Environmental Research 216 (2023) 114481

Contents lists available at ScienceDirect

Environmental Research

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

Long-term air pollution exposure and COVID-19 case-severity: An analysis of individual-level data from Switzerland

Anton Beloconi [a,b], Penelope Vounatsou [a,b,*]

[a] Swiss Tropical and Public Health Institute, Allschwil, Switzerland
[b] University of Basel, Basel, Switzerland

ARTICLE INFO

Keywords:
$PM_{2.5}$
NO_2
Intensive care unit
Mortality
Bayesian inference

ABSTRACT

Several studies are pointing out that exposure to elevated air pollutants could contribute to increased COVID-19 mortality. However, literature on the associations between air pollution exposure and COVID-19 severe morbidity is rather sparse. In addition, the majority of the studies used an ecological study design and were applied in regions with rather high air pollution levels. Here, we study the differential effects of long-term exposure to air pollution on severe morbidity and mortality risks from COVID-19 in various population subgroups in Switzerland, a country known for clean air. We perform individual-level analyses using data covering the first two major waves of COVID-19 between February 2020 and May 2021. High-resolution maps of particulate matter ($PM_{2.5}$) and nitrogen dioxide (NO_2) concentrations were produced for the 6 years preceding the pandemic using Bayesian geostatistical models. Air pollution exposure for each patient was measured by the long-term average concentration across the municipality of residence. The models were adjusted for the effects of individual characteristics, socio-economic, health-system, and climatic factors. The variables with an important association to COVID-19 case-severity were identified using Bayesian spatial variable selection. The results have shown that the individual-level characteristics are important factors related to COVID-19 morbidity and mortality in all the models. Long-term exposure to air pollution appears to influence the severity of the disease only when analyzing data during the first wave; this effect is attenuated upon adjustment for health-system related factors during the entire study period. Our findings suggest that the burden of air pollution increased the risks of COVID-19 in Switzerland during the first wave of the pandemic, but not during the second wave, when the national health system was better prepared.

Anton Beloconi: Conceptualization, Methodology, Software, Validation, Formal analysis, Investigation, Data curation, Writing – original draft, Writing – review & editing, Visualization. Penelope Vounatsou: Conceptualization, Methodology, Resources, Data curation, Writing – review & editing, Supervision, Project administration, Funding acquisition.

1. Introduction

The severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2), which causes the coronavirus disease 2019 (COVID-19) (Zhu et al., 2020a), continues to be an important global public health problem. COVID-19 infections can manifest in a variety of ways, from asymptomatic to very severe forms. The latter usually require mechanical ventilation, cause the admission to the intensive care unit (ICU), and might lead to death. Older age and comorbidities have consistently been reported as risk factors for an unfavorable COVID-19 prognosis; however, younger patients without known risk factors are also being admitted to ICU, although in smaller numbers and with different symptoms. Comorbidities that have been reported include hypertension, obesity, diabetes, cardiovascular disease, chronic obstructive pulmonary disease, chronic kidney disease, and cancer (Guan et al., 2020; Bourdrel et al., 2021).

Air pollution is one of many determinants that have received additional attention since the start of the COVID-19 pandemic as a factor that may facilitate the spread, the severity, and the mortality of the disease (Brunekreef et al., 2021). There is a large body of literature in environmental epidemiology that includes well-established methods and findings on the effects of air pollution on health issues, similar to the ones found for coronavirus. For example, exposure to air pollution

* Corresponding author. University of Basel, Basel, Switzerland.
E-mail address: penelope.vounatsou@swisstph.ch (P. Vounatsou).

https://doi.org/10.1016/j.envres.2022.114481
Received 12 July 2022; Received in revised form 27 September 2022; Accepted 30 September 2022
Available online 4 October 2022

contributes to the development of diabetes, high blood pressure, heart and lung diseases (Cohen et al., 2017), decreases immunity (Mostafavi et al., 2019) and induces inflammation (Chen and Schwartz, 2008). An increasing number of studies suggest that exposure to elevated air pollutants also contributes to enhanced susceptibility and severity of the course of a COVID-19 infection (Copat et al., 2020; Marquès and Domingo, 2022).

