the range between the 50%- and 90%-percentile (96–135 μg/m^3), this weather type is also of particular importance for MI frequencies in Augsburg. In contrast, the appearances of the weather types "S", "NW", and "ANW" are associated with reduced daily maximum O_3 concentrations. The weather type "S" is characterized by relatively dry and warm air masses. However, probably due to low concentrations of precursor emissions in the air masses, reduced O_3 concentrations result. In case of the weather types "ANW" and in particular "NW", the advection of relatively cold and humid air masses from northerly directions leads to reduced O_3 concentrations. However, due to their relatively low occurrence frequencies, they do not play a distinctive role.

The daily maximum 1-hour O_3 concentrations show a notable non-linear relationship with MI frequencies in Augsburg. Hence, an increase in O_3 concentrations is not paralleled by an increase in MI frequencies, but an enhanced MI risk occurs mainly at median to moderately high O_3 concentrations. For the city of Augsburg a significantly enhanced MI risk occurs for O_3 concentrations in the range between 96 μg/m^3 and 138 μg/m^3. A linear fit up to the maximum RR at approx. the 75%- O_3 percentile (116 μg/m^3) yields a significant increase of 3.41% (95% CI: [1.33%, 5.53%]) of the myocardial infarction frequency per 10 μg/m^3 increase in O_3. At higher O_3 concentrations a decrease of the MI risk occurs. However, it should be noted that a linear fit of the decrease above the 75%- O_3 percentile shows non-significant values. As comparison, for the city of Toulouse RR for acute MI was 1.05 for an increase in daily average O_3 of 5 μg/m^3 (Ruidavets et al., 2005). For Denver an increase in average daily O_3 concentrations from 20 to 29.7 ppb was associated with an 18, 12, and 21% change in risk of hospitalization among elderly people for acute myocardial infarction, coronary atherosclerosis, and pulmonary heart disease, respectively (Koken et al., 2003). In contrast, for London associations between O_3 exposure and cardiac admissions remained inconclusive (Wong et al., 2002). With respect to cardiovascular mortality rates the APHEA2 project (Air Pollution and Health: A European Approach, Gryparis et al., 2004) found an increase of 0.49% (95% CI: 0.34, 0.64) in cardiovascular mortality per 10 μg/m^3 increase in maximum 1-hour O_3 during the warm season pooled across 23 European cities. The slope of the dose-response curve of O_3 and daily number of deaths also showed a flattening at high (approx. 100 μg/m^3) O_3 values, but did not involve an overall decreasing trend at values above as in our study. In general, the association between O_3 and MI is highly variable across different cities and across the different studies, due to differences in the local characteristics of air pollution, climate and meteorology and different methodological approaches. The decrease of MI risk at very high O_3 concentrations found in our study might also be associated with adaptation measures of the population. Since high O_3 concentrations often occur simultaneously with high air temperatures, a combined air pollution-thermal load situation can occur, which is countered by sheltering and avoidance of outdoor physical activity. Sarnat et al. (2005), comparing personal exposure and ambient concentrations of O_3, found that the time spent indoors at home with or without air conditioning strongly modified personal exposure to O_3.

In addition, the non-linear exposure-response association, with a significantly enhanced MI risk between the 50% and 90% percentiles (96–135 μg/m^3) of daily maximum 1-hour O_3, implies that the current information threshold (1-hour O_3 of 180 μg/m^3) and target value (maximum eight-hour mean of 120 μg/m^3 at no more than 25 days per year) are suitable to only a limited extent. This stands in accordance to an assessment by the WHO (2013), which comes to the conclusion that the current target values for the protection of human health are set too high.

With respect to the impact of weather types on daily MI frequencies, one can distinguish between a direct effect and an indirect effect. The direct effect relates to weather types, which were selected in the GAMs as predictors for MI frequencies. This involves in particular the very frequent weather type Anticyclonic (A), which is characterized by warm and moderately humid high-pressure conditions and which is related to a reduction in MI frequencies. In contrast, cold and humid low-pressure conditions due to cyclonic activity over the target region (weather type "C"), in particular in connection with a northerly flow ("CN") yields adverse effects on MI. However, it can be noted that the adverse weather types have only a low occurrence frequency during the months from March to September. The indirect effect of weather types on MI frequencies operates via the contribution of specific weather types to MI-relevant O_3 concentrations. Here, the weather type "U" plays an important role, due to the high occurrence frequency in spring and summer and because of its strong contribution to the occurrence of MI-relevant O_3 concentrations.

In summary, a complex picture of the relationships between weather types, meteorological conditions, O_3 concentrations and MI frequencies in the city of Augsburg became apparent. Yet, it was shown that O_3 constitutes an air pollution substance, which has to be seen in connection with enhanced MI frequencies. Besides, the present study indicates that an adverse health impact occurs already at medium to moderate high values of daily maximum 1-hour O_3 concentrations. In the present study only one O_3 measuring station was used, which could introduce some uncertainties in the assessment. Thus, further studies could aim for a more detailed spatial representation of air pollution, also involving other air pollutants like particulate matter or nitrogen oxides. Furthermore, ozone effects can be stronger on hot days as was shown for instance in a study for British conurbations by Pattenden et al. (2010). Thus, a particular focus should also be given to situations when a combined, interactive thermal and air pollution load occurs.

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.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://

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