Master's Thesis

submitted in partial fulfilment of the requirements of the

Master of Science in Epidemiology (MSc)

Charité – Universitätsmedizin Berlin

Berlin School of Public Health

The association between different timeframes of air pollution exposure and COVID-19 incidence, morbidity and mortality in German counties in 2020

26 November 2023

by Sophie Hermanns

Matriculation Number 4000265

Primary Advisor: Dr. Erika von Schneidemesser, Research Institute For Sustainability Helmholtz Centre Potsdam

Secondary Advisor: Dr. Susanne Koch, Charité Universitätsmedizin Berlin

Table of Contents

Statutory Declaration

I hereby declare that I have prepared this thesis independently and without the unauthorized assistance of third parties and that I have not used any sources or aids other than those indicated in this text. Data and concepts taken directly or indirectly from other sources are marked with an indication of the source.

The submitted written version of the work corresponds to the one on the electronic storage medium.

Furthermore, I assure that this work has not already been submitted in the same or a similar form as proof of performance elsewhere.

Berlin, November 26th 2023

Sophie Hermanns

List of Tables

List of Figures

1. Introduction

Ambient air pollution is a significant driver of disease and death in Germany. For 2018, the European Environment Agency attributes 63,000 premature deaths in Germany to particulate matter (PM) and 9,000 premature deaths to nitrogen dioxide (NO_2).[1] The Institute for Health Metrics and Evaluation estimates that air pollution was the 10th greatest health risk in Germany in 2019, with 29,252 attributable deaths or 3.05% of all deaths, while Lelieved et al. estimate that 11,000 annual deaths in Germany are attributable to road traffic emissions alone.[2,3] Many studies have shown that exposure to air pollution increases the risk and severity of several chronic health conditions, including pulmonary, cardiovascular and renal diseases as well as obesity and diabetes.[4] However, the link between air pollution and infectious diseases is less well understood. Since the outbreak of the COVID-19 pandemic, a growing body of research has looked specifically at the association between exposure to air pollutants and COVID-19 incidence, mortality and other non-fatal outcomes.[5]

The first confirmed COVID-19 case in Germany was reported on January 27th. Between early 2020 and June 2023, Germany's *Robert-Koch-Institut* (RKI) had counted 38.5 million confirmed cases and 174,400 associated deaths.[6] Yet only few studies so far have looked at the association between air pollution and COVID-19 in Germany.

Several mechanisms have been hypothesized by which air pollution could causally contribute to transmission and severe courses of COVID-19 and other diseases caused by SARS-viruses. First, air pollution exacerbates inflammatory response which may lead to worse health outcomes for patients with COVID-19.[7,8] Second, exposure to ambient air pollution exacerbates chronic diseases, in part due to increased inflammation, that have been linked to higher susceptibility and more severe outcomes from COVID-19.[9] Third, viruses may be able to attach to PM and thereby stay airborne for longer and increase transmission. There is no conclusive evidence for or against either of these three hypothesized mechanisms yet. Exposure timeframes may offer some insight: if SARS-CoV-2 was spread more easily in places with high PM pollution, this suggests effects on COVID-19 disease burden through short-term pollution exposure. If ambient air pollution affects COVID-19 primarily through chronic diseases, long-term exposure would be required to see effects. For heightened

inflammatory response as a causal pathway, both long-term and short-term exposure may have cumulative or distinct effects on vulnerability to COVID-19.
Most studies on COVID-19 and air pollution so far have focused on either long-term exposure to air pollution, over several years preceding the pandemic, or on short-term exposure immediately before or during the period in which infections, hospital admissions and deaths occurred.[5] However, many populations that experienced high ambient air pollution during the pandemic were also exposed to high pollution in the preceding years and vice versa. Making it difficult to compare or distinguish the associations between long- and short-term exposure and COVID-19.

In this study, we estimate the effects of both long- and short-term exposure to NO_2 and PM with a diameter of 2.5 µm or less ($PM_{2.5}$) on COVID-19 disease burden at the level of German counties (*Landkreise*) during the first wave of the pandemic in 2020. We build on the methods and data sources utilized in a study by Koch et al. (2022), which found positive and statistically significant associations between NO_2 between 2010 and 2019 on COVID-19 outcomes. We provide a new analysis of the effects of long-term exposure, considering 10 years and 2 years prior (2010-19 and 2018-19) and, additionally, estimate the effects of short-term exposure (48 hours, 7 days and 4 weeks). While most ecological studies on air pollution focus on COVID-19 incidence and mortality, we, like Koch et al., leverage data from German hospitals to include admission on intensive care units and mechanical ventilation of COVID-19 patients in the analysis.[10]

2. Methods

2.1 Setting and population

The unit of analysis are German counties (*Landkreise* and *kreisfreie Städte*), which correspond to the Nomenclature of Territorial Unit for Statistics level 3 (NUTS-3). Most large cities and some smaller towns constitute their own counties. On March 15th, schools in Germany and national borders closed, followed by restaurants, shops and churches. Federal states started imposing social distancing rules from March 22nd onwards, limiting meetings between different households to two persons. Some states also restricted residents' movement outside their homes. By April 15, these rules started to be lifted. Schools reopened on May 4th and borders started to be re-opened from May 15.[11] Different regions were affected differently by the first wave, with high incidence in the large southern states of Bavaria and Baden-Württemberg and large cities, as well as cluster events during the February carnival festivities in the Rhine region. Many counties in the north and east were comparatively less affected during the first wave (see figure 3).

2.2 Data sources

2.2.1 COVID-19 data

The DIVI-register tracks intensive care capacities and COVID-19 patient numbers in German hospitals.[12] Daily reporting to the register became mandatory for all hospitals on April 16, 2020. Data on COVID-19 patient-days on intensive care units and on mechanical ventilation was extracted for the period between April 16 and May 16, 2020. Using demographic data, we calculated the rate of patient-days per 100,000 residents.

The Robert-Koch-Institute (RKI), Germany's national public health institute, provides a public-access database of COVID-19 cases and deaths reported for each county by local public health offices.[13] Incidence (based on reported date of symptom onset) and mortality for each county were calculated per 100,000 residents. To account for the fact that counties started being affected by the pandemic at different time-points, we calculated the number of days between the first officially reported case and the start of the study period as a control variable.

The database only included cases after the patients tested positive and tests in the spring of 2020 were limited to patients who showed symptoms. Therefore, case numbers do not reflect asymptomatic cases. Associations modeled in this paper may indicate the effect of air pollution on the development of symptoms rather than on an increased risk of infections. A sero-epidemiological study in one German community affected by a super-spreader event in February 2020 found that the number of infections was five-fold higher that the number of reported cases.[14]

All 401 counties in Germany reported cases and deaths from January onwards. However, only 396 counties reported to the DIVI-register and consistent data is only available from April 16th onwards. The primary analysis of all outcomes is therefore limited to the DIVI-reporting counties and the period from April 16 to May 16, when most restrictions on social meetings, shops and schools began to be lifted. However, looking at the entire first wave starting on March 4th, the day social restrictions were imposed in most of the country, only 18% of cases and deaths occurred in the shorter period starting on April 16th. Therefore this longer period, which aligns with the RKI's definition of the first wave, is used for secondary analysis.[11]

2.2.2 Air pollution data

As in Koch et al (2022), the APExpose dataset (version 2.0) was used to analyze the association between long-term exposure to air pollution and COVID-19 outcomes. The data combines observed data from the European Environmental Agency's Airbase, with modelled global reanalysis data from the Copernicus Atmospheric Monitoring Service (CAMS) to create a complete dataset for all German counties for the period 2010 - 2019. The data includes parameters for nitrogen dioxide (NO_2), nitrogen oxide (NO), ozone (O_3), and particulate matter with an aerodynamic diameter smaller than 2.5 µm and 10 µm ($PM_{2.5}$ and PM_{10}), as well as three different scenarios (urban, rural, average). The parameters for NO_2, NO, $PM_{2.5}$ and PM_{10} are given as annual means while O_3 is provided as maximum value over an 8-hour period. To analyze the effects of long-term exposure to air pollution, we calculated the means of each pollutant in each county over the ten-year period (January 2010 – December 2019) and a two-year-period (2018 – 2019) prior to the COVID-19 outbreak.[15,16]

To analyze the association of short-term air pollution exposure and COVID-19 outcomes, a new dataset was created, based on the same sources and methodology as APExpose at the daily time resolution. The data contains daily observation for the period from March 4th to May 16th, 2020, with values for NO_2, O_3 and $PM_{2.5}$, averaged over the preceding 48-hour, 7-day, and 4-week time periods of interest.

2.2.3 Demographic data and German Index of Social Deprivation

The Federal Statistical Office of Germany provides data for each county on population size, population in each age and sex group as well as area size. Data from 2019 was used to calculate population density and the share of the population aged over 64 years, as well as the fraction of the population that is female. Population density is assumed to increase risk of transmission and male sex and old age have been linked to increased risk of severe outcomes and death from COVID-19.[17,18]

The German Index of Social Deprivation (GISD), developed by RKI, is a measure of relative regional socio-economic disadvantage. The GISD indicators are selected to align with the concept of individual socio-economic status (SES) in social epidemiology, which combines education, occupation, and income dimensions.The index score is on a scale from 0 to 1. A higher score indicates more deprivation.[19] For each county, we calculated the mean GISD-score between 2010 and 2019. Several ecological studies in Germany and other OECD countries have shown an association between income/ social status and COVID-19 incidence. In the first wave of the pandemic, regions with higher income and education experienced higher incidence, possibly due to more international business and leisure travel.[20,21] Studies found increased risk of mortality for socially deprived regions in Germany starting from the second wave of the pandemic, though findings for the first wave are less conclusive.[20,22] Studies in the USA and UK have found increased risks for hospitalization and death for patients and regions with greater social deprivation.[23–27]

2.4 Statistics

NO and PM_{10} are highly correlated with NO_2 and $PM_{2.5}$, respectively, therefore no separate models were included in the main analysis. Annual mean O_3 pollution (based on measurements of 8-hour daily maximums) exceeded WHO-recommended thresholds in all counties between 2010 and 2019, but remained low during the first wave of the pandemic and was therefore excluded from the main analysis. Separate models for mean annual NO_2 and mean annual $PM_{2.5}$ were fitted for the ten- and two-year exposure periods and as averages for the 48-hours, 7-days and 4-weeks preceding each date. Sensitivity analyses were conducted with tri-pollutant models with NO_2, $PM_{2.5}$ and O_3 as combined exposures (see tables S1-2).

Separate models were fit for each outcome, pollutant and exposure time-window. The analysis has four outcome variables: new cases (incidence), new deaths (mortality), patient-days on ICUs and patient-days on mechanical ventilation. All outcomes were calculated as rates per 100,000 residents. There were two long-term exposure periods, from 2010 to 2019 (ten years) and 2018 to 2019 (two years). For the long-term exposures, pollution and COVID-19 disease parameters were calculated as means per county. Exposures and outcomes were included for each date in a given county. The main analysis is limited to dates and counties for which data on patient-days on ICUs and mechanical ventilation were available through the DIVI-register, between April 16th and May 16th 2020. A sensitivity analysis includes data for incidence and mortality from 401 counties between March 4th and May 16th 2020 (see tables S4 and S6).

Negative binomial distributions were chosen due to overdispersion of the outcome variables. Because variables in the model operate at different scales, the control variables were scaled. Since many counties experienced some days without new cases or deaths or patients on intensive care, the data used to model short-term exposure contained a high proportion of zeros (27 – 95%, varying by outcome). Therefore, zero-inflation was applied. This was not necessary for the long-term exposure models, as only few counties reported zeros for outcomes aggregated over the entire study period (0 – 14%). To account for the repeat measurements at county-level and unmeasured factors affecting outcomes, random intercepts were fit for each county.

Statistical analysis was conducted in R Statistical Software (version 4.3.1). Data processing was conducted with the dplyr-package and models were fit with the MASS- and glmmTMB-packages.[28–31]

3. Results

3.1 Descriptive analysis

3.1.1 NO_2 and $PM_{2.5}$

The data for analysing short-term exposure contains 11,822 observations from 396 counties between April 16th and May 16th 2020. Data for the secondary analysis covering the entire first wave from March 4th to May 16th included 29,269 observations from 401 counties.

Mean $PM_{2.5}$ and NO_2 pollution was slightly lower in 2018-19 ($PM_{2.5}$: 12.5 µg/ m^3; NO_2: 16.6 µg/ m^3) than in 2010-2019 ($PM_{2.5}$: 13.1 µg/ m^3; NO_2: 17.8 µg/ m^3). The mean values of both pollutants averaged over two-, seven- and 28-day periods in the spring of 2020 were lower than the annual means from the preceding years. Mean pollution was only slightly lower between April and May 2020 than in the longer period between March and May (see figure 1).

The counties with the highest pollution-levels between April and May 2020 were mainly located in the industrial Rhine-area: Bonn, Duisburg, Cologne and Dortmund all had mean NO_2 values of over 24 μg/m^3, while Gelsenkirchen, Essen, Dortmund and Monchengladbach had mean $PM_{2.5}$ values over 12 μg/m^3. The lowest pollution levels were recorded in parts of southern Germany and in the northeast. This broadly matches the geographic patterns of pollution averaged over the preceding ten and two years, with a few divergences: over the 2010-2019 period, Berlin had the 5th highest recorded annual mean of $PM_{2.5}$ but ranked only 133rd in the April-May 2020 period, and Frankfurt and Mainz, both in the Rhine-Main region in southwestern Germany, had the highest and third-highest levels of NO_2 -pollution and ranked 23rd and 29th in the spring of 2020 (see tables S12 – 15).

Over the period 2010-2019, all counties included in this study exceeded the WHO-recommended levels of concentration for $PM_{2.5}$ (5 μg/ m^3*)*. For NO_2, only 7.2% of counties stayed below the WHO-recommended threshold of 10 μg/m^3 between 2010 and 2019 (10.2% between 2018 and 2019). Between March and May 2020, 18.2% of counties had, on the mean, below-threshold levels of NO_2 and none had below-threshold levels of $PM_{2.5}$. However, the figures from spring 2020 are only indicative, as the WHO-thresholds are meant to evaluate annual means, not short-term pollution.

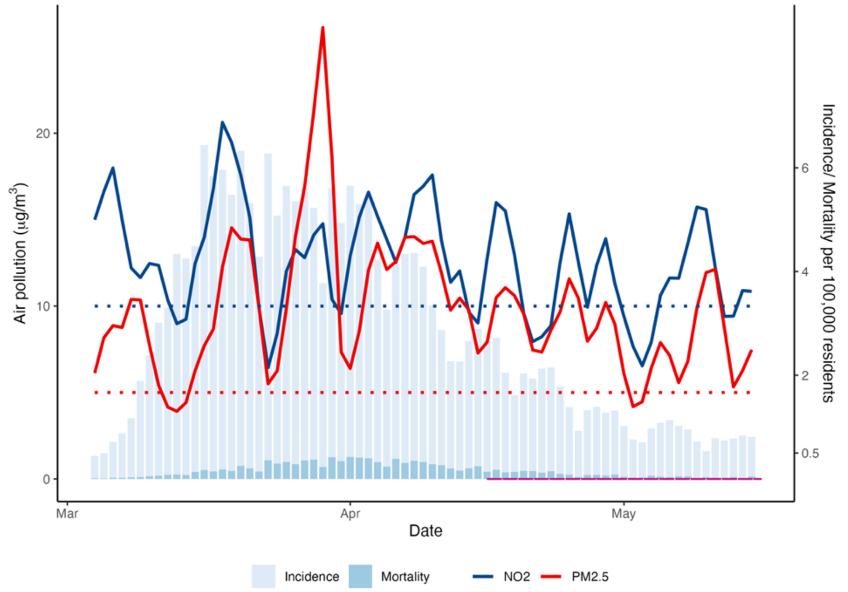

Figure 1: Incidence and mortality and NO_2-levels and $PM_{2.5}$-levels over time in March – May 2020. Pollution variables for a given date are given as average of the previous 48 hours. The dashed coloured lines are WHO-recommended thresholds annual average levels of NO_2 and $PM_{2.5}$. The pink line indicates the period for which data is available in the DIVI-register.

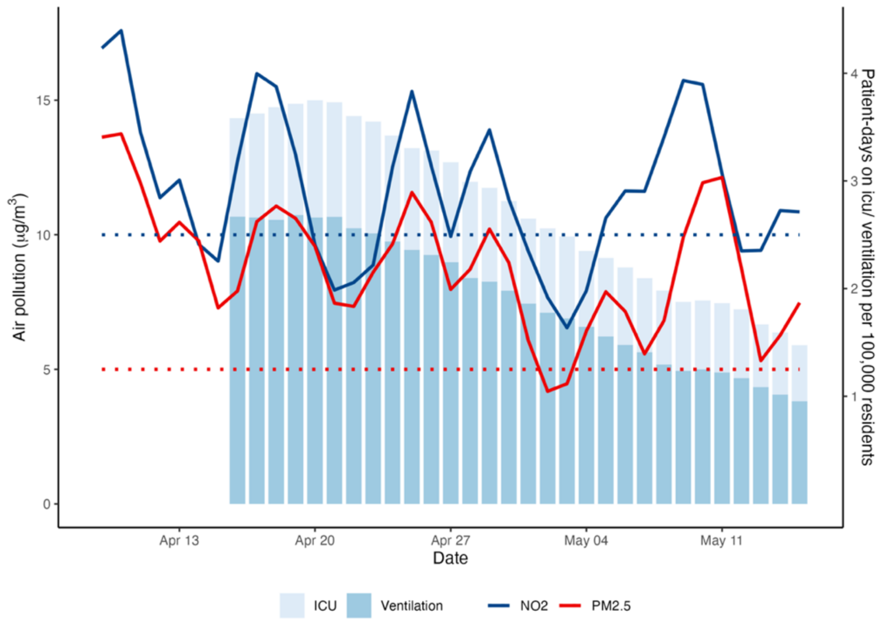

Figure 2: Patient-days on ICU and on mechanical ventilation and NO_2-levels and $PM_{2.5}$-levels over time in April – May 2020. The dashed coloured lines are WHO-recommended thresholds for annual average levels of NO_2 and $PM_{2.5}$.

3.1.2 Disease outcomes

Between April 16th and May 16th, in the 396 counties that reported to the DIVI-register, a total of 64,621 patient-days on ICUs and 46,234 patient-days on mechanical ventilation were recorded, as well as 31,660 new cases and 1,615 deaths. These made up 18% of all 173,160 new cases and of 8,815 deaths recorded between March 4th and May 16th. The average county reported 40.2 cases and 2.2 deaths per 100,000 residents between April 16th and May 16th, 54.5 patient-days on ICUs and 37.1 on mechanical ventilation per 100,000 residents (see table 1).

Of the ten counties with the highest reported incidence and mortality, eight and nine, respectively, are located in the federal state Bavaria. Seven of the counties with the highest rate of patient-days on ICU and on mechanical ventilation are also located in Bavaria. Three of the ten counties with the highest mortality (Tirschenreuth, Neustadt a.d. Waldnaab, and Langenzenn) did not report to the DIVI register on ICU and mechanical ventilation (see tables S9 and S10). Of the top 100 counties (top quartile) with the highest mean NO_2 pollution, all but one reported to the DIVI-register. Of the top 100 counties with the highest mean $PM_{2.5}$ pollution, 96 reported to the DIVI-register.

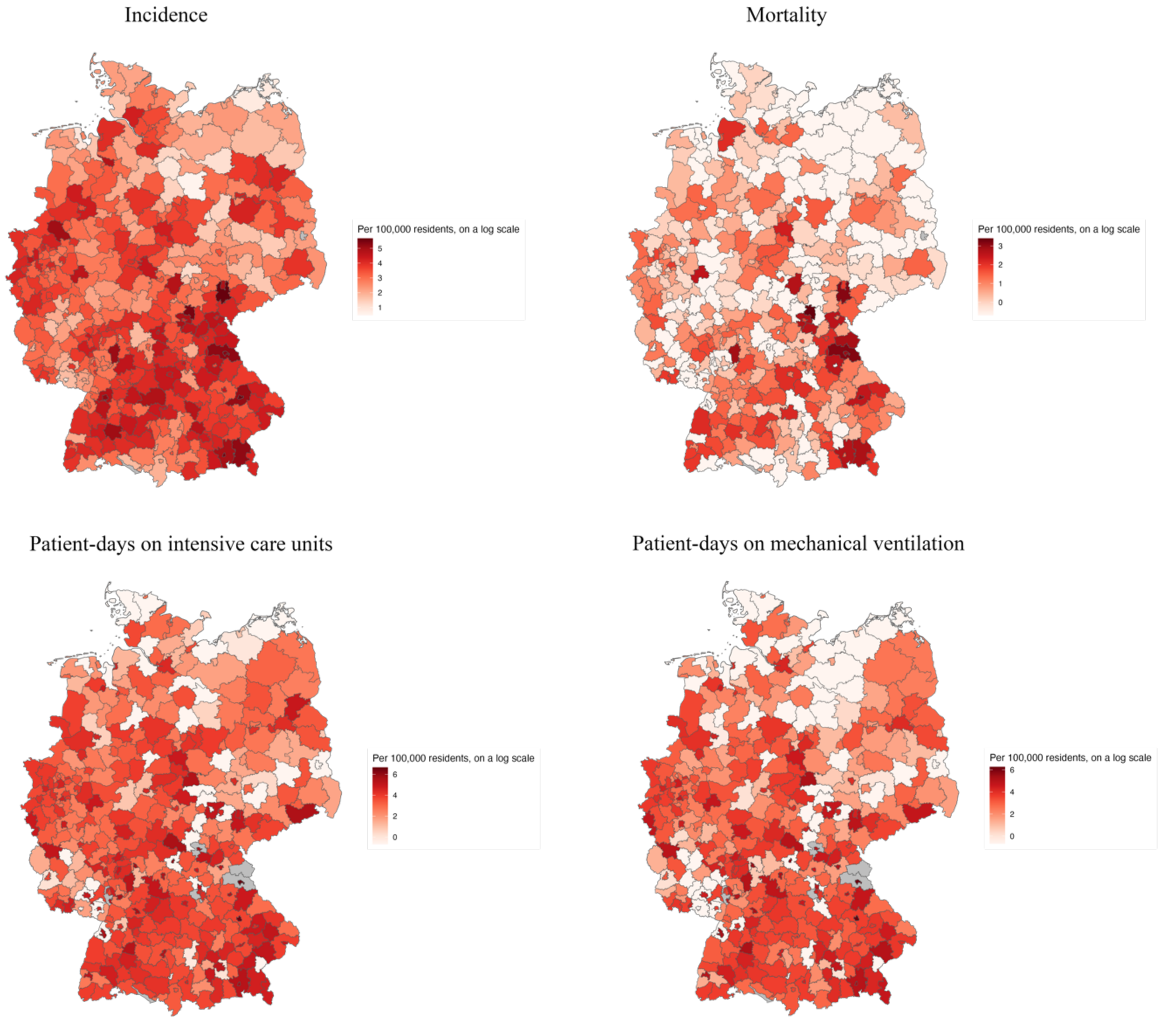

Figure 3: COVID-19 disease parameters per county for the period April 16th to May 16th 2020. Darker colors indicate higher values. Counties with missing data are marked in grey.

