

Short-term effects of air quality and thermal stress on non-accidental morbidity—a multivariate meta-analysis comparing indices to single measures

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Abstract Air quality and thermal stress lead to increased morbidity and mortality. Studies on morbidity and the combined impact of air pollution and thermal stress are still rare. To analyse the correlations between air quality, thermal stress and morbidity, we used a two-stage meta-analysis approach, consisting of a Poisson regression model combined with distributed lag non-linear models (DLNMs) and a meta-analysis investigating whether latitude or the number of inhabitants significantly influence the correlations. We used air pollution, meteorological and hospital admission data from 28 administrative districts along a north-south gradient in western Germany from 2001 to 2011. We compared the performance of the single measure particulate matter (PM10) and air temperature to air quality indices (MPI and CAQI) and the biometeorological index UTCI. Based on the Akaike information criterion (AIC), it can be shown that using air quality indices instead of single measures increases the model strength. However, using the UTCI in the model does not give additional information compared to mean air temperature. Interaction between the 3-day average of air quality (max PM10, max CAQI and max MPI) and meteorology (mean air temperature and mean UTCI) did not improve the models.

Using the mean air temperature, we found immediate effects of heat stress (RR 1.0013, 95% CI: 0.9983–1.0043) and by 3 days delayed effects of cold stress (RR: 1.0184, 95% CI: 1.0117–1.0252). The results for air quality differ between both air quality indices and PM10. CAQI and MPI show a delayed impact on morbidity with a maximum RR after 2 days (MPI 1.0058, 95% CI: 1.0013–1.0102; CAQI 1.0068, 95% CI: 1.0030–1.0107). Latitude was identified as a significant meta-variable, whereas the number of inhabitants was not significant in the model.

Keywords Air quality index · Biometeorological index · Hospital admission · Morbidity · Distributed lag non-linear model · Multivariate meta-analysis

Introduction

According to the European Environment Agency (EEA 2013), air pollution leads to a reduction in life expectancy of 8.6 months per person in Europe. Together with the changing climate that will increase air temperature and hence thermal stress (Smith et al. 2013; Lokys et al. 2015a), air pollution is one of the major health concerns according to the World Health Organisation (Quantification of the Health Effects of Exposure to Air Pollution 2000). The effect of air pollution and thermal stress on mortality has been subject to numerous research projects throughout the past years (Vanos et al. 2014, 2015; Lelieveld et al. 2015; Williams et al. 2014; Guo et al. 2011; Gabriel and Endlicher 2011; Ruckerl et al. 2011). The high number of recent publications on this topic indicates that the effects of air pollution and thermal stress are of high interest, but not yet completely understood. The study by Grass (2008) shows that there are mainly two approaches to analyse health effects caused by air pollution and

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biometeorological variables: (1) early studies treat either thermal components or air pollution as independent variable, without considering confounders. Later, this changed to the use of the other variable as a confounder. (2) Recent studies (Buchholz et al. 2010; Vanos et al. 2014, 2015; Breitner et al. 2014) analyse the simultaneous effects of meteorological and air quality variables. However, these studies are still rare and especially the combined, but also, the single effects can vary across locations and population characteristics (Liu et al. 2011; Li et al. 2015a).

The combined effects of air pollutants, especially particulate matter (PM₁₀) and ozone, with temperature on mortality were shown to be significant by some studies (Breitner et al. 2014; Baccini et al. 2008; Vanos et al. 2014, 2015), while others did not find a significant confounding effect of air pollution to the impact of temperature on mortality (Basu et al. 2008). Only few studies suggested a possible interaction between air pollutants and temperature on the effect on mortality (Ren et al. 2006, 2008; Park et al. 2011). There is a lack of studies on the combined effect of air pollution and thermal stress on morbidity. Firoz et al. (2013) highlight the fact that mortality is only a small fraction of the burden of morbidity. As morbidity is, in most cases, a precursor for mortality, the understanding of air quality and thermal stress as drivers for morbidity can help to reduce the burden of both health endpoints.

Neither air quality nor human thermal stress is sufficiently described by a single pollutant or thermal measure like air temperature, respectively (de Freitas and Grigorieva 2014). Therefore, several indices have been developed to describe air quality and human thermal stress in total instead of using single measures. Air quality indices with verbal categories like “good”, “moderate” or “poor” and biometeorological indices with categories like “cold stress”, “no thermal stress” or “heat stress” are easy to understand for the public. They are widely used in Europe for policy support or direct information for the public about air quality and thermal stress (van den Elshout et al. 2008; Jendritzky et al. 2012). In this context, Li et al. (2015b) showed that the Air Pollution Index (API) is suited to communicate the health risks of air pollution. As this is a less common index in Europe, we investigate if the indices used in Europe are equally suited. Lokys et al. (2015b) compared different health impact-related air quality indices. The authors showed that the indices are correlated but differ especially at higher air pollution levels. The current study assesses if the “Common air quality index” (CAQI) (van den Elshout et al. 2008), the “Multi Pollutant Index” (MPI) (Gurjar et al. 2008) and the “Universal Thermal Climate Index” (UTCI) (Jendritzky et al. 2012) are suited to describe the associations between air quality, thermal stress and morbidity. In particular, we were interested if air quality and thermal indices are equally or even better suited than single measures (PM₁₀ and air temperature) to determine the health impact of air pollution

and thermal stress on humans at the level of morbidity based on hospital admissions.