The majority of publicly available COVID-19 outcome data are area-level counts. As a result, most of the studies assessing the effects of exposure to air pollution have applied an ecological study design; i.e., the air pollution estimates were averaged over the same level of spatial aggregation as the COVID-19 data and these aggregates were compared to the COVID-19 incidence, deaths, and/or case fatality rates. Examples include descriptive analyses based on several correlation indices (such as Pearson and Spearman) between the COVID-19 outcomes and the exposures to different air pollutants in separate cities or countries around the world (Bashir et al., 2020; Daes et al., 2021; Fatorini and Regoli, 2020; Telo-Leal and Macías-Hernandez, 2021; Zoran et al., 2020a; Zoran et al., 2020b), regression analyses evaluating the association between air pollution exposures and COVID-19 incidence, severity, and lethality, such as simple linear regression models (Li et al., 2020), multivariate Poisson (Jiang et al., 2020) and negative binomial (De Angelis et al., 2021; Aloisi et al., 2022) regression models that account for demographic, socio-economic, and meteorological variables; generalized additive models (GAM) (Zhu et al., 2020b) and hierarchical multiple regression models (Coccia, 2020).

The main advantage of the ecological regression analysis is that it offers a simple and cost-effective approach for examining potential associations between past air pollution exposure and greater susceptibility to COVID-19 in large representative populations. The disadvantage is that it is not designed to account for individual-level risk factors such as age and comorbidities (Wu et al., 2020). In the context of COVID-19, this is a severe limitation, as individual-level risk factors are known to highly affect the health outcomes of the disease, leading to ecological fallacy (Wakefield, 2008). A critical assessment of the methodological considerations for epidemiological studies of air pollution and COVID-19 concluded that ecological analyses are susceptible to important sources of bias (Villeneuve and Goldberg, 2020).

To alleviate the effect of ecological bias, Konstantinoudis et al. (2021) (Konstantinoudis et al., 2021) proposed downscaling the coarse spatial resolution of COVID-19 deaths data in the UK. This allowed exploiting the variability of air pollution exposure at high geographical resolution and a more adequate adjustment of the effects of the confounders. The findings provided some evidence of an association between average exposure to NO_2 during 2014–2018 and the COVID-19 mortality, whereas the role of $PM_{2.5}$ was more uncertain.

Until today, only a limited number of studies analyzing individual-level data have been published. In one of the studies, a regression *probit* model was used to evaluate the effects of long- and short-term exposure to $PM_{2.5}$ on the probability of dying from COVID-19 in Mexico City (López-Feldman et al., 2021). To adjust the effect of air pollution exposure for potential confounders, a set of individual- and municipal-level covariates were used. The results revealed a positive relationship between $PM_{2.5}$ and the mortality risk after contracting COVID-19. A different study investigated the risk factors (including air pollution) for COVID-19 mortality using the community-based UK Biobank cohort (Elliott et al., 2021). Univariate, multivariate logistic, and penalized (LASSO) regression models were fitted to COVID-19 deaths. Demographic, social, lifestyle, biological, medical, and environmental risk factors were evaluated. The results have shown that there was a small effect of PM pollution on the risk of death due to COVID-19 in the univariate analyses, but this effect was attenuated upon adjustment for other factors in multivariate models. Analyzing data from the Italian IQVIA Longitudinal Patient Database, researchers have found a positive association between PM_{10} levels and the likelihood of experiencing pneumonia due to COVID-19 (Pegoraro et al., 2021). A multiple mixed-effects logistic regression model was employed accounting for sex, age, and comorbidities. A more recent retrospective, individual-level study on hospitalized patients in Catalonia (Spain) revealed that long-term exposure to PM_{10} levels increased the number of severe COVID-19 cases and COVID-19 deaths (Marquès et al., 2022).