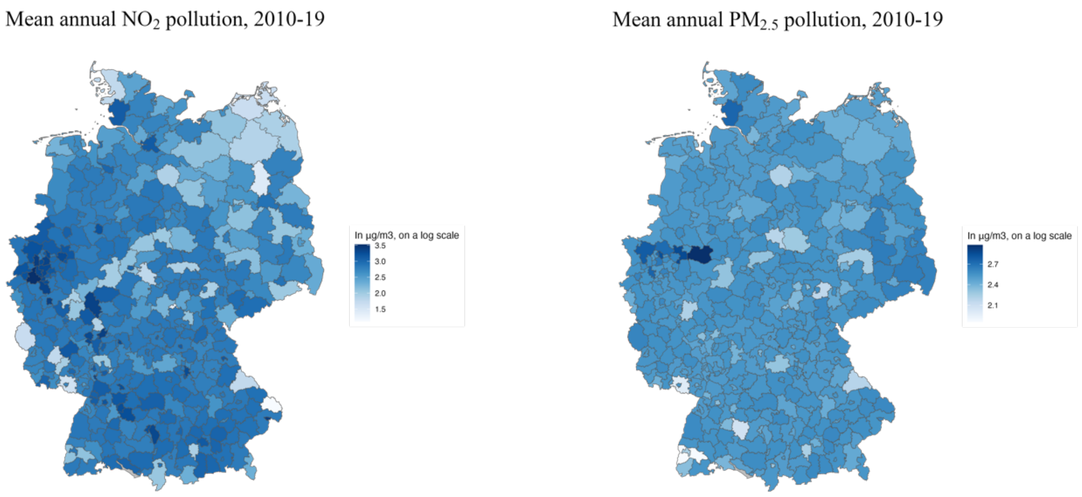

Figure 4: Air pollutants per county as mean of the annual means for the period 2010-2019. Darker colors indicate higher values.

Table 1: Disease outcomes and air pollution levels by state. All disease parameters are given as means per 100,000 residents for the entire period April 16 – May 16 2020. PM2.5 and NO2 levels are proved as means of the annual means for the periods 2010 – 2019 and 2018 – 2019. For the period April 16 – May 16 2020, the means of the 48-hour means per county were calculated. Standard deviations for all parameters are given in parentheses.

	COVID-19 Disease Parameters				Air Pollutants					
	April - May 2020				2010 - 2019		2018 - 2019		April - May 2020	
State	**Incidence**	**Mortality**	**ICU**	**Mechanical ventilation**	**$PM_{2.5}$ (µg/m^3)**	**NO_2 (µg/m^3)**	**$PM_{2.5}$ (µg/m^3)**	**NO_2 (µg/m^3)**	**$PM_{2.5}$ (µg/m^3)**	**NO_2 (µg/m^3)**
Baden-Württemberg	53.6 (39.6)	2.7 (2.3)	78.7 (68.9)	52.9 (49.6)	12.8 (1.3)	19.6 (3.8)	12.1 (1.4)	18.4 (3.7)	8.1 (2.4)	12.3 (5.3)
Bayern	60.7 (49.1)	3.8 (5.1)	90.7 (125.0)	63.1 (87.0)	12.9 (0.6)	18.6 (3.4)	12.5 (0.8)	17.5 (3.8)	8.4 (2.4)	11.2 (4.4)
Berlin	33.6 (-)	1.4 (-)	74.3 (-)	59.6 (-)	16.7 (-)	20.0 (-)	13.7 (-)	18.4 (-)	8.4 (2.6)	13.6 (3.8)
Brandenburg	27.2 (23.1)	0.9 (1.1)	27.2 (35.2)	12.6 (13.8)	14.0 (1.4)	14.0 (3.4)	12.7 (0.8)	12.6 (3.6)	7.4 (2.5)	8.0 (2.8)
Bremen	82.5 (47.0)	3.3 (1.5)	66.4 (53.0)	38.5 (25.2)	13.4 (0.3)	21.8 (0.4)	12.8 (0.1)	20.0 (0.7)	8.2 (3.2)	13.4 (5.0)
Hamburg	36.4 (-)	3.1 (-)	82.0 (-)	67.5 (-)	14.1 (-)	23.5 (-)	12.9 (-)	22.9 (-)	8.1 (2.8)	16.9 (4.7)
Hessen	39.3 (33.4)	2.0 (3.4)	56.5 (44.1)	40.8 (35.7)	13.2 (0.5)	18.2 (6.1)	12.4 (0.9)	16.9 (6.5)	8.3 (2.6)	11.8 (6.7)
Mecklenburg-Vorpommern	6.1 (2.9)	0.1 (0.3)	6.1 (8.1)	3.7 (5.3)	12.6 (0.4)	10.5 (4.4)	12.0 (0.8)	10.0 (4.4)	7.1 (3.3)	6.6 (4.0)
Niedersachsen	21.1 (18.6)	1.3 (2.0)	27.1 (31.9)	18.3 (25.2)	12.6 (0.8)	15.6 (3.0)	12.2 (0.9)	14.6 (2.8)	8.0 (2.3)	9.6 (3.5)
Nordrhein-Westfalen	42.0 (26.1)	1.9 (2.1)	47.1 (31.1)	34.2 (26.9)	14.0 (1.3)	21.9 (4.4)	13.3 (1.5)	20.8 (4.8)	9.4 (3.1)	15.9 (7.2)
Rheinland-Pfalz	23.6 (20.2)	1.2 (1.7)	36.8 (47.4)	23.7 (36.5)	12.9 (1.1)	17.1 (5.4)	12.3 (1.1)	15.8 (5.5)	8.6 (2.6)	11.1 (5.6)
Saarland	31.8 (11.8)	2.7 (3.0)	46.2 (39.0)	21.4 (17.7)	13.1 (0.5)	17.7 (2.5)	12.5 (0.7)	16.3 (2.6)	8.3 (2.3)	11.0 (3.3)
Sachsen	23.3 (19.3)	1.1 (1.6)	39.5 (64.1)	23.0 (30.7)	13.5 (1.0)	16.4 (3.8)	12.7 (1.3)	13.9 (3.9)	8.0 (2.3)	9.6 (3.7)
Sachsen-Anhalt	14.8 (13.4)	0.6 (1.1)	17.7 (21.9)	10.0 (15.3)	13.7 (1.2)	15.8 (3.3)	12.5 (0.9)	14.4 (3.6)	8.1 (2.6)	10.2 (3.8)
Schleswig-Holstein	19.7 (18.4)	0.7 (1.4)	13.5 (13.1)	10.0 (10.5)	12.6 (0.8)	14.7 (3.4)	12.6 (1.1)	13.8 (3.7)	8.1 (2.6)	10.8 (5.0)
Thüringen	48.3 (75.5)	3.8 (7.8)	53.1 (64.6)	37.5 (49.6)	12.7 (1.2)	15.7 (4.5)	12.1 (1.3)	14.3 (4.3)	8.6 (2.6)	9.9 (3.7)
Total	**40.3 (40.4)**	**2.2 (3.7)**	**54.4 (76.2)**	**37.1 (54.0)**	**13.1 (1.1)**	**17.8 (4.7)**	**12.5 (1.1)**	**16.6 (4.9)**	**9.8 (4.3)**	**12.6 (6.0)**

3.2 Regression analysis

In our analysis, for the long-term exposure models for 10- and 2-year timeframes, $PM_{2.5}$ has no statistically significant association with any outcome. In contrast, for NO_2, the long-term exposure models show positive and statistically significant associations with all the health outcomes examined: a one unit (1 µg/ m^3) increase in mean annual NO_2 between 2010 and 2019 was linked to a 3.4% (95% CI 1.010 – 1.058) increase in incidence, a 4.2 % (95% 95% CI 0.998 – 1.079) increase in mortality, an additional 5% (95% CI 1.017 – 1-084) patient-days on ICU and a 5.7% (95% CI 1.021 – 1.095) additional patient-days on mechanical ventilation. The effect estimates for the exposure timeframe 2018-19 are very similar and within less than 1 percentage point of the 2010-19 estimates. All estimates were statistically significant at the 5%-level, except for the estimated effect on mortality. When the full first wave was included in the model, the estimate increased slightly (4.2%; 95% CI 1.015 – 1.069) and achieved statistical significance. Further sensitivity analyses employing a tri-pollutant model, which accounted for NO_2, $PM_{2.5}$ and O_3, yielded results that were consistent with the primary findings.

In the models for short-term exposure to NO_2 and $PM_{2.5}$, a mean increase of 1 µg/ m^3 over the preceding 2, 7 or 28 days is associated with an increase in all COVID-19 disease parameters and all estimates are statistically significant at the 5%-level. The effect sizes are generally highest for pollution averaged over seven days preceding disease outcomes and larger in the $PM_{2.5}$-models than in the NO_2 -models. A mean increase of 1 µg/ m^3 in $PM_{2.5}$ in the 7 preceding days was associated with an 18.2 % (95% CI 1.163 – 1.201) increase in incidence and a 36.8% (95% CI 1.278 – 1.464) increase in mortality. A mean increase of 1 µg/ m^3in NO_2 in the 7 preceding days was associated with an 3.6% % (95% CI 1.023 – 1.049) increase in incidence and an 8.1% (95% CI 1.037 – 1.127) increase in mortality. Figure 5 shows the exponentiated effect estimates of $PM_{2.5}$ and NO_2 on COVID-19 outcomes, adjusting for socio-demographic data. Each estimate is derived from a separate model.

For patient-days on ICU and on mechanical ventilation, the effects are largest after 28 days, with increases of 1 µg/m^3 in either pollutant associated with increases of over 20% for both outcomes. However, these results should be regarded as only indicative, as the models for both outcomes exhibited poor fit and high dispersion values, ranging from 94 to 10^9, with a median of 9×10^6.

The models' random effects indicated substantial variability at the county level (mean variance = 1.83, mean standard deviation = 1.33). This suggests that there are distinct county-specific patterns.

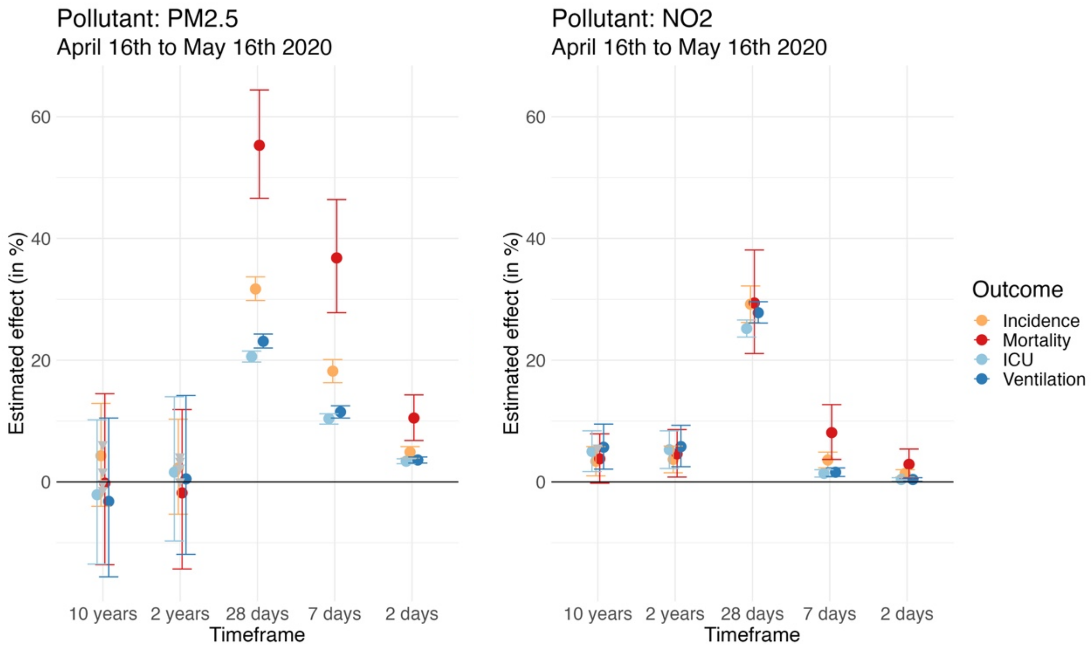

Figure 5: Effect estimates for the association of $PM_{2.5}$ and NO_2 on COVID-19 outcomes. Bars indicate 95% confidence intervals. Statistically non-significant estimates are marked with a grey triangle. Each estimate is derived from a separate, single-pollutant model.

4. Discussion

Germany, like most European countries, saw significant reductions in NO_2 (30%) and PM_{10}-levels (10%) in April 2020, compared to previous years, likely due to lockdown measures.[1] Even at these reduced levels, we found short-term exposure effects of $PM_{2.5}$ and NO_2 on COVID-19 disease burden. NO_2 also appears to have long-term effects, whereas no significant association was observed between long-term exposure to $PM_{2.5}$ and increased COVID-19 risks, indicating possible different causal pathways for the two pollutants. The effects over a 2-year period were lower compared to those over 10 years, potentially reflecting a decrease in pollution levels, especially in 2019. The short-term effects were most pronounced with exposure to pollution in the preceding 7 and 28 days. This suggests that short-term pollution exposure heightens susceptibility to developing COVID-19 symptoms and increases the risk of severe and fatal outcomes. These effects are measurable as soon as 48 hours post-exposure to higher levels of pollution and intensify with longer exposure over one to four weeks. Studies and meta-analyses from similar contexts estimated the mean incubation period in spring 2020 as 6.5 days and the mean duration between symptom onset and hospitalization as 5.7 days.[32,33] The significant impact of the 7-day exposure window on severe outcomes therefore suggests that pollution exacerbates the course of existing infections.

These findings are consistent with other studies that have found positive and statistically significant associations between air pollution and COVID-19. In a systematic review of 139 studies on long-term exposure, Bhaskar et al. found that 127 reported statistically significant positive associations.[34] Carballo et al reviewed 355 pollutant-COVID-19 estimates from 116 long- and short-term exposure studies and found that approximately half reported positive significant associations for incidence (52.7%) and mortality (48.1%), with a slightly lower rate for non-fatal severe outcomes (41.2%).[5] Similarly, a meta-analysis of studies using data from individual patients reported 66% higher odds of COVID-19 infection and 127% higher odds for severe non-fatal outcomes per additional 10 µm/g of $PM_{2.5}$, in addition to a positive but statistically not significant association with mortality.[35] Another study of short-term air pollution exposure and COVID-19 during spring 2020 in Germany found positive effects of PM_{10} on incidence and mortality, with the most pronounced effects five to seven days after illness onset.[36]

High levels of air pollution cause oxidative stress and inflammation.[37, 38] The SARS-CoV-2 spike protein binds to cells' receptors for the angiotensin-converting-enzyme 2 (ACE-2), which plays an important role in regulating inflammation. Air pollution and COVID-19 may therefore have an additive effect on the body's inflammatory response. Air pollution may re-enforce SARS-CoV-2 effect on the body's inflammatory response. Many COVID-19 patients with severe outcomes experienced inflammation in the lungs leading to pneumonia, acute respiratory distress syndrome and death. Another common complication and cause of death among COVID-19 patients was multi-organ damage and failure, which is also linked to inflammation.[39] Some COVID-19 patients also experienced cardiovascular complications, exacerbated by chronic health conditions, for which people exposed to air pollution have elevated risks.

The results of this and other studies are thus compatible with multiple causal pathways through which both long- and short-term exposure to high levels of NO_2 and $PM_{2.5}$ could contribute to higher rates of symptomatic COVID-19 cases, severe illness and death: Long-term exposure may contribute through increased prevalence of chronic diseases and through higher inflammation, while short-term exposure right before and during infection worsens inflammation, which together with the heightened inflammatory response caused by SARS-CoV-2 may lead to severe outcomes such as respiratory failure or multi-organ failure. Other factors, such as further physical spread of virus through particle matter, may also play a role, though this specific mechanism cannot explain the effects of NO_2.

4.1 Limitations

COVID-19 incidence and outcomes, as well as individual-level air pollution exposure, are determined by many different factors, some of which are not yet fully understood. Unmeasured confounding is therefore likely. For example, regional variations in prevention measures such as social distancing regulations are not accounted for in the model. Data from public health offices is likely to be incomplete and dating of case notifications may not accurately reflect disease onset. Case numbers are likely to be an underestimate and do not account for asymptomatic cases. Moreover, the data on cases and deaths has reporting-lags on weekends, when public health offices were closed. Data for Saturdays, Sundays and Mondays (when the weekend notifications were processed) therefore likely has systematic errors. Data on ICU occupancy and mechanical ventilation was collected primarily for resource coordination in a health emergency, not scientific purposes, and may contain systematic and unsystematic errors.

The ecological study design does not allow for adjustment on patient-level risk factors. Some counties, especially major cities such as Berlin, Hamburg or Munich, are very large and heterogeneous. They encompass sub-populations that experience very high and very low levels of social deprivation, that skew very young and very old, live near traffic and in green suburbs. In this study, we could not differentiate between these sub-populations or capture complexities in pollution exposure through factors such as mobility. For example, the county Hochtaunuskreis has some of the lowest levels of pollution in Germany, but many residents work in nearby Frankfurt and Mainz, which have some of the highest levels of pollution. Similarly, not all patient-days on ICUs may be due to residents of the county in which the reporting hospital is located: three of the ten counties with the highest reported incidence do not have ICUs and residents who required intensive care and ventilation were therefore likely reported by hospitals in nearby counties. Further research using patient-level data or disaggregating population-data by age-groups and sex could mitigate this limitation to some extent.

5. Conclusion

Our findings contribute to the emerging literature on the link between COVID-19 and air pollution by showing a positive association between $PM_{2.5}$ and NO_2 on incidence and mortality between April and May 2020 in Germany, with the strongest association one to four weeks after exposure to high pollution levels. These findings contribute to a larger evidence-base on the negative effects of air pollution on population health. Not only would reductions in air pollution ease the burden of many chronic diseases on the German health system, improved air quality might also make populations more resilient against the now endemic SARS-COV-2 and similar infectious diseases in the future. Further research is needed to contrast and distinguish the effects of long- versus short-term pollution exposure. If a causal link between short-term air pollution and specific types of infectious diseases were confirmed, additional tools could be deployed during future health emergencies, such as limiting industrial production and construction projects in population centers, and some existing tools, such as indoor air filters, facial masks or lockdowns, could have additional justification.

6. References

1. Air quality in Europe - 2020 report [Internet]. European Environment Agency (EEA); 2020 [cited 2023 Nov 26]. Report No.: 09/2020. Available from: https://www.eea.europa.eu/publications/air-quality-in-europe-2020-report

2. Institute for Health Metrics and Evaluation (IHME). Global Burden of Disease (GBD) Compare [Internet]. 2020 [cited 2023 Sep 15]. Available from: https://vizhub.healthdata.org/gbd-compare/

3. Lelieveld J, Pozzer A, Pöschl U, Fnais M, Haines A, Münzel T. Loss of life expectancy from air pollution compared to other risk factors: a worldwide perspective. Cardiovascular Research. 2020 Sep 1;116(11):1910–7.

4. Pryor JT, Cowley LO, Simonds SE. The Physiological Effects of Air Pollution: Particulate Matter, Physiology and Disease. Frontiers in Public Health [Internet]. 2022 [cited 2023 Nov 4];10(2). Available from: https://www.frontiersin.org/articles/10.3389/fpubh.2022.882569

5. Hernandez Carballo I, Bakola M, Stuckler D. The impact of air pollution on COVID-19 incidence, severity, and mortality: A systematic review of studies in Europe and North America. Environ Res. 2022 Dec;215(Pt 1):114155.

6. Robert-Koch-Institut. Antworten auf häufig gestellte Fragen (FAQ) zu akuten Atemwegserkrankungen und COVID-19. [Internet]. 2023 [cited 2023 Oct 10]. Available from: https://www.rki.de/SharedDocs/FAQ/COVID-19/FAQ-gesamt.html?nn=13490888

7. Lai A, Chang ML, O'Donnell RP, Zhou C, Sumner JA, Hsiai TK. Association of COVID-19 transmission with high levels of ambient pollutants: Initiation and impact of the inflammatory response on cardiopulmonary disease. Science of The Total Environment. 2021 Jul 20;779:146464.

8. Paital B, Agrawal PK. Air pollution by NO2 and PM2.5 explains COVID-19 infection severity by overexpression of angiotensin-converting enzyme 2 in respiratory cells: a review. Environ Chem Lett. 2021 Feb 1;19(1):25–42.

9. Mehta S, Shin H, Burnett R, North T, Cohen AJ. Ambient particulate air pollution and acute lower respiratory infections: a systematic review and implications for estimating the global burden of disease. Air Qual Atmos Health. 2013 Mar 1;6(1):69–83.

10. Koch S, Hoffmann C, Caseiro A, Ledebur M, Menk M, von Schneidemesser E. Air quality in Germany as a contributing factor to morbidity from COVID-19. Environ Res. 2022 Nov 1;214(Pt 2):113896.

11. Schilling J, Buda S, Fischer M, Goerlitz L, Grote U, Haas W, et al. Retrospektive Phaseneinteilung der COVID-19- Pandemie in Deutschland bis Februar 2021. Epidemiologisches Bulletin. 2021;(15).

12. Robert-Koch-Institut. Intensivkapazitäten und COVID-19-Intensivbettenbelegung in Deutschland [Internet]. Zenodo; 2023 [cited 2023 Apr 4]. Available from: https://zenodo.org/record/7798669

13. Koch-Institut R. SARS-CoV-2 Infektionen in Deutschland [Internet]. Zenodo; 2023 [cited 2023 Jul 17]. Available from: https://zenodo.org/record/8153118

14. Streeck H, Schulte B, Kümmerer BM, Richter E, Höller T, Fuhrmann C, et al. Infection fatality rate of SARS-CoV2 in a super-spreading event in Germany. Nat Commun. 2020 Nov 17;11(1):5829.

15. Caseiro A, von Schneidemesser E. APExpose_DE, an air quality exposure dataset for Germany 2010–2019. Sci Data. 2021 Oct 28;8(1):287.

16. Caseiro A, von Schneidemesser E. APExpose_DE. Zenodo; 2021.

17. Booth A, Reed AB, Ponzo S, Yassaee A, Aral M, Plans D, et al. Population risk factors for severe disease and mortality in COVID-19: A global systematic review and meta-analysis. PLoS One. 2021;16(3):e0247461.

18. Dessie ZG, Zewotir T. Mortality-related risk factors of COVID-19: a systematic review and meta-analysis of 42 studies and 423,117 patients. BMC Infect Dis. 2021 Aug 21;21(1):855.

19. Michalski N, Reis M, Tetzlaff F, Herber M, Kroll LE, Hövener C, et al. German Index of Socioeconomic Deprivation (GISD): Revision, update and application examples. 2022 Dec 9 [cited 2023 Jul 17]; Available from: https://edoc.rki.de/handle/176904/10494

20. Plümper T, Neumayer E. The pandemic predominantly hits poor neighbourhoods? SARS-CoV-2 infections and COVID-19 fatalities in German districts. European Journal of Public Health. 2020 Dec 11;30(6):1176–80.

21. Dragano N, Hoebel J, Wachtler B, Diercke M, Lunau T, Wahrendorf M. Soziale Ungleichheit in der regionalen Ausbreitung von SARS-CoV-2. Bundesgesundheitsbl. 2021 Sep;64(9):1116–24.

22. Hoebel J, Michalski N, Diercke M, Hamouda O, Wahrendorf M, Dragano N, et al. Emerging socio-economic disparities in COVID-19-related deaths during the second pandemic wave in Germany. International Journal of Infectious Diseases. 2021 Dec 1;113:344–6.

23. Federgruen A, Naha S. Crowding Effects Dominate Demographic Attributes in COVID-19 Cases. International Journal of Infectious Diseases. 2021 Jan 1;102:509–16.

24. Ramírez IJ, Lee J. COVID-19 Emergence and Social and Health Determinants in Colorado: A Rapid Spatial Analysis. Int J Environ Res Public Health. 2020 Jun;17(11):3856.

25. Wadhera RK, Wadhera P, Gaba P, Figueroa JF, Joynt Maddox KE, Yeh RW, et al. Variation in COVID-19 Hospitalizations and Deaths Across New York City Boroughs. JAMA. 2020 Jun 2;323(21):2192–5.

26. Fielding-Miller RK, Sundaram ME, Brouwer K. Social determinants of COVID-19 mortality at the county level. PLoS One. 2020;15(10):e0240151.

27. Price-Haywood EG, Burton J, Fort D, Seoane L. Hospitalization and Mortality among Black Patients and White Patients with Covid-19. N Engl J Med. 2020 May 27;NEJMsa2011686.

28. R Core Team. R Statistical Software [Internet]. Vienna, Austria: R Foundation for Statistical Computing; Available from: https://www.R-project.org

29. Wickham H, François R, Henry L, Müller K. dplyr: A Grammar of Data Manipulation [Internet]. 2023. Available from: https://github.com/tidyverse/dplyr

30. Ripley B, Venables B, Bates DM, ca 1998) KH (partial port, ca 1998) AG (partial port, Firth D. MASS: Support Functions and Datasets for Venables and Ripley's MASS [Internet]. 2023 [cited 2023 Nov 26]. Available from: https://cran.r-project.org/web/packages/MASS/index.html

31. Brooks ME, Kristensen K, Benthem KJ van, Magnusson A, Berg CW, Nielsen A, et al. glmmTMB Balances Speed and Flexibility Among Packages for Zero-inflated Generalized Linear Mixed Modeling. The R Journal. 2017;9(2):378–400.

32. Alene M, Yismaw L, Assemie MA, Ketema DB, Gietaneh W, Birhan TY. Serial interval and incubation period of COVID-19: a systematic review and meta-analysis. BMC Infect Dis. 2021 Mar 11;21(1):257.

33. Faes C, Abrams S, Van Beckhoven D, Meyfroidt G, Vlieghe E, Hens N. Time between Symptom Onset, Hospitalisation and Recovery or Death: Statistical Analysis of Belgian COVID-19 Patients. Int J Environ Res Public Health. 2020 Oct;17(20):7560.

34. Bhaskar A, Chandra J, Hashemi H, Butler K, Bennett L, Cellini J, et al. A Literature Review of the Effects of Air Pollution on COVID-19 Health Outcomes Worldwide: Statistical Challenges and Data Visualization. Annual Review of Public Health. 2023;44(1):1–20.

35. Sheppard N, Carroll M, Gao C, Lane T. Particulate matter air pollution and COVID-19 infection, severity, and mortality: A systematic review and meta-analysis. Science of The Total Environment. 2023 Jul 1;880:163272.

36. Isphording IE, Pestel N. Pandemic meets pollution: Poor air quality increases deaths by COVID-19. Journal of Environmental Economics and Management. 2021 Jul 1;108:102448.

37. Lederer AM, Fredriksen PM, Nkeh-Chungag BN, Everson F, Strijdom H, De Boever P, et al. Cardiovascular effects of air pollution: current evidence from animal and human studies. American Journal of Physiology-Heart and Circulatory Physiology. 2021 Apr;320(4):H1417–39.

38. Lakey PSJ, Berkemeier T, Tong H, Arangio AM, Lucas K, Pöschl U, et al. Chemical exposure-response relationship between air pollutants and reactive oxygen species in the human respiratory tract. Sci Rep. 2016 Sep 8;6(1):32916.

39. Vincent JL, Taccone FS. Understanding pathways to death in patients with COVID-19. The Lancet Respiratory Medicine. 2020 May 1;8(5):430–2.

Supplementary Material

Code

Code and details on data processing and analysis are available at
https://github.com/sophiemhermanns/airpolC19

Geographic distribution of air pollutants

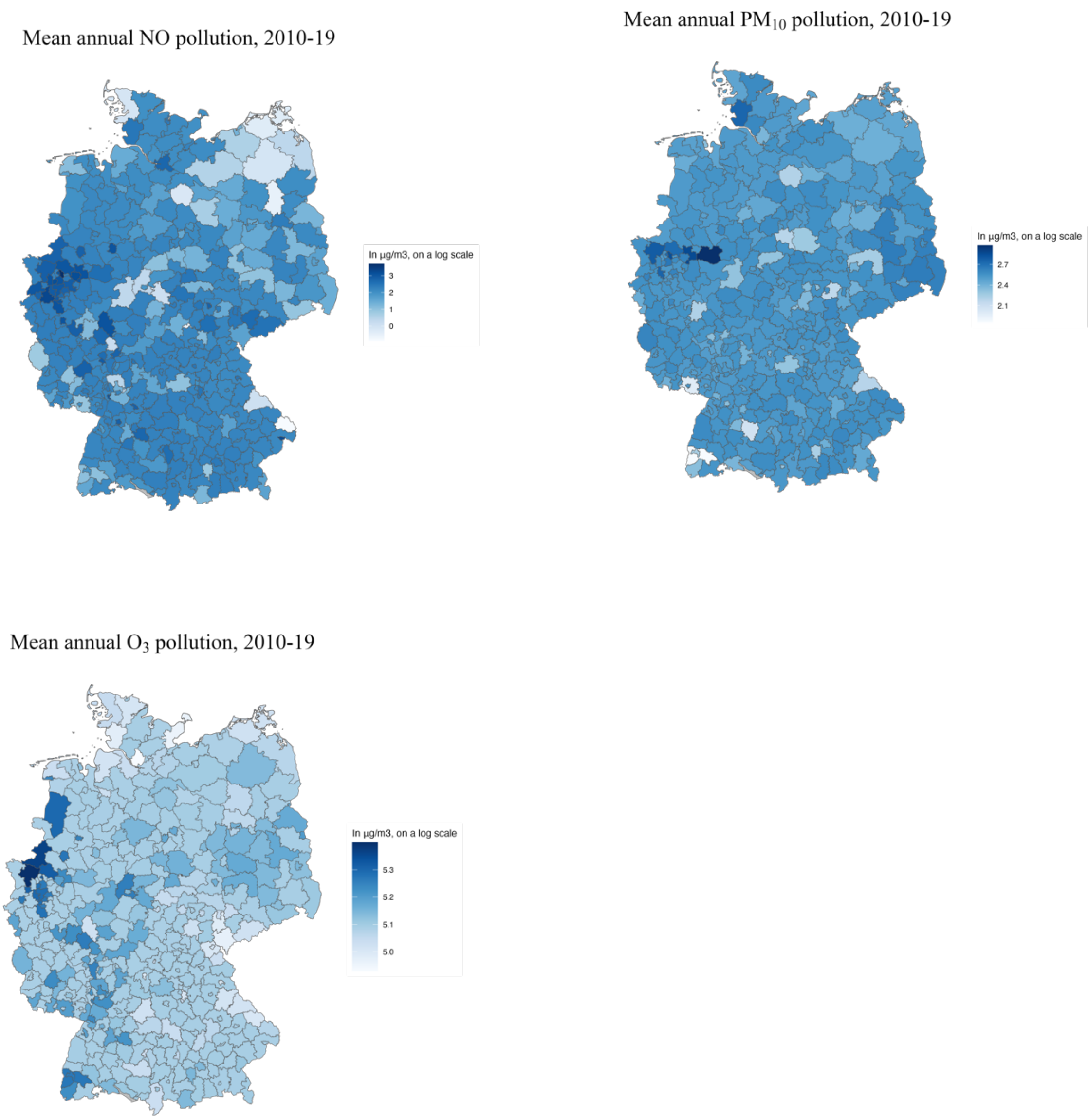

Figure S1: Geographic distributions of NO- , PM_{10}- and O_3-levels per county as means of the mean annual values for the period 2010-2019, in µg/ m^3, on a log scale.

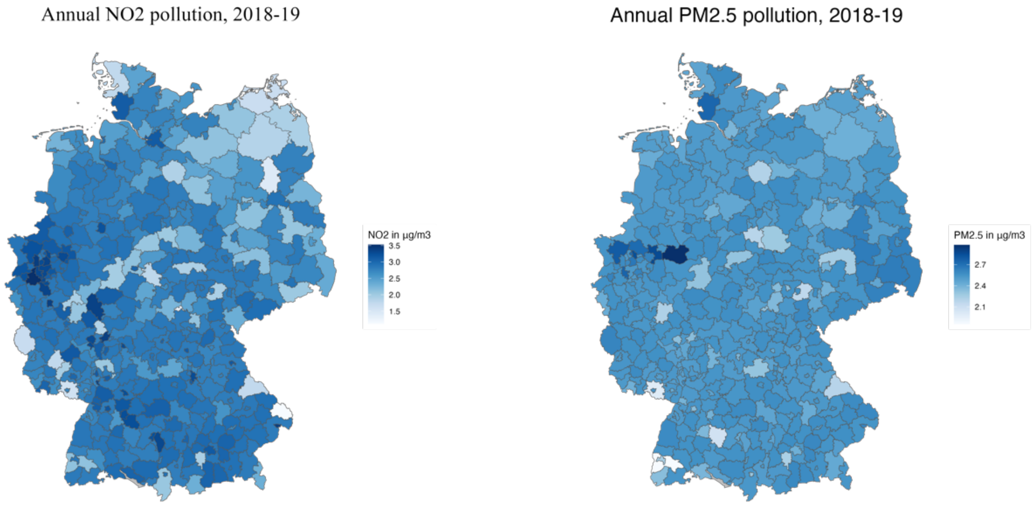

Figure S2: Geographic distributions of NO_2- and $PM_{2.5}$-levels per county as means of the mean annual values for the period 2018-2019, in µg/ m^3, on a log scale.

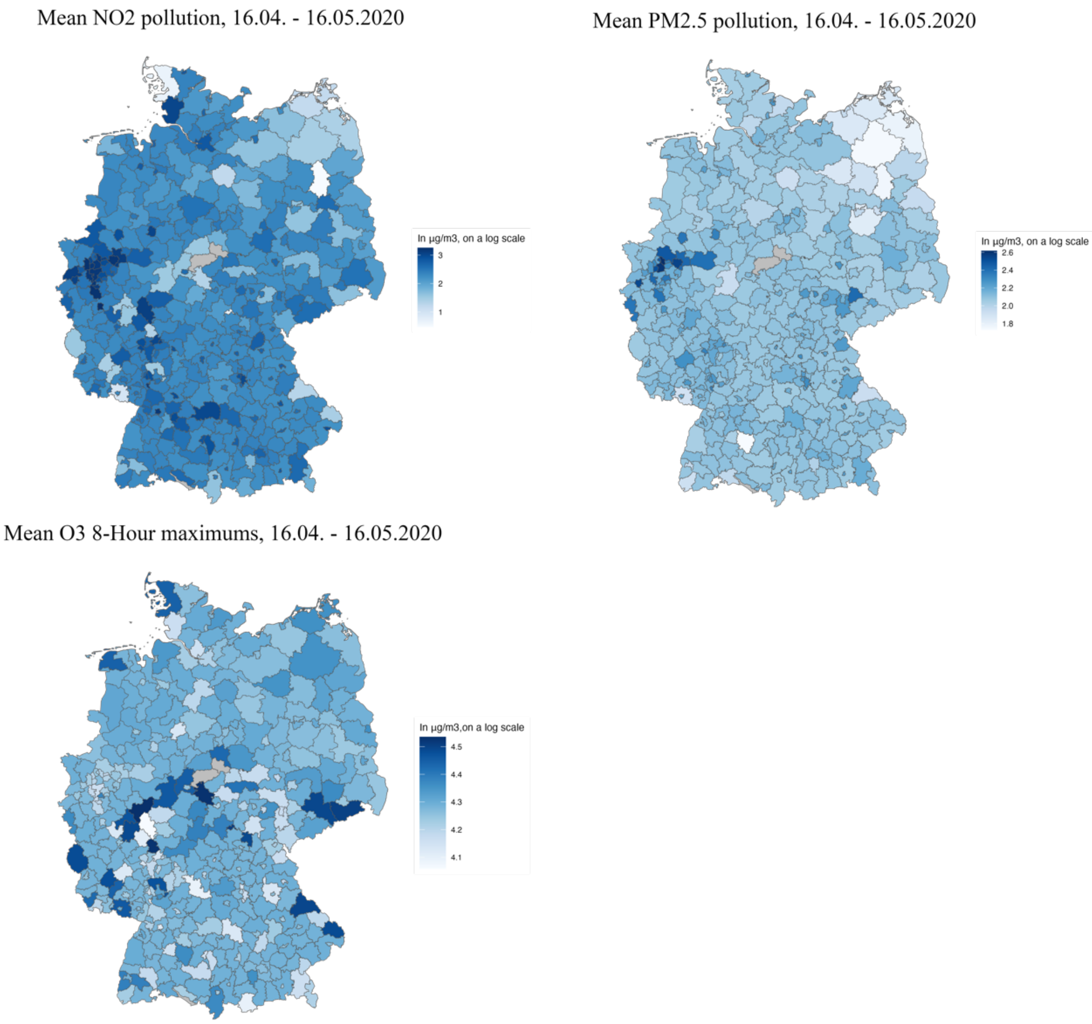

Figure S3: Geographic distributions of NO_2-levels and $PM_{2.5}$-levels per county as means of 48-hour-periods and of O_3-levels as means of 8-hour maximums, averaged over 48h-hour periods for the period April 16 – May 16 2020, in µg/ m^3, on a log scale.

Pollutant-levels by year

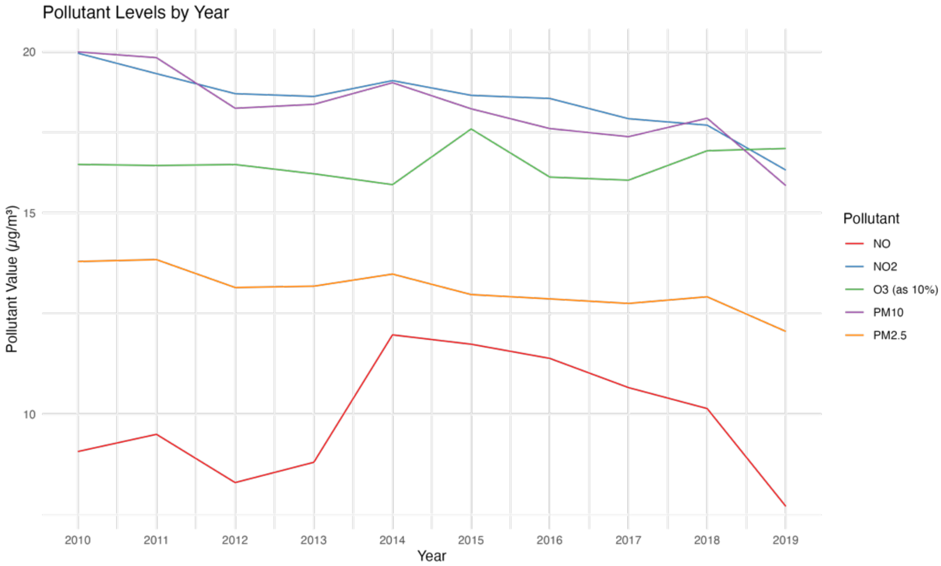

Figure S4: Mean pollutant levels by year for the period 2010 – 2019. O_3 is presented as means of 8-hour-maximums and shown as 10% of its values, for better readability.

Geographic distribution of control variables

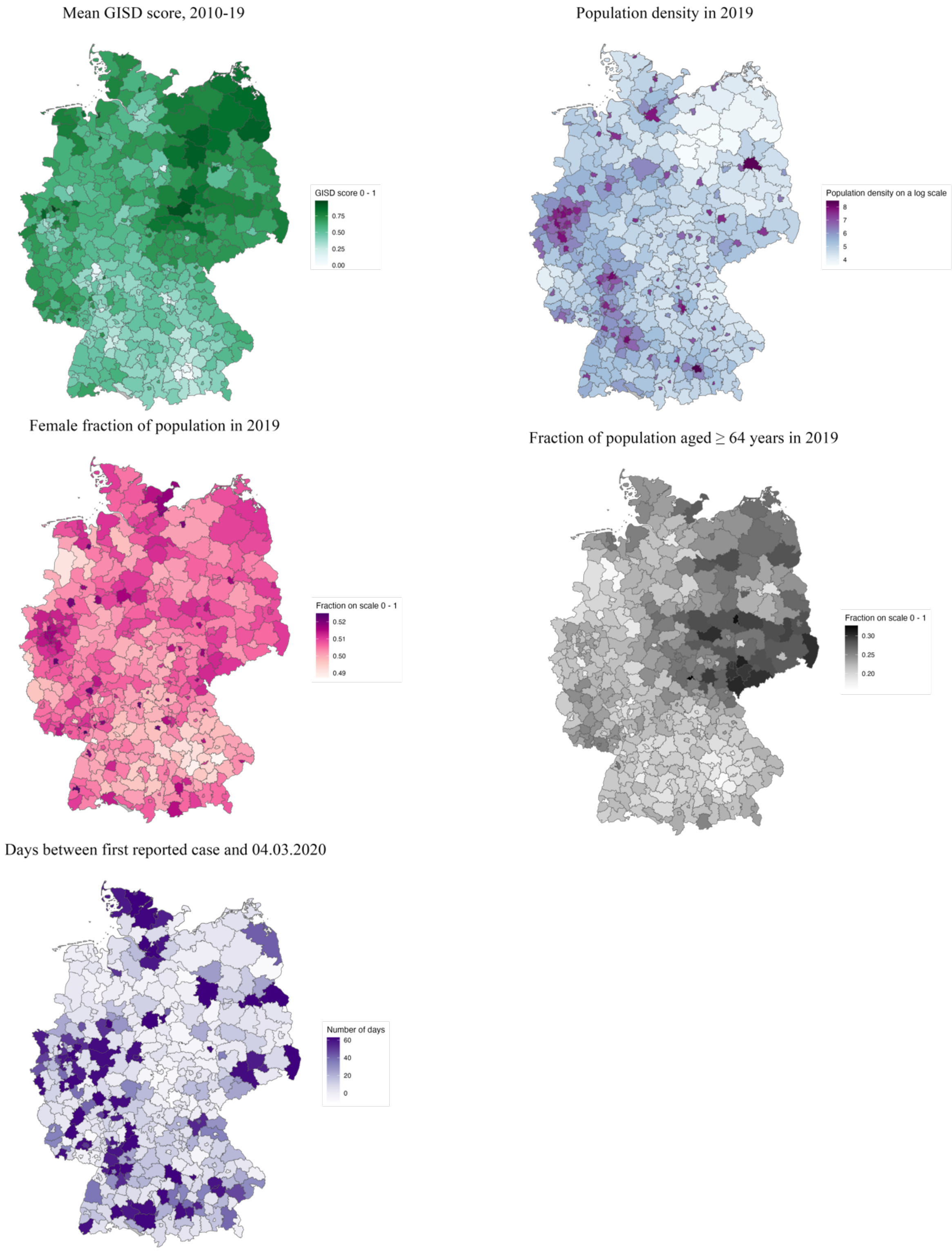

Figure S5: GISD-scores, log of population density in 2019, fraction of the population that were female and fraction of the population aged 64 years or older in 2019, and number of days between the first reported COVID-case in a county and March 4th 2020. GISD-scores are shown as means of annual values for the period 2010 – 2019.

Tri-pollutant models

Table S1: Effect estimates for the association between long-term NO2-, PM2.5- and O3-pollution 2010 – 19 and COVID-19 parameters at county-level April 16 – May 16 2020, in tri-pollutant models.

Air pollutants	Estimate (odds ratio)	95% Confidence Interval	p-value
Incidence			
NO2	1.037	1.026 - 1.048	0.001
PM2.5	0.981	0.941 - 1.021	0.638
O3	0.992	0.988 - 0.996	0.045
Mortality			
NO2	1.055	1.036 - 1.074	0.005
PM2.5	0.910	0.840 - 0.980	0.179
O3	0.986	0.979 - 0.993	0.045
Patient-days on ICU			
NO2	1.055	1.039 - 1.071	0.001
PM2.5	0.957	0.901 - 1.013	0.424
O3	0.991	0.985 - 0.997	0.124
Patient-days on mechanical ventilation			
NO2	1.063	1.046 - 1.080	0.000
PM2.5	0.937	0.876 - 0.998	0.284
O3	0.993	0.987 - 0.999	0.253

Table S2: Effect estimates for the association between long-term NO2-, PM2.5- and O3-pollution 2018 – 19 and COVID-19 parameters at county-level March 4 – May 16 2020, in tri-pollutant models.

Air pollutants	Estimate (odds ratio)	95% Confidence Interval	p-value
Incidence			
NO2	1.033	1.026 - 1.040	0.000
PM2.5	0.976	0.950 - 1.002	0.345
O3	0.994	0.991 - 0.997	0.017
Mortality			
NO2	1.049	1.036 - 1.062	0.000
PM2.5	0.935	0.889 - 0.981	0.144
O3	0.990	0.985 - 0.995	0.036
Patient-days on ICU			
NO2	1.055	1.039 - 1.071	0.001
PM2.5	0.957	0.901 - 1.013	0.424
O3	0.991	0.985 - 0.997	0.124
Patient-days on mechanical ventilation			
NO2	1.063	1.046 - 1.080	0.000
PM2.5	0.937	0.876 - 0.998	0.284
O3	0.993	0.987 - 0.999	0.253

Single-pollutant models: NO_2

Table S3: Effect estimates of the association between NO_2-pollution and COVID-19 disease parameters between April 16 and May 16 2020, at county-level.

Outcome	Timeframe	Estimate (odds ratio)	95% Confidence Interval	p-value
Incidence				
	10 years	1.050	1.017 - 1.084	0.0015
	2 years	1.053	1.022 - 1.084	0.0003
	2 days	1.004	1.001 - 1.007	0.0030
	7 days	1.014	1.008 - 1.020	0.0000
	28 days	1.252	1.238 - 1.266	0.0000
Mortality				
	10 years	1.034	1.010 - 1.058	0.0030
	2 years	1.037	1.015 - 1.059	0.0006
	2 days	1.014	1.008 - 1.020	0.0000
	7 days	1.036	1.023 - 1.049	0.0000
	28 days	1.292	1.262 - 1.322	0.0000
ICU				
	10 years	1.038	0.998 - 1.079	0.0528
	2 years	1.046	1.008 - 1.086	0.0114
	2 days	1.029	1.006 - 1.054	0.0150
	7 days	1.081	1.037 - 1.127	0.0000
	28 days	1.294	1.211 - 1.381	0.0000
Ventilation				
	10 years	1.057	1.021 - 1.095	0.0010
	2 years	1.058	1.025 - 1.093	0.0003
	2 days	1.004	1.001 - 1.007	0.0110
	7 days	1.016	1.009 - 1.023	0.0000
	28 days	1.278	1.261 - 1.296	0.0000

Table S4: Effect estimates of the association between NO_2-pollution and COVID-19 disease parameters between March 4 and May 16 2020, at county-level.

Outcome	Timeframe	Estimate (odds ratio)	95% Confidence Interval	p-value
Incidence				
	10 years	1.032	1.017 – 1.047	0.0000
	2 years	1.031	1.017 – 1.045	0.0000
	2 days	1.028	1.025 - 1.031	0.0000
	7 days	1.073	1.068 - 1.079	0.0000
	28 days	1.134	1.122 - 1.146	0.0000
Mortality				
	10 years	1.042	1.015 – 1.069	0.0012
	2 years	1.042	1.017 – 1.067	0.0005
	2 days	1.029	1.020 - 1.038	0.0000
	7 days	1.089	1.073 - 1.104	0.0000
	28 days	1.294	1.257 - 1.333	0.0000

Single-pollutant models: $PM_{2.5}$

Table S5: Effect estimates of the association between $PM_{2.5}$-pollution and COVID-19 disease parameters between April 16 and May 16 2020, at county-level.

Outcome	Timeframe	Estimate (odds ratio)	95% Confidence Interval	p-value
Incidence				
	10 years	1.043	0.960 - 1.129	0.3068
	2 years	1.023	0.947 - 1.103	0.5486
	2 days	1.049	1.039 - 1.058	0.0000
	7 days	1.182	1.163 - 1.201	0.0000
	28 days	1.317	1.298 - 1.337	0.0000
Mortality				
	10 years	0.998	0.864 - 1.145	0.9793
	2 years	0.982	0.857 - 1.119	0.7813
	2 days	1.105	1.068 - 1.143	0.0000
	7 days	1.368	1.278 - 1.464	0.0000
	28 days	1.553	1.466 - 1.644	0.0000
ICU				
	10 years	0.979	0.865 - 1.102	0.6999
	2 years	1.016	0.903 - 1.140	0.7588
	2 days	1.034	1.030 - 1.038	0.0000
	7 days	1.104	1.095 - 1.112	0.0000
	28 days	1.206	1.197 - 1.215	0.0000
Ventilation				
	10 years	0.968	0.844 - 1.105	0.5997
	2 years	1.005	0.881 - 1.142	0.9356
	2 days	1.036	1.031 - 1.041	0.0000
	7 days	1.115	1.105 - 1.125	0.0000
	28 days	1.231	1.220 - 1.243	0.0000

Table S6: Effect estimates of the association between $PM_{2.5}$-pollution and COVID-19 disease parameters between March 4 and May 16 2020, at county-level.

Outcome	Timeframe	Estimate (odds ratio)	95% Confidence Interval	p-value
Incidence				
	10 years	1.021	0.968 – 1.074	0.4454
	2 years	1.020	0.971 – 1.070	0.4315
	2 days	1.046	1.043 - 1.049	0.0000
	7 days	1.092	1.087 - 1.096	0.0000
	28 days	0.951	0.945 - 0.956	0.0000
Mortality				
	10 years	0.996	0.908 – 1.088	0.9302
	2 years	1.001	0.919 – 1.088	0.9841
	2 days	1.086	1.078 - 1.095	0.0000
	7 days	1.233	1.218 - 1.247	0.0000
	28 days	1.139	1.121 - 1.157	0.0000

Top 10 counties by variable

All COVID-19 parameters are calculated per 100,000 residents. All pollution-levels for the period April 16 – May 16 2020 are calculated as means of pollutant-levels averaged over 48-hour-periods preceding any given date between April 16 and May 16.

Table S7: The ten counties with the highest COVID-19 incidence between April 16 and May 16 2020.

		COVID-19 Disease Parameters				Air Pollutants			
		April - May 2020				April - May 2020		2010 - 2019	
Rank	**County**	**Incidence**	**Mortality**	**ICU**	**Ventilation**	**$PM_{2.5}$ (μg/m³)**	**NO_2 (μg/m³)**	**$PM_{2.5}$ (μg/m³)**	**NO_2 (μg/m³)**
1	Greiz	289.5	22.6	145.8	129.4	11.4	12.9	13.7	17.5
2	Straubing	261.6	20.9	73.2	43.9	10.0	14.5	13.1	18.3
3	Rosenheim	240.8	3.1	299.0	206.1	10.5	18.2	13.0	18.8
4	Sonneberg	239.1	29.5	12.1	6.9	9.7	8.0	13.2	8.8
5	Weiden i.d.OPf.	203.5	18.7	779.1	460.9	10.4	18.3	12.8	21.3
6	Neustadt a.d.Waldnaab	189.5	23.3	-	-	9.5	10.2	13.0	17.3
7	Traunstein	186.7	15.8	106.0	67.1	10.4	15.3	12.4	19.0
8	Pforzheim	183.4	1.6	76.2	59.5	8.8	23.7	12.0	22.7
9	Straubing-Bogen	174.1	11.9	120.6	44.5	9.5	10.6	13.0	17.8
10	Odenwaldkreis	167.5	17.6	191.3	155.1	9.6	13.6	13.5	17.3

Table S8: The ten counties with the highest COVID-19 incidence between March 4 and May 16 2020.

		COVID-19 Disease Parameters				Air Pollutants			
		March - May 2020				March - May 2020		2010 - 2019	
Rank	**County**	**Incidence**	**Mortality**	**ICU**	**Ventilation**	**$PM_{2.5}$ (μg/m³)**	**NO_2 (μg/m³)**	**$PM_{2.5}$ (μg/m³)**	**NO_2 (μg/m³)**
1	Tirschenreuth	1562.9	194.3	-	-	9.6	10.7	13.2	17.9
2	Wunsiedel i.Fichtelgebirge	891.9	56.4	39.9	30.3	11.8	11.5	13.5	18.7
3	Straubing	866.3	100.4	73.2	43.9	10.0	14.5	13.1	18.3
4	Neustadt a.d.Waldnaab	850.2	78.3	-	-	9.5	10.2	13.0	17.3
5	Halfing	848.4	74.6	199.0	145.8	9.5	10.5	13.1	19.0
6	Rosenheim	789.9	36.2	299.0	206.1	10.5	18.2	13.0	18.8
7	Weiden i.d.OPf.	732.3	49.1	779.1	460.9	10.4	18.3	12.8	21.3
8	Traunstein	698.2	49.1	106.0	67.1	10.4	15.3	12.4	19.0
9	Hohenlohekreis	674.6	41.7	104.7	46.2	9.6	11.4	13.3	19.0
10	Zollernalbkreis	613.1	39.1	103.0	73.4	9.6	11.4	13.6	19.7

Table S9: The ten counties with the highest COVID-19 mortality between April 16 and May 16 2020.

		COVID-19 Disease Parameters				Air Pollutants			
		April - May 2020				April - May 2020		2010 - 2019	
Rank	**County**	**Incidence**	**Mortality**	**ICU**	**Ventilation**	**$PM_{2.5}$ ($\mu g/m^3$)**	**NO_2 ($\mu g/m^3$)**	**$PM_{2.5}$ ($\mu g/m^3$)**	**NO_2 ($\mu g/m^3$)**
1	Sonneberg	29.5	239.1	12.1	6.9	8.3	7.6	13.2	8.8
2	Neustadt a.d.Waldnaab	23.3	189.5	-	-	7.9	9.2	13.0	17.3
3	Greiz	22.6	289.5	145.8	129.4	9.6	10.7	13.7	17.5
4	Straubing	20.9	261.6	73.2	43.9	8.7	13.1	13.1	18.3
5	Weiden i.d.OPf.	18.7	203.5	779.1	460.9	9.0	15.8	12.8	21.3
6	Odenwaldkreis	17.6	167.5	191.3	155.1	8.2	11.5	13.5	17.3
7	Tirschenreuth	16.7	83.3	-	-	8.0	9.7	13.2	17.9
8	Traunstein	15.8	186.7	106.0	67.1	8.8	14.0	12.4	19.0
9	Bad Rodach	15	131.4	-	-	8.3	10.5	12.9	17.2
10	Halfing	14.2	144.6	199.0	145.8	7.9	9.4	13.1	19.0

Table S10: The ten counties with the highest COVID-19 mortality March 4 and May 16 2020.

		COVID-19 Disease Parameters				Air Pollutants			
		March - May 2020				March - May 2020		2010 - 2019	
Rank	**County**	**Mortality**	**Incidence**	**ICU**	**Ventilation**	**$PM_{2.5}$ ($\mu g/m^3$)**	**NO_2 ($\mu g/m^3$)**	**$PM_{2.5}$ ($\mu g/m^3$)**	**NO_2 ($\mu g/m^3$)**
1	Tirschenreuth	194.3	1562.9	-	-	9.6	10.7	13.2	17.9
2	Straubing	100.4	866.3	73.2	43.9	10.0	14.5	13.1	18.3
3	Neustadt a.d.Waldnaab	78.3	850.2	-	-	9.5	10.2	13.0	17.3
4	Halfing	74.6	848.4	199.0	145.8	9.5	10.5	13.1	19.0
5	Odenwaldkreis	65.1	415.7	191.3	155.1	9.6	13.6	13.5	17.3
6	Wunsiedel i.Fichtelgebirge	56.4	891.9	39.9	30.3	11.8	11.5	13.5	18.7
7	Altötting	51.1	522.8	0.0	0.0	10.4	14.4	13.3	19.4
8	Amberg-Sulzbach	50.5	460.9	31.1	26.2	9.5	10.6	12.8	16.7
9	Langenzenn	49.2	439.5	-	-	9.8	12.9	13.3	18.8
10	Traunstein	49.1	698.2	106.0	67.1	10.4	15.3	12.4	19.0

Table S11: The ten counties with the highest rate of patient-days on ICUs due to COVID-19 between April 16 and May 16 2020.

		COVID-19 Disease Parameters				Air Pollutants			
		April - May 2020				April - May 2020		2010 - 2019	
Rank	**County**	**ICU**	**Incidence**	**Mortality**	**Ventilation**	**$PM_{2.5}$ ($\mu g/m^3$)**	**NO_2 ($\mu g/m^3$)**	**$PM_{2.5}$ ($\mu g/m^3$)**	**NO_2 ($\mu g/m^3$)**
1	Weiden i.d.OPf.	779.1	203.5	18.7	460.9	9.0	15.8	12.8	21.3
2	Regensburg	697.6	86.9	1.3	523.9	9.5	17.4	13.0	17.8
3	Schweinfurt	387.5	84.2	0.0	327.6	9.3	14.8	12.5	20.5
4	Aschaffenburg	305.6	11.3	0.0	236.6	8.2	18.0	12.1	29.0
5	Rosenheim	299	240.8	3.1	206.1	9.4	16.8	13.0	18.8
6	Heilbronn	274.9	34.0	0.8	183.3	8.7	18.9	12.7	23.5
7	Coburg	272.7	53.6	4.9	136.3	8.9	13.7	12.7	16.5
8	Heidelberg	272.5	15.5	0.0	148.0	9.2	12.9	13.6	22.6
9	Rhön-Grabfeld	265	38.9	3.8	141.9	8.1	9.6	13.1	18.0
10	Baden-Baden	255.5	27.2	0.0	204.8	8.5	12.5	12.7	16.3

Table S12: The ten counties with the highest levels of NO_2 – pollution between 2010 and 2019.

		Air Pollutants				COVID-19 Disease Parameters			
		2010 - 2019		April - May 2020		April - May 2020			
Rank	**County**	**NO_2 (μg/m³)**	**$PM_{2.5}$ (μg/m³)**	**NO_2 (μg/m³)**	**$PM_{2.5}$ (μg/m³)**	**Incidence**	**Mortality**	**ICU**	**Ventilation**
1	Frankfurt am Main	32	13.6	20.4	9.3	53.3	2.0	118.3	95.0
2	Essen	31.8	16.2	23.2	13.4	25.4	0.9	98.8	88.5
3	Mainz	30.6	13.9	19.3	10.3	79.6	5.0	14.6	6.4
4	Köln	30.3	13.4	24.9	10.9	26.4	0.6	63.4	45.9
5	Passau	30	13.9	18.7	8.7	13.3	0.0	136.4	60.6
6	Mülheim an der Ruhr	29.8	14.1	23.5	12.3	25.8	1.8	56.3	41.6
7	Leverkusen	29.6	13.6	22.7	9.7	26.9	0.6	15.3	10.4
8	Dortmund	29.2	16.4	24.3	12.8	17.7	0.0	33.0	26.3
9	Düsseldorf	29.2	16.0	23.7	11.3	66.1	0.3	69.1	44.2
10	Aschaffenburg	29	12.1	18.0	8.2	11.3	0.0	305.6	236.6

Table S13: The ten counties with the highest levels of NO_2 – pollution between April 16 and May 16 2020.

		Air Pollutants				COVID-19 Disease Parameters			
		April - May 2020		2010 - 2019		April - May 2020			
Rank	**County**	**NO_2 (μg/m³)**	**$PM_{2.5}$ (μg/m³)**	**NO_2 (μg/m³)**	**$PM_{2.5}$ (μg/m³)**	**Incidence**	**Mortality**	**ICU**	**Ventilation**
1	Bonn	26	9.7	14.0	28.8	41.3	0.3	116.5	85.2
2	Duisburg	25.3	9.5	14.1	24.0	78.2	5.6	60.8	44.9
3	Köln	24.9	10.9	13.4	30.3	26.4	0.6	63.4	45.9
4	Dortmund	24.3	12.8	16.4	29.2	17.7	0.0	33.0	26.3
5	Mettmann	23.9	8.9	13.1	28.7	35.8	2.7	19.6	15.4
6	Pforzheim	23.9	7.8	12.0	22.7	183.4	1.6	76.2	59.5
7	Düsseldorf	23.7	11.3	16.0	29.2	66.1	0.3	69.1	44.2
8	Speyer	23.7	10.4	13.7	26.1	53.4	2.0	183.9	136.5
9	Mülheim an der Ruhr	23.5	12.3	14.1	29.8	25.8	1.8	56.3	41.6
10	Essen	23.2	13.4	16.2	31.8	25.4	0.9	98.8	88.5

Table S14: The ten counties with the highest levels of $PM_{2.5}$ – pollution between 2010 and

2019.

		Air Pollutants				COVID-19 Disease Parameters			
		2010 - 2019		April - May 2020		April - May 2020			
Rank	**County**	**$PM_{2.5}$ (µg/m^3)**	**NO_2 (µg/m^3)**	**$PM_{2.5}$ (µg/m^3)**	**NO_2 (µg/m^3)**	**Incidence**	**Mortality**	**ICU**	**Ventilation**
1	Gelsenkirchen	17.7	28.6	23.2	13.7	43.5	1.2	22.7	16.6
2	Recklinghausen	17.3	23.3	17.1	11.9	66.9	2.1	19.7	5.9
3	Wesel	17.1	25.0	10.6	8.2	28.5	0.4	54.1	23.0
4	Berlin	16.7	20.0	13.6	8.4	33.6	1.4	74.3	59.6
5	Soest	16.7	18.8	15.5	11.0	9.6	0.0	10.3	6.3
6	Unna	16.7	25.6	22.7	11.3	26.1	0.5	16.2	8.9
7	Dortmund	16.4	29.2	24.3	12.8	17.7	0.0	33.0	26.3
8	Elbe-Elster	16.3	15.4	9.6	8.7	3.9	0.0	0.0	0.0
9	Essen	16.2	31.8	23.2	13.4	25.4	0.9	98.8	88.5
10	Düsseldorf	16	29.2	23.7	11.3	66.1	0.3	69.1	44.2

Table S15 The ten counties with the highest levels of $PM_{2.5}$ – pollution between April 16 and May 16 2020.

		Air Pollutants				COVID-19 Disease Parameters			
		April - May 2020		2010 - 2019		April - May 2020			
Rank	**County**	**$PM_{2.5}$ (µg/m^3)**	**NO_2 (µg/m^3)**	**$PM_{2.5}$ (µg/m^3)**	**NO_2 (µg/m^3)**	**Incidence**	**Mortality**	**ICU**	**Ventilation**
1	Gelsenkirchen	13.7	23.2	17.7	28.6	43.5	1.2	22.7	16.6
2	Essen	13.4	23.2	16.2	31.8	25.4	0.9	98.8	88.5
3	Dortmund	12.8	24.3	16.4	29.2	17.7	0.0	33.0	26.3
4	Mönchengladbach	12.5	21.4	13.9	21.0	54.4	0.8	70.5	57.5
5	Mülheim an der Ruhr	12.3	23.5	14.1	29.8	25.8	1.8	56.3	41.6
6	Recklinghausen	11.9	17.1	17.3	23.3	66.9	2.1	19.7	5.9
7	Düsseldorf	11.3	23.7	16.0	29.2	66.1	0.3	69.1	44.2
8	Unna	11.3	22.7	16.7	25.6	26.1	0.5	16.2	8.9
9	Altenburger Land	11.2	10.6	12.7	18.1	22.4	0.0	5.6	4.5
10	Soest	11	15.5	16.7	18.8	9.6	0.0	10.3	6.3