The numerous studies on the correlations between air quality or thermal stress on the one hand and human health on the other reveal that there are many factors that confound the relationships. Besides confounding factors such as influenza (Guo et al. 2011) or holidays, the composition of particulate matter (Krein et al. 2007, 2008) or socio-economic factors (Stafoggia et al. 2006) as well as geographic aspects (Perez et al. 2015; Gasparrini et al. 2015; Cakmak et al. 2016) may influence the relationship. To address geographic dependence and the influence of population size as a proxy for the socio-economic situation, we analysed if latitude and the number of inhabitants can significantly reduce the heterogeneity amongst study regions.

In our study, we address the following three research questions: (1) Can biometeorological indices and air quality indices (compared to single measures) improve regression models for the relationship between air quality, thermal stress and non-accidental morbidity? (2) Which time lag or lag period is leading to the maximum increase in relative risk (RR) for morbidity as caused by air quality and thermal stress? (3) Can we characterize the impact of latitude and population size on the relationship between air quality, thermal stress and non-accidental morbidity?

Materials and methods

Data

The analysis was conducted in 28 administrative districts along a north-south gradient in the western part of Germany (Fig. 1) covering the period from 2001 to 2011. The total number of inhabitants in the study is 3.7 million, with a daily average of 6.17 (SD 0.72) all-case hospital admissions and 1.30 (SD 0.21) hospital admission related to cardiovascular and respiratory diseases per 10,000 inhabitants.

Datasets for each district included data on air quality, meteorology and non-accidental hospital admissions (morbidity). Regular doctor visits were not taken into account, as reliable statistics on these are not available. The air quality and meteorological data was provided by regional air quality monitoring networks of the federal states of Lower Saxony (Niedersächsisches Ministerium für Umwelt, Energie und Klimaschutz), Rhineland-Palatine (Landesamt für Umwelt Rheinland-Pfalz) and “AirBase – the European air quality database” provided by the European Environment Agency (EEA Airbase) for Rhineland-Palatine. Monitors for air quality and thermal data can be different, due to local measurement setups. The concentrations of NO₂, SO₂, O₃ and PM₁₀ were reported on an hourly or daily basis. Data on air temperature, wind speed, relative humidity and global radiation was

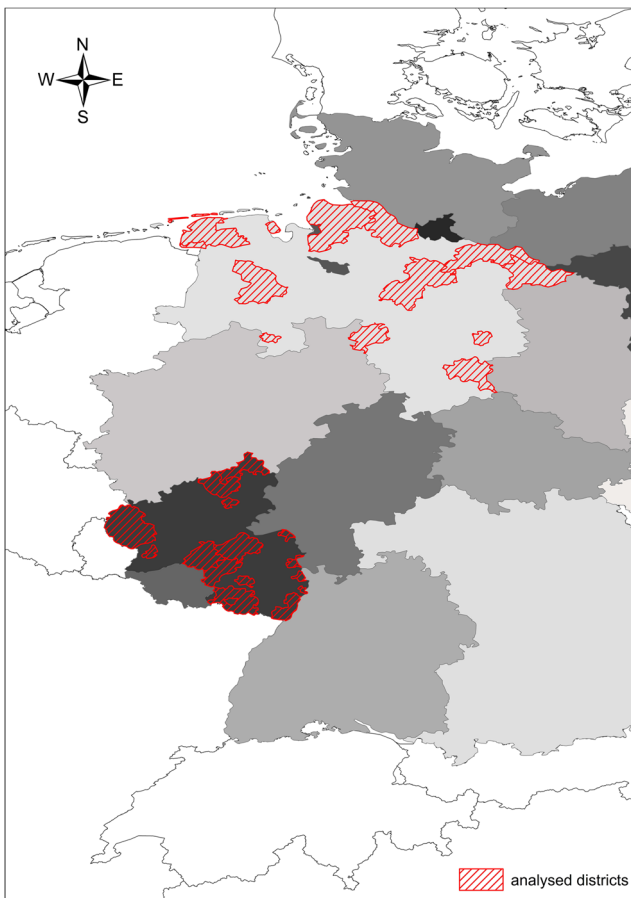


Fig. 1 Twenty-eight analysed administrative districts along a north-south gradient in the western part of Germany located in Lower Saxony and Rhineland-Palatine

obtained on an hourly basis. In case of hourly data, the daily mean, maximum and minimum were calculated if at least 75% of the data was available (2001/752/EC). Otherwise, the day was marked with missing data. In addition, we calculated daily values of common air quality and biometeorological indices. The indices to describe air quality and human thermal comfort are used to assess if these are equally or even better suited than the single measures PM10 and mean air temperature to determine effects of air pollution and thermal stress on hospital admissions.

For air quality, we calculated the non-aggregating “Common Air Quality Index” (CAQI) (van den Elshout et al. 2008) and the aggregating “Multi Pollutant Index” (MPI) (Gurjar et al. 2008) based on the daily maximum pollution levels. An aggregating index takes into account the conjoint effect of all pollutants included in the index, while the non-aggregating index is only based on the highest daily sub-index per pollutant (Plaia and Ruggieri 2010). Lokys et al. (2015b) demonstrated that both indices show a linear correlation, but the spread between them increases at high pollution levels. Hence, we expect differences in the regression at least at high index levels.

To assess the short-term effects of biometeorological stress on hospital admission, we used daily mean air temperature and daily mean UTCI. Mean air temperature is common in many studies that analyse the effect of thermal stress on morbidity or mortality (Ye et al. 2012; Breitner et al. 2014). Comparisons of different temperature measures conducted by Anderson and Bell (2009) and Guo et al. (2011) showed that mean air temperature was the best predictor for mortality. However, de Freitas and Grigorieva (2014) concluded from the high number of existing biometeorological indices that the thermal environment for humans is not sufficiently described by air temperature. Therefore, the “Universal Thermal Climate Index” (UTCI, Jendritzky et al. 2012) that does not only take into account the air temperature but also wind speed, relative humidity and mean radiant temperature was calculated. Regression results for mean air temperature and UTCI were compared. We used the freely available RayMan Pro model Ver. 2.1 (Matzarakis et al. 2007) to calculate the UTCI based on mean hourly data for air temperature, wind speed, relative humidity and global radiation. For the calculations, we used a clothing value of 0.1 *clo*, an activity of 80 *W* (standing).

Hospital admission data was provided by the “RDC of the Federal Statistical Office and the Statistical Offices of the federal states”, [Krankenhausstatistik (Teil II: Diagnosen)], [2000–2011] on request and is only available for academic use, restricted to personal use of the applicant and only available for temporary use within the premises of the data centre. The dataset includes gender, age (categorized in 5-year groups), date of admission and main diagnosis according to the International Classification of Diseases (ICD-10) on a daily basis per administrative district. We analysed non-accidental hospital admissions that can be related to air pollution or thermal stress including cardiovascular and respiratory diseases (ICD-10: A15-16 (tuberculosis); A37 (whooping cough); H01-H11 (disorders of eyelid, lacrimal system, orbit and conjunctiva); I05-I99 (diseases of the circulatory system); J05-J84 (diseases of the respiratory system); O03, O05-O06 (pregnancy with abortive outcome); R00-R07, R09 (symptoms and signs involving the circulatory and respiratory systems); R51 (headache); R53 (malaise and fatigue)).

Data analysis

To analyse the 28 districts, we used a two-stage meta-analysis approach proposed by Gasparrini et al. (2012) using the R statistics package “mvmeta”. The first stage consists of district-specific Poisson regression models, controlled for overdispersion, combined with distributed lag non-linear models (DLNMs) (Gasparrini 2011) to analyse the correlation between air quality, thermal stress and morbidity based on the selected non-accidental hospital admission. We compare models using air quality and thermal indices to models including the single pollutants and meteorological data. The first

model includes the covariates CAQI and UTCI as measures for air quality and human thermal comfort. The second model uses the aggregating air quality index MPI instead of the CAQI. Both models were compared to a third model containing maximum daily PM10 and daily mean air temperature. The models can be summarized as follows:

$$\text{LogE}(Y_t/X_t) \sim \beta_1 X_{1,t-1} + \beta_2 X_{2,t-1} + \text{ns}(\text{time}, df) + \text{DOW}_t + \text{Hol}_t + \text{Infl}_t \quad (1)$$

With Y_t being daily number of hospital admission related to the diseases selected by ICD-10 codes. X_1 describes the air quality component (max CAQI, max MPI or max PM10) and X_2 is the thermal component (mean UTCI, mean air temperature). In all models, we controlled for a long-term and seasonal trend using a natural cubic spline with 7 degrees of freedom (df) per year (Bhaskaran et al. 2013), day of the week (DOW_t), holidays (Hol_t) and influenza (Infl_t). To control for influenza, we used the hospital admission for ICD-10 codes J09–J11. An occurrence of influenza in the respective region leads to the whole week being marked for influenza (Guo et al. 2011). Within the DLNM, we choose a cubic B-spline to model the non-linear effects of air pollution and thermal stress with equally spaced knots placed at the quantiles. For the lag space, we selected a natural spline with knots placed along the logarithmic scale to account for a higher variability at lower lags up to a maximum lag of 14 days. Analitis et al. (2008), Baccini et al. (2008) and Breitner et al. (2014) showed that a maximum lag of 14 days is sufficient to represent the delayed effects of cold stress. The degrees of freedom for the covariates and lag were determined using the minimum of the Akaike information criterion (AIC) summed over all districts. Resulting degrees of freedom for the lag was 4 and 5 for all other covariates. To calculate the relative risks, we centred the DLNMs on the mean of each air quality covariate. For the thermal covariates such as UTCI, we used 17.5 °C, the mean of the “No thermal stress” category and 17.0 °C for temperature (Gasparrini and Armstrong 2013).

In addition to the three basic models, we test all models for interaction between a 3-day average (main impact period) for the air quality and thermal measure. The model including the interaction can be described as follows:

$$\text{LogE}(Y_t/X_t) \sim \beta_1 X_{1,t-1} + \beta_2 X_{2,t-1} + \beta_1 X_{1_{avg}} X_{2_{avg}} + \text{ns}(\text{time}, df) + \text{DOW}_t + \text{Hol}_t + \text{Infl}_t \quad (2)$$

With $X_{1_{avg}}$ being the average of the air pollution component (max CAQI, max MPI or max PM10) from $t-3$ to t and $X_{2_{avg}}$ being the average of the thermal component (mean UTCI or mean air temperature) from $t-3$ to t .

The second stage consists of a multivariate meta-analysis based on the “mvmeta” package for R statistics provided by Gasparrini et al. (2012). The meta-analysis enables us to

determine the effect of the covariates in all districts and its confidence interval based on the first-stage analysis per district. In addition, we can compare the districts and include meta-variables such as latitude or the number of inhabitants in the study. The estimation and interpretation of the meta-analysis are similar to linear mixed models, where the fixed part of the model represents the population-averaged outcomes. The random part of the model described by the between-study (co)variance matrix explains the deviation from the population averages (Gasparrini et al. 2012). We choose the restricted maximum likelihood (REML, Patterson and Thompson 1971) method to estimate the between-study (co)variance matrix as it is suitable for small sample sizes and takes into account only the random effects between study sites by accounting for the loss in degrees of freedom resulting from the estimated fixed effects (Harville 1977). The results of the multivariate meta-analysis are summarized overall and for the 10th and 90th percentile of the covariates. In order to analyse the variation between districts, we calculated the I^2 statistic (Higgins and Thompson 2002), which determines the heterogeneity also for smaller sample sizes than Cochran’s Q (Cochran 1950).

To assess if the meta-variables latitude and the number of inhabitants per district explain parts of the heterogeneity, we included them in the meta-analysis separately. We introduced the meta-variable “census”, describing the number of inhabitants in the administrative district, as a proxy for urban and rural districts with different population density and different exposure patterns to air pollution. The meta-variable “latitude”, calculated as the centroid’s latitude value of each administrative district, is used to assess if differences regarding the impact of air pollution and thermal stress occur along the north-south gradient.

We calculated the effects over all districts as well as the effects at the 25th and the 75th percentile of the meta-variables. The analyses were done for the whole range of the covariates as well as their 10th and 90th percentile. The Wald statistic was calculated to determine if the introduced meta-variables describe a significant modification to the original model. To identify a modification in remaining heterogeneity, we calculated the I^2 statistic (Higgins and Thompson 2002) in order to compare it to the models without meta-variables.

Results

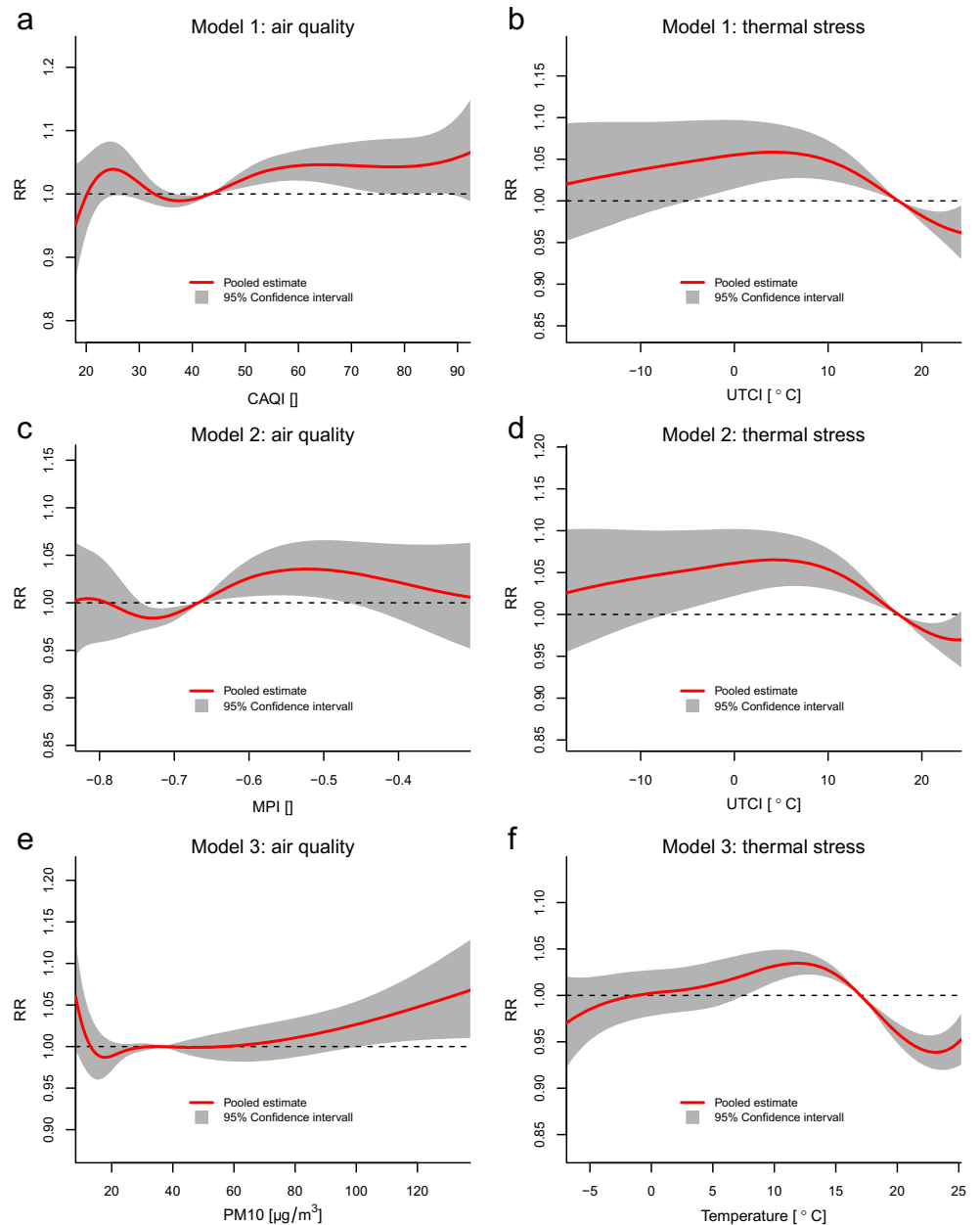
Based on the AIC, the strongest model is model 2 including MPI and UTCI (summed AIC for all regions: 397.950), followed by model 1 (CAQI, UTCI, AIC: 397.966). The model 3 with max PM10 and mean air temperature ranks third with an AIC of 521.211. This gives a first indication that the use of indices instead of single air pollutants is beneficial to determine the impact of air pollution and thermal stress on human

morbidity. Significant interactions between the 3-day average of air quality and the 3-day average for thermal stress were not found.

The meta-analysis for the 28 regions shows the overall effects of every variable based on the three-dimensional results from the DLNMs in the predictor and lag space. The overall cumulative summary does not show the lag space but considers the overall effect of the variable over the whole lag of 14 days (Fig. 2). All models show an increased RR for air pollution higher than the average air pollution level of CAQI = 43 (Fig. 2a), MPI = -0.67 (Fig. 2c) and PM10 = 36.6 (Fig. 2e). The increased RR for the MPI is not significant regarding the 95% confidence interval. The increase in RR below the average air quality is not

significant for any of the three models. The thermal stress is shown on the right hand side of Fig. 2. The results for the UTCI are similar for model 1 (Fig. 2b) and model 2 (Fig. 2d). Both show a slightly, but not significantly increased RR for UTCI below 17.5 and a slightly decreased RR for UTCI above that value. The decreased RR above the centre value of 17.5 °C results from the fact that the harmful effect of high temperatures occurs immediately after the event and remains only for a few days. A detailed analysis of this fact will be performed based on the predictor-specific summary for the variables along the lag space. The mean air temperature (Fig. 2f) shows a similar pattern as the UTCI. Mean air temperature suggests though that very low temperatures, below -5 °C, reduce the RR.

Fig. 2 Overall cumulative summary for model 1 including max CAQI (a) and mean UTCI (b), model 2 including max MPI (c) and mean UTCI (d) and model 3 including max PM10 (e) and mean air temperature (f) over the lag of 14 days. The pooled estimate is represented by the red line. Grey area shows the 95% confidence interval



The impact of air pollution and thermal stress along the lag space was analysed using the predictor-specific summary at the 10th and 90th percentile of each variable. Figure 3 shows that UTCI and air temperature show the same patterns at low and high values. At the 10th percentile, air temperature (Fig. 3a) and UTCI (Fig. 3c) have a delayed adverse effect on human morbidity with an increased RR after 1–2 days with a maximum RR (1.0110, 95% CI 1.0066–1.0153 for mean air temperature, RR: 1.0184, 95% CI: 1.0117–1.0252 UTCI) after 3 days. The impact of high temperatures and high UTCI at the 90th percentile is immediate but overall lower than the effect of cold stress. The maximum RR at the 90th percentile of UTCI is 1.0011 (95% CI: 1.0005–1.0018) (Fig. 3d), whereas it is slightly higher for mean air temperature (RR 1.0013, 95% CI: 0.9983–1.0043) but with a wider confidence interval (Fig. 3b). As the overall patterns are similar, the use of mean

UTCI is valid to identify the impact of thermal stress on human morbidity. Furthermore, it is able to detect significant changes in RR, when mean air temperature is not (heat stress).

The predictor-specific summary for air quality shows differences between the air quality indices and PM10 especially at high air pollution levels (Fig. 4). All three air quality measures have an increased RR at the 90th percentile from lag 0. The indices CAQI (Fig. 4a) and MPI (Fig. 4b) have the maximum RR (CAQI: 1.0068, 95% CI: 1.0030–1.0107, MPI: 1.0058, 95% CI: 1.0013–1.0102) after a lag of 2 days, while the maximum RR of 1.0021 (95% CI: 0.9976–1.0068) for PM10 occurs immediately. The effect of PM10 is not significant at any lag and percentile. The RR at 10th percentile over 14 days is 0.989 (95% CI: 0.96–1.018) while high PM10 concentrations lead to a slight increase in RR (RR at 90th percentile over 14 days: 1.001, 95% CI: 0.982–1.021). The

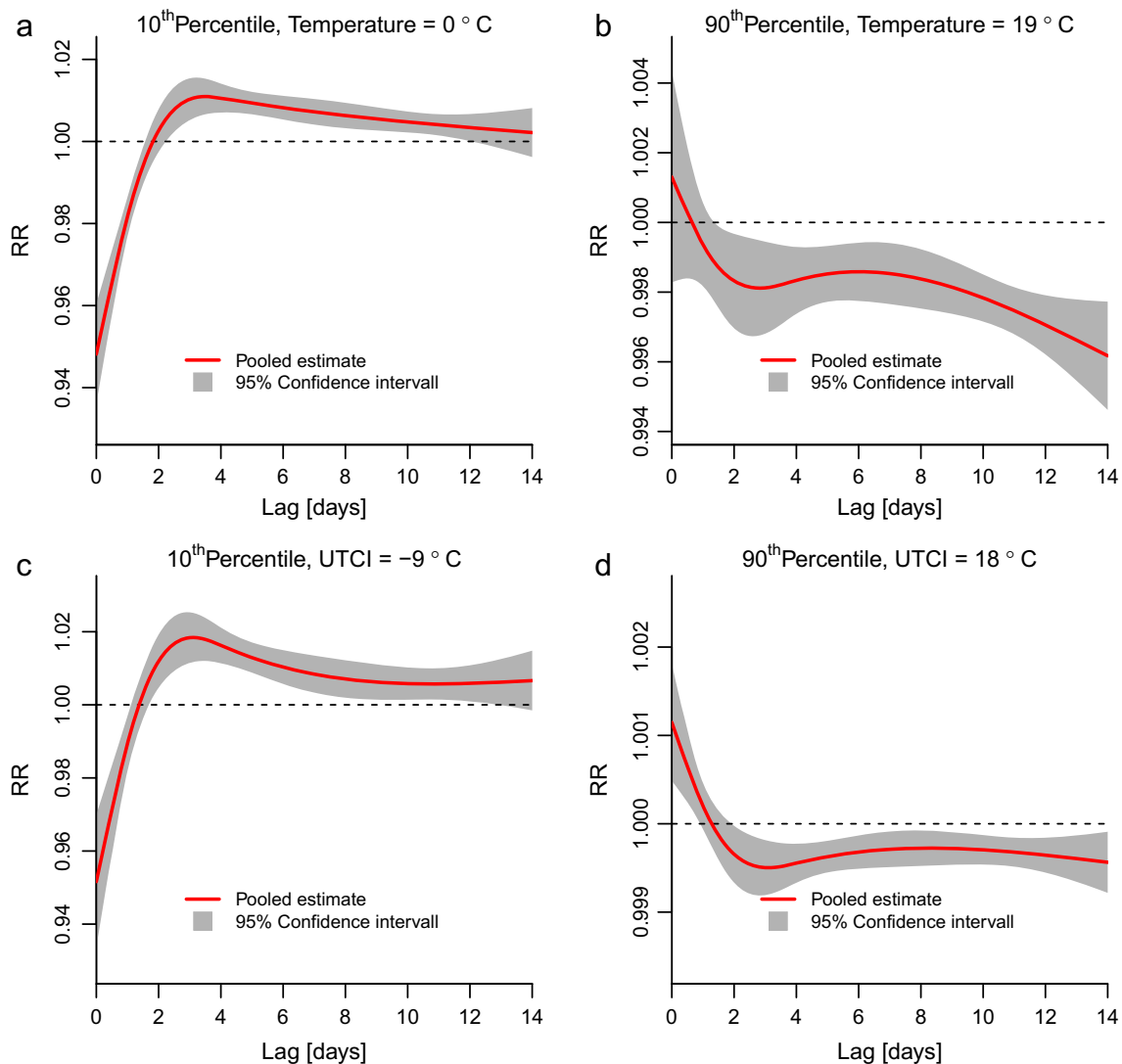


Fig. 3 Predictor specific summary for biometeorological variables. The upper panels show the results for mean air temperature at the 10th percentile (a) and 90th percentile (b). The lower panels show the results

for mean UTCI at 10th percentile (c) and 90th percentile (d). The pooled estimate is represented by the red line. Grey area shows the 95% confidence interval

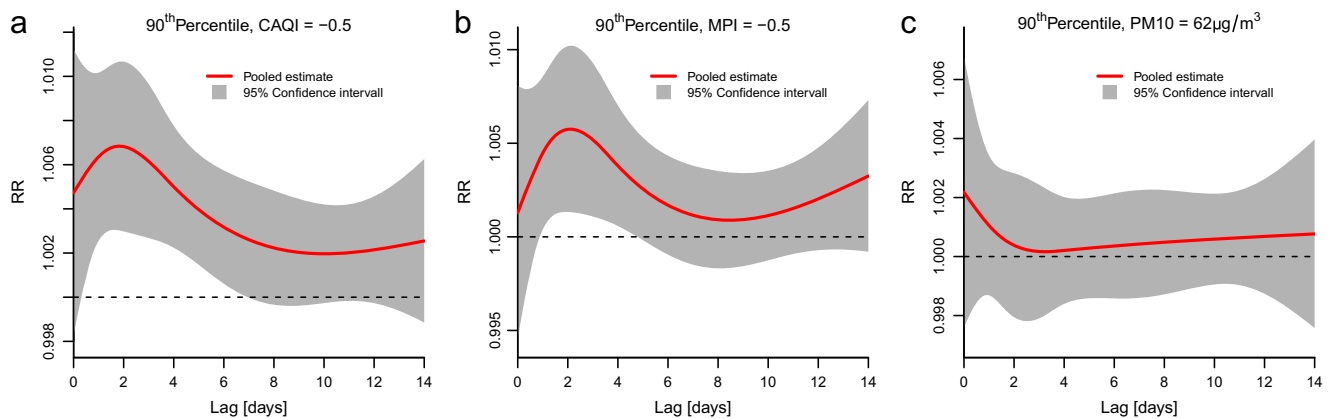


Fig. 4 Predictor-specific summary of the air quality variables at the 90th percentile along the lag of 14 days showing results for the CAQI (a), MPI (b) and PM10 (c). The pooled estimate is represented by the red line. Grey area shows the 95% confidence interval

confidence interval for PM10 always includes values below an RR of 1 (Fig. 4c). Therefore, we conclude that the use of the PM10 to describe air quality does not allow the detection of adverse effects of air pollution on human morbidity along the lag space.

The assessment of heterogeneity between the 28 administrative districts based on I^2 revealed that there is moderate heterogeneity (Higgins et al. 2003) for the air quality variables (I^2 between 36.7 and 48.7%), whereas thermal-stress-related measures only show low heterogeneity amongst the study regions (I^2 between 9.7 and 28.5%). The introduction of the meta-variable “census” did not explain the detected heterogeneity amongst regions as it did not significantly decrease I^2 for most predictor variables. Only for the MPI, the Wald test showed a significant decrease in the overall I^2 ($W = 0.034$). For 10th and 90th percentile, the Wald test does not result in a significant decrease in I^2 . We conclude that the number of inhabitants does not significantly influence the impact of air pollution and thermal stress on human morbidity. It has to be analysed in detail, if this is due to the fact that there is no difference in the correlation in urban and rural areas or due to the fact that the number of inhabitants is an inappropriate proxy for urbanization.

The introduction of the meta-variable “latitude” representing the north-south gradient within the studied administrative districts leads to a significant (UTCI $W = 0.03$, CAQI $W = 0.01$, MPI $W = 0.005$) or highly significant (PM10 $W = 0$) reduction of heterogeneity for all predictor variables (UTCI $I^2 = 20.1\%$, CAQI $I^2 = 32.0\%$, MPI $I^2 = 39.0\%$) except temperature. This means a reduction in heterogeneity by 2.7 to 4.7%.

The results from the meta-analysis including latitude reveal that overall the increase in RR is higher in the northern regions. The effect of air pollution, described by the CAQI, shows different patterns between northern and southern districts (Fig. 5a, b). The northern districts, at the 75th percentile of latitude, show a similar pattern as in the original model

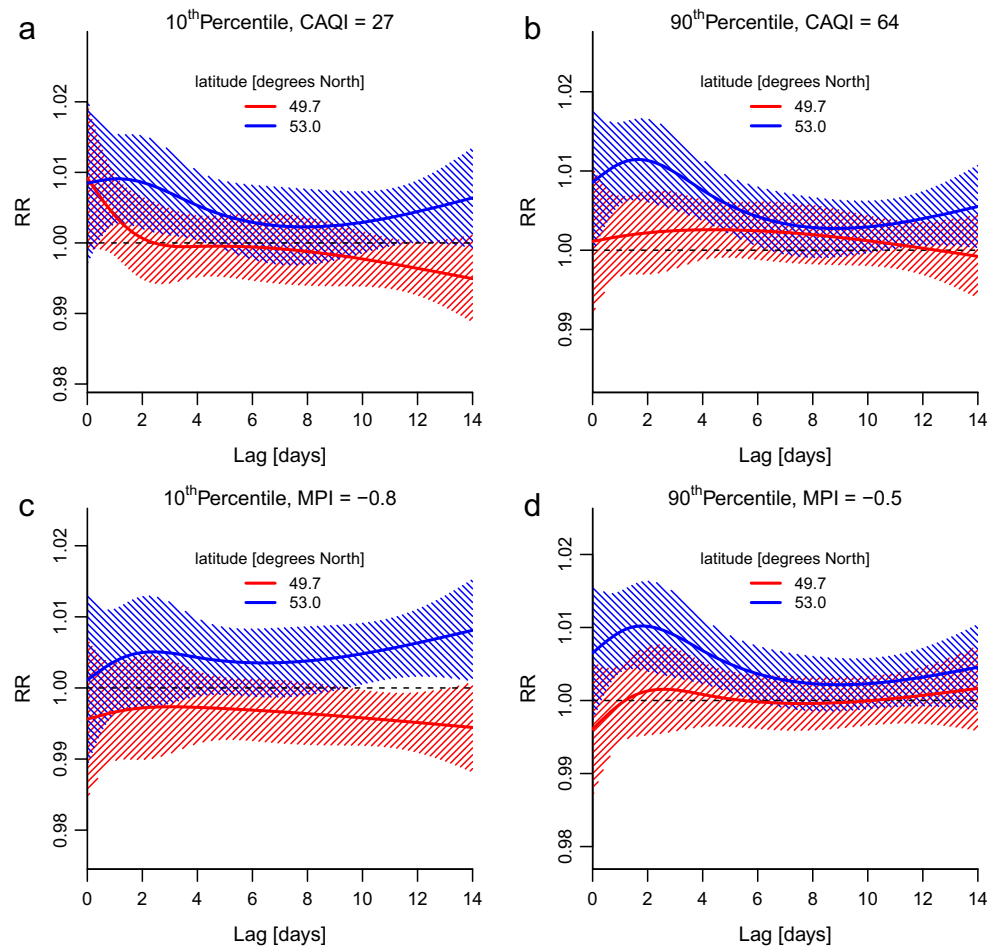
(Fig. 4). The southern districts, at the 25th percentile, exhibit a different pattern, not showing the delayed effect of high CAQI values after 2 days (Fig. 5b). High MPI values at the 75th percentile (Fig. 5d) show the delayed effect of air pollution at higher and lower latitude. Despite this pattern, the MPI shows a lower RR at all lags and for both high and low MPI values for the southern regions (Fig. 5c, d).

The results from the models including the meta-variable “latitude” indicate that the regional differences significantly influence the models. It is therefore important to detect the correlations between air quality, thermal stress and human morbidity based on the specific region of interest. In case a generalized association between those variables is needed, the driving factors for these differences have to be identified first, in order to be included in the models.

Discussion

We show that the short-term correlations between air quality, thermal stress and human health can be described by a DLNM using morbidity data. We included the variables max PM10 and mean air temperature in a DLNM with a maximum lag of 14 days for 28 regions in western Germany. Model strength improved using indices that include more than one pollutant or meteorological measures. The model including the aggregating air quality index MPI and the biometeorological index UTCI was identified as the strongest model out of the three calculated ones to describe the correlations along the north-south gradient in western Germany. This shows the suitability of these indices to describe the impact of air pollution and thermal stress on human health, also on health endpoints precedent to death. Li et al. (2015b) also showed the suitability of an air quality index for southern China, using mortality data. The model using the non-aggregating air quality index CAQI was only slightly worse than the previously mentioned model. The AIC for the model consisting of max PM10 and mean air temperature is about 1.3

Fig. 5 Predictor-specific summary for air quality indices at the 25th (red) and 75th (blue) percentile of the meta-variable latitude. 95% confidence interval is represented by the hatched area of the same colour. The results for CAQI are shown in the upper panel, showing low air pollution at the 10th percentile of CAQI (a) and high air pollution at the 90th percentile of CAQI (b). The results for MPI are shown in the lower panel, showing low air pollution at the 10th percentile of MPI (c) and high air pollution at the 90th percentile of MPI (d)



times higher, showing that the use of the indices is not only useful to communicate the current air quality or thermal stress level to the public. In order to clearly determine if indices or single measures perform better in the regression, it would be necessary to perform regressions for all possible combinations. Hence, it remains unclear if a model using for example the MPI and mean air temperature would perform even better than the three tested ones.

Comparing our study to studies on the correlation of air quality and or thermal stress on morbidity, we confirmed the findings (Breitner et al. 2014; Li et al. 2015a) that high and low temperatures lead to an increased relative risk. Also, the pattern of immediate response to high (Hajat and Kosatky 2010), but delayed response to cold temperatures was confirmed. Our findings are in line with the results from Perez et al. (2015), who showed a higher adverse effect of cold over heat stress. The pattern and resulting relative risks at the 10th and 90th percentile of mean air temperature and UTCI are similar, indicating that the use of the UTCI does not provide any additional information to the use of air quality in the model. However, the results for the 90th percentile of PM10 are not significant during the first 2 days. This indicates that for immediate effects of heat stress, the additional variables used in the UTCI improve the results. This underlines the

findings of Blazejczyk et al. (2012) who compare different more and less complex thermal indices. According to their work, the UTCI is suited to describe human thermal comfort in any situation, whereas more simple approaches may be suitable under specific meteorological conditions. Heat stress due to air temperature may be amplified by increased humidity or decreased by increased wind, leading to difficulties to solely describe heat stress by air temperature. Notwithstanding the missing significance for immediate heat stress represented by mean air temperature, we suggest using mean air temperature rather than a biometeorological index in order to improve and maintain comparability to other studies.

The studies from Li et al. (2015a, 2015b) showed an immediate impact of air pollution on morbidity with harvesting effects after 2–3 days. Contrary to this, our study showed a delayed effect of 2 days for the air quality indices, while showing an immediate effect for PM10. The 95% confidence interval for the non-aggregating index CAQI resembles the results of the non-aggregating air quality index used in the study by Li et al. (2015b). The delayed effect of the aggregated air quality index MPI might be caused by the fact that besides PM10 also ozone, NO₂ and SO₂ are always taken into account, even if they do not represent the highest pollutant on

this day. The use of indices increases model strength. Together with the significant increase in RR for both air quality indices compared to only PM10, this justifies the use of indices compared to single measures. As both air quality indices show a similar behaviour along the lag-response and dose-response relationship, it cannot be determined if an aggregating or non-aggregating index is performing better. As non-aggregating air quality indices are more frequently used, we suggest using this type of indices to ease comparison of the results.

The inclusion of the meta-variable latitude, describing the north-south gradient from Lower Saxony to Rhineland Palatine further improved the model results. Latitude significantly reduced the heterogeneity amongst the analysed 28 regions, and hence was identified as an important meta-variable for the model. This underlines the findings of Baccini et al. (2008), who analysed the effects of heat on mortality in 15 European cities and showed that the temperature-mortality relationship varies across geographical locations and climate conditions. A geographical dependence based on spatial synoptic classification, giving similar results to latitude, for the relationship between air quality and cardiovascular mortality was shown by Cakmak et al. (2016). The number of inhabitants per region, however, did not significantly reduce heterogeneity. Our analysis showed that the population at higher latitudes is more vulnerable to air pollution. Regarding thermal stress, no significant differences were found. The cause of the geographically different impact of air pollution on human morbidity could not be determined by this study, but the remaining heterogeneity might be associated to environmental conditions such as the composition of particulate matter (Krein et al. 2007, 2008) or other socio-economic factors (Stafoggia et al. 2006). Due to data protection issues in Germany, it is very difficult to acquire a complete dataset including socio-economic factors with a high spatial resolution. It might be considered to study these relationships in other European countries, e.g. Denmark (Lyngge et al. 2011), where datasets are more complete and easily available for scientific purposes.

Investigating the interaction between the air quality and thermal stress variables, we did not find a significant effect for any of the three models. This finding is contrary to the findings of Li et al. (2015a), Park et al. (2011) and Qian et al. (2008) who analysed the interaction for the association with mortality. The lack of accordance may be due to the fact that morbidity is less prone to interactive effects than mortality. In addition, Park et al. (2011) found the strongest effect modifications for SO₂ which was not analysed in the present study. All three aforementioned studies were conducted outside Europe. Regional differences in relations between air quality thermal stress and human health may contribute to the differences in the results. However, our results go in line with Breitner et al. (2014) who showed no significant interaction between air pollution and thermal stress on mortality in Germany. This underlines the assumption that the study area influences the results.

Conclusion

We found that using the indices MPI for air quality and UTCI for thermal stress increases the strength of the association between air quality, thermal stress and morbidity compared to a model using the single measures PM10 and mean air temperature. To determine if a combination of one index and a single measure would further increase the strength of the model, additional analyses are needed. The results showed heterogeneity along a north-south gradient within Germany, which was significantly reduced by including the meta-variable latitude, underlining the influence of geographical location on the association. The agreement of our findings with studies regarding mortality underlined the importance of these studies, while also showing some differences, regarding for example the interaction. Missing agreement with some other studies regarding interactions highlights the importance of studies in different regions and regarding the different health endpoints mortality and morbidity. Therefore, we suggest further investigation of the correlation between air quality, thermal stress and certain diseases such as cardiovascular or respiratory diseases.

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Compliance with ethical standards

Ethical approval Ethical approval to the use of hospital admission data was given by the “RDC of the Federal Statistical Office and the Statistical Offices of the federal states” together with the signature to statistical confidentiality in accordance with section 16 (7) of the Federal Statistics Act (BStatG). It is ensured by the contract not to be able to identify individual data from the published results.

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