Most of the previous studies based on individual-level data have focused on the associations between air pollution exposure and the mortality from COVID-19, rather than the severe morbidity. Additionally, the majority of these studies have been performed in regions with rather high air pollution levels and have focused on exposure to particulate matter. Here, we study the differential effects of long-term exposure to $PM_{2.5}$ and NO_2 on severe morbidity and mortality risks from COVID-19 in various population subgroups in Switzerland – a country known for low air pollution levels when compared to other regions worldwide. To date, only one study has investigated the evolution of COVID-19 in-hospital mortality in Switzerland while also accounting for risk factors (Roelens et al., 2021), but air pollution exposure was not considered. Our work aims to evaluate whether even small changes in air pollution levels affect the severity and lethality of the infection. We propose a Bayesian spatial logistic model fitted to individual-level data. In particular, we investigate the risk factors for COVID-19 case-severity and mortality during the first two major waves of the pandemic in Switzerland (February 2020–April 2021), focusing on the effect of the long-term exposure to $PM_{2.5}$ and NO_2 concentrations estimated at high spatial resolution using Bayesian geostatistical models for the years 2014–2019. Our modelling endeavors improve the understanding of the effect of air pollution exposure on COVID-19 morbidity and mortality.

2. Materials and methods

2.1. Data sources

2.1.1. Individual level COVID-19 data

The COVID-19 dataset covering the period: 25/02/2020–30/04/2021 was obtained from the Swiss Federal Office of Public Health (FOPH). The dataset represents individual-level information on patients that were confirmed SARS-CoV-2 positive (through a PCR test) including: the dates of positive registered case, dates of hospitalization, admission to ICU, and death; sex, gender, age, smoking status, and the comorbidities of the patient (including diabetes, cardio, hypertension, chronic respiratory disease, cancer, immunosuppression, adiposity, and chronic kidney disease). There were only two levels for each comorbidity: a) patient has underlying disease; and b) patient does not have underlying disease or is not filled. We therefore assumed that if a particular disease was not filled then the patient did not have it. Additionally, we received information on the municipality of residence of the patient.

To isolate the effect of exposure to air pollution from other confounding factors, in addition to the individual-level patient characteristics, we extracted three categories of aggregated-level variables: (i) climatic data (at municipality-level); (ii) socio-economic factors (at municipality-level); and (iii) health-system-related factors (at cantonal level). There were a total of 2205 municipalities and 26 cantons in Switzerland in 2020.

2.1.2. Air pollution and climatic data

For each year between 2014 and 2019, air pollution data ($PM_{2.5}$ and NO_2 concentrations) were modelled on a European scale at 1 km^2 spatial resolution. A Bayesian geostatistical modelling framework was applied following our earlier works (Beloconi et al., 2018; Beloconi and Vounatsou, 2020, 2021). The analyses incorporated information from the pan-European in-situ monitoring network (Eionet), the Swiss national observations network (NABEL), simulations of the surface pollutant concentrations from the state-of-the-art chemical transport models, high-resolution satellite-based proxies of PM and NO_2, as well as additional high-resolution products related to land-use/cover, meteorology and climate. More information on the models and data used is provided in the Supplementary Information (SI). The accuracy of the exposure models was evaluated using the 5-fold-cross-validation method, as discussed in Beloconi and Vounatsou (2020, 2021) (Beloconi and Vounatsou, 2020, 2021); the results for each year are presented in table A1 (in SI). Averaged concentrations of both pollutants at 1 km^2 spatial resolution over the period 2014–2019 are shown in Fig. 1 (top). The data was aggregated on a municipality scale (Fig. 1 bottom) and assigned to each patient living in that particular municipality.

To adjust for potential effects of climate on the seasonality of the disease, we accessed the average monthly climatic data for the period February 2020–April 2021. In particular, we used the Google Earth Engine API (Gorelick et al., 2017) to process and extract the near-surface air temperature and the near-surface specific humidity data from the Famine Early Warning Systems Network (FEWS NET) Land Data Assimilation System (Amy McNally NASA/GSFC/HSL, 2018; McNally et al., 2017), as well as the precipitation from Climate Hazards Group InfraRed Precipitation with Station data (CHIRPS) (Funk et al., 2015). The climatic proxies were aggregated on a municipality scale and were assigned to each patient that got tested positive in the particular municipality and month.

2.1.3. Socio-economic and health-system factors

The socio-economic data with information available in the years closest to the years of the COVID-19 pandemic (i.e., 2020–2021) were extracted for each municipality from the Statistical Atlas of Switzerland compiled by the Federal Office of Statistics (FSO) (Swiss Federal office of statistics). The information consists of indices related to the distribution of the population (i.e., population count, population density, age-structure, and proportion of the permanent foreign population), the predominant national language, the urbanization status, the living conditions (i.e., average household size and share of households with five or more people), the distribution of deaths, and the economic indicators across municipalities (i.e., income per resident, social assistance rate, and number of employees in different economic sectors).

The Statistical Atlas of Switzerland was also used to extract factors related to the healthcare system. This information, available only at cantonal level, was assigned to individuals according to their residence. The data is related to the capacities of the hospitals (i.e., hospitalization rate in acute care, number of hospital beds, length of hospital stay, number of patients in nursing homes, average length of stay in a nursing home), and the number of workers in the health sector (i.e., density of doctors in the outpatient sector, nursing home staff, number of employees in the hospital and spitex facilities). Table A2 in the SI provides a detailed description of each variable.

2.2. Statistical modelling

The individual-level analyses were based on the subset of the patients that were hospitalized; therefore, those who died outside the hospital were excluded from the analyses. Missing hospitalization cases were imputed based on the contextual information, i.e., the hospitalization date and the date of the admission to ICU, when available.

Two outcomes were considered to measure the COVID-19 severity: (i) ICU – whether the patient went to the intensive care unit after hospitalization (1 – yes, 0 – no); and (ii) Death – whether the patient died after hospitalization (1 – yes, 0 – no). Bayesian spatial conditional autoregressive (CAR) logistic regression models were fitted. For patient $i = 1, \ldots, n$ and municipality $j = 1, \ldots, M$, we assume that:

$$y_{ij} \sim Bernoulli\left(\pi_{ij}\right)$$

$$\log\left(\frac{\pi_{ij}}{1-\pi_{ij}}\right) = \boldsymbol{X}_{ij}^{T}\boldsymbol{\beta} + \omega_j + \varepsilon_j \tag{1}$$

where $\boldsymbol{X}$ is a set of the selected covariates, $\boldsymbol{\beta}$ are the regression coefficients, and ω_j is a random effect quantifying spatial variation among municipalities. We assigned a CAR prior distribution to $\boldsymbol{\omega} =$

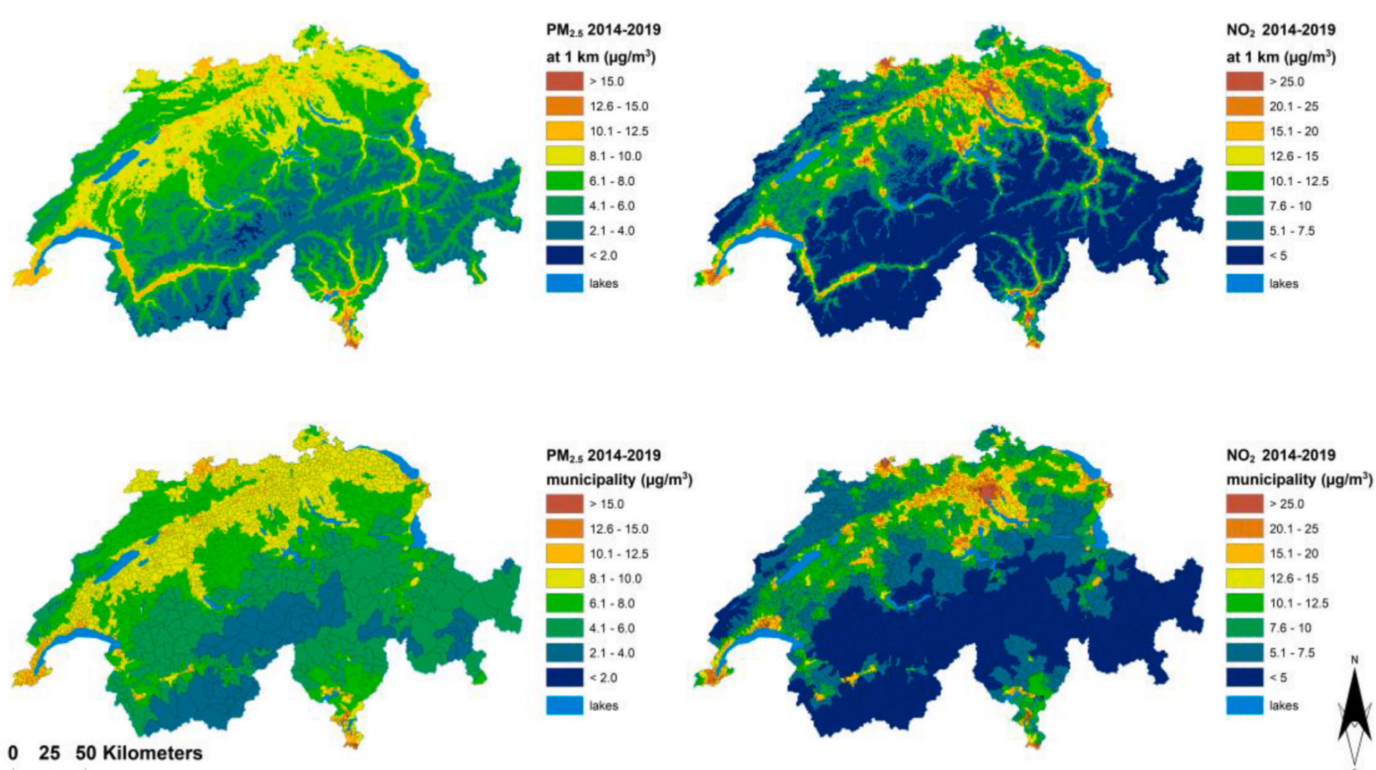

Fig. 1. Average $PM_{2.5}$ and NO_2 exposure in Switzerland during 2014–2019 at 1 km^2 spatial resolution (top) and aggregates at the municipality level (bottom).

$(\omega_1, \omega_2, \ldots, \omega_M)^T$ such as $\omega_j \Big| \boldsymbol{\omega}_{-j} \sim N\left(\overline{\omega}_{\delta_j}, \frac{\sigma_\omega^2}{m_{\delta_j}}\right)$, where $\overline{\omega}_{\delta_j} = m_{\delta_j}^{-1} \sum_{\delta_j \in \partial_j} \omega_j$, ∂_j and m_{δ_j} represents the set of neighbors and the number of neighbors of municipality j, and ε_j is a random effect quantifying non-spatial variation, $\boldsymbol{\varepsilon}_j \sim N(0, \sigma_\varepsilon^2)$. This formulation is known as the Besag-York-Mollié (BYM) model (Besag et al., 1991). The deviance information criteria (DIC) was used to compare the goodness-of-fit of the models to their corresponding non-spatial analogues (i.e., the same formulation as in Eq. (1) but excluding the spatial random effect ω_j).

First, univariate analyses were performed to evaluate the associations of ICU and death with the individual-level characteristics of the patients. For the multivariate modelling, several additional data cleaning steps were undertaken. The patients with missing sex characteristics (3 patients) and missing municipality information (350 patients) were excluded. Only ~45% of the patients reported their smoking status (No/Yes); therefore, this variable was excluded from the multivariate analyses. The ages were grouped into four categories: (i) ≤39; (ii) 40–59; (iii) 60–79; and (iv) 80+ years. The comorbidities were grouped as follows: (i) 0; (ii) 1; (iii) 2; and (iv) 3 or more comorbidities. The elapsing time variable was calculated as the difference between the date of hospitalization and the case date (usually the date of test); if the patient was already in the hospital, a value of zero was assigned. All the variables were standardized to reduce the computational time and to allow direct comparison of the covariate effects.

The development over time of the laboratory-confirmed COVID-19 deaths in Switzerland (depicted in Fig. 2) reveals two major waves of deaths due to the pandemic in 2020–2021. The first wave starts a few weeks after the identification of the first case, and the second one starts around October 1st, 2020. In order to understand the differences and similarities between the unexpected first wave and the second wave when the country's health system was better prepared, two separate analyses were performed using: (i) data covering only the first wave (i.e., before October 2020); and (ii) the entire time series.

To identify the factors that have an important association to each of the outcomes, Bayesian variable selection (BVS) was applied using stochastic search (George and McCulloch, 1996) and adopting a spike and slab prior distribution for the regression coefficients (Chammartin et al., 2013). This method identifies regressors with a non-zero effect and it was chosen because it can account for potential spatial correlation in the data (Scheipl et al., 2012). For each predictor X_k, a binary indicator parameter γ_k is introduced with Bernoulli probability p_k corresponding to the inclusion of the X_k in the model. For the coefficient β_k, we assume a prior distribution to be a mixture of two normal distributions, $\beta_k \sim \delta(\gamma_{k-1}) N(0, \tau_k^2) + (1 - \delta(\gamma_{k-1})) N(0, \vartheta_0 \tau_k^2)$, where δ(.) is the Dirac delta function, that is a non-informative Normal prior distribution if X_k is included in the model, i.e., $\beta_k \sim N(0, \tau_k^2)$ (slab) and an informative normal prior shrinking β_k to zero (spike) if X_k is excluded from the model, i.e., $\beta_k \sim N(0, \vartheta_0 \tau_k^2)$, where $\vartheta_0 = 10^5$ is a very large number shrinking the variance to zero. A Beta(1,1) hyperprior was adopted for p_k and a Gamma(0.01,0.01) for the precision parameter τ_k^2.

The BVS analyses were performed separately for each of the two periods defined in the previous subsection. To avoid multi-collinearity, when two or more predictors had an absolute correlation coefficient of >0.8, only one was used in the model selection. In the case of the air pollution estimates, also strongly intercorrelated, a separate Bayesian variable selection was performed, i.e., the probability of $PM_{2.5}$ and NO_2 inclusion in the multivariate models was separately evaluated when accounting for the other predictors.

The BVS was implemented in Just Another Gibbs Sampler (JAGS) (Plummer, 2003). For each analysis, 50′000 iterations and two chains were used. The initial iterations, equivalent to 10 per cent of the total iterations utilized in each chain, were discarded as burn-in. The predictors with a posterior mean inclusion probability $E(\gamma_k)$ greater than 0.5 were selected for the final models, which were fitted using the Integrated Nested Laplace Approximation (INLA) algorithm (Rue et al., 2009; Lindgren et al., 2011) implemented in the R-INLA package (Rue et al., 2013), available within the R software (R Core Team, 2021).

3. Results

3.1. Descriptive statistics and univariate analyses

We analyzed 28540 patients hospitalized with COVID-19 infection from the start of the pandemic at the end of February 2020 until the end of April 2021. Out of these, 5849 (20.5%) patients were admitted to ICU and 5234 (18.3%) died. The spatial distribution of the percentage of people admitted to ICU and of those that died out of those hospitalized in each municipality is depicted in Fig. 3.

The results of the logistic regression models measuring the univariate associations between the individual level characteristics and the risks of admission to the ICU and mortality are shown in Table 1. As expected, there is a gradual increase in the odds of ending up in ICU, or dying, with the increasing age of the patients; being male also increases these odds. The analysis of the comorbidities reveals that there is a significant increase in the odds ratios of both outcomes when a patient possesses at least one disease. These odds are lower for adiposity and diabetes and higher for cardiovascular and chronic kidney diseases as well as cancer. Patients that reported no previous disease had 70% lower odds of being

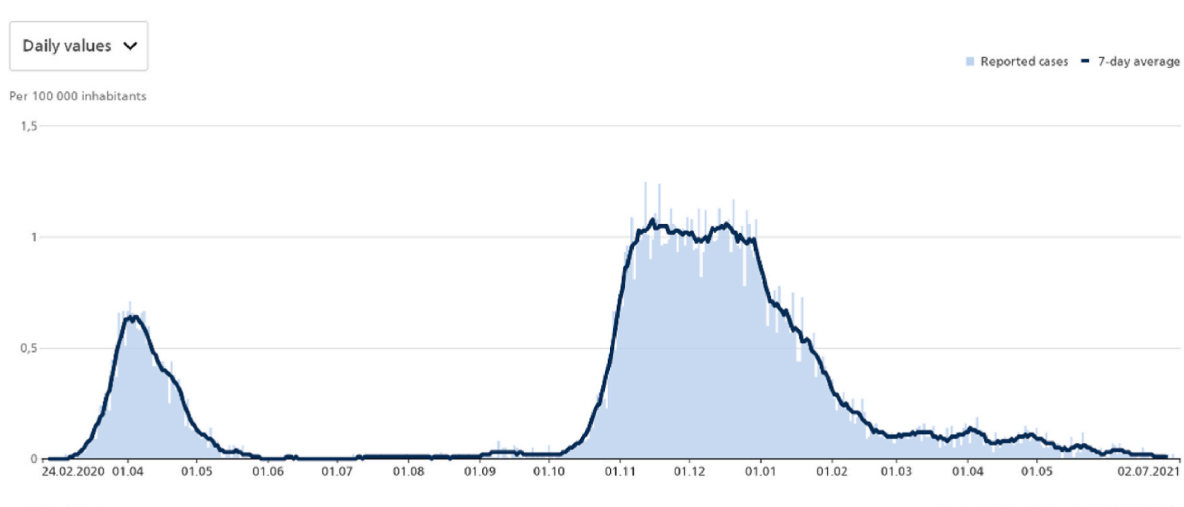

Fig. 2. Development over time of the laboratory-confirmed COVID-19 deaths in Switzerland per 100′000 inhabitants.

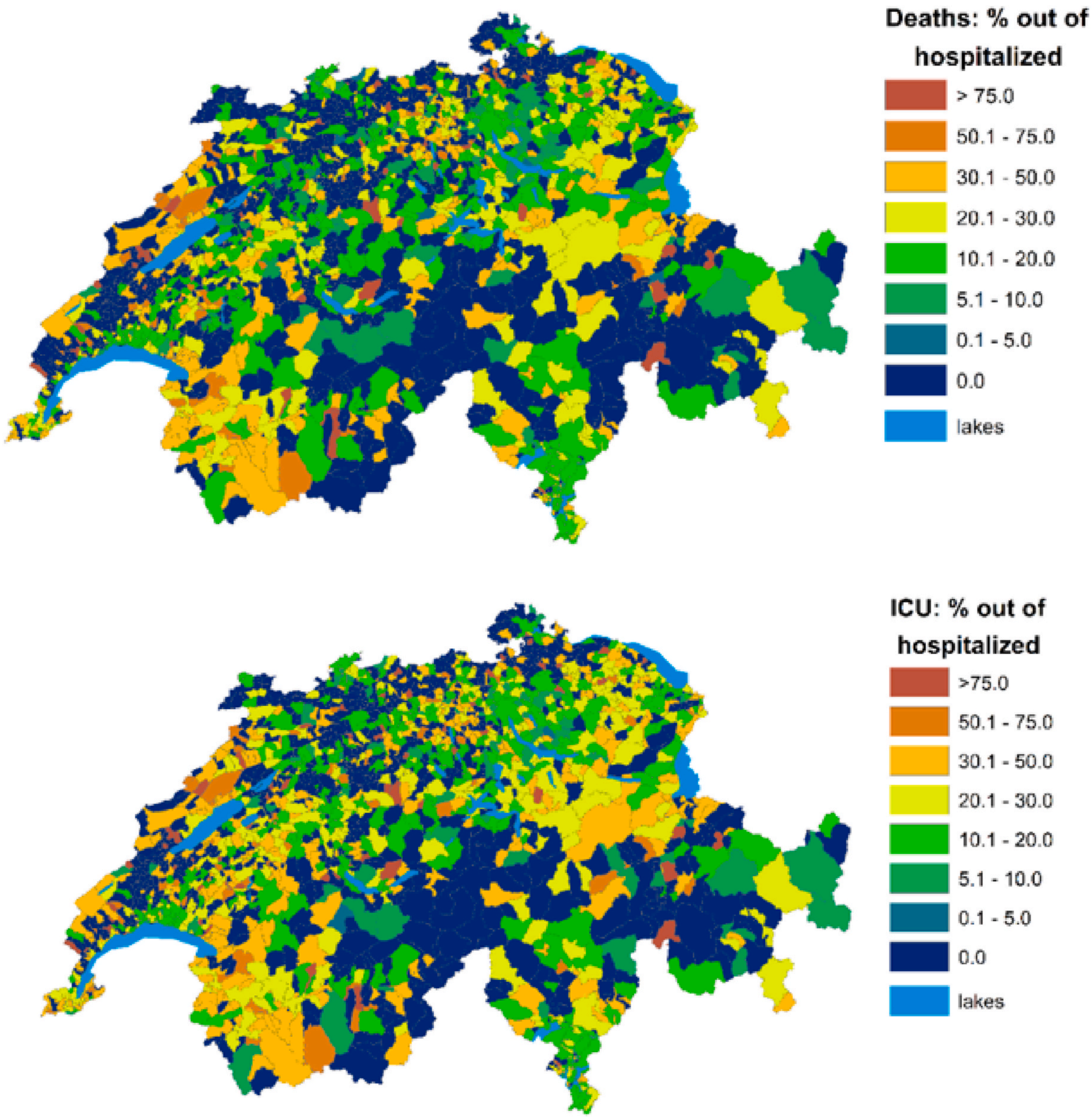

Fig. 3. The percentage of patients admitted to the intensive care unit (top) or died (bottom) out of all hospitalized patients in each municipality.

in ICU and 80% lower odds of dying. The analysis on the smoking status, based on 45% of patients that reported it, indicated an increase in the odds of both outcomes, although marginally in the case of death.

There was a difference in the severe COVID-19 outcomes during the first wave of the disease compared to the entire period. In particular, the mortality risk (MR) in the hospitalized patients during the first wave of the pandemic MR = 20.0% (95% CI: 18.9%, 21.2%) was higher than during the entire study period MR = 18.3% (17.9%, 18.8%). Similarly, the ICU risk was: 25.1% (23.9%, 26.3%) during the 1st wave and 20.5% (20.0%. 21.0%) overall. There were differences also in the potential risk factors. For example, the average elapsing time from the case-date to hospitalization date in the first wave was shorter: 1.55 (95% CI: 1.42, 1.67) days when compared to the analyses of all the time series: 2.60 (2.53, 2.66) days. The air temperature, calculated based on the time when the people were hospitalized with coronavirus, was higher on average during the first period: 8.89 °C (95% CI: 8.73 °C, 9.05 °C) versus 5.90 °C (5.85 °C, 5.96 °C).

3.2. Multivariable analysis

Eight separate Bayesian variable selection models were fitted, corresponding to the combination of two pollutants ($PM_{2.5}$ and NO_2), two study periods (Feb 20–Apr 21 and Feb 20–Sept 20), and two outcomes (admission to ICU and mortality risks). The resulting probabilities of inclusion for NO_2 and $PM_{2.5}$ variables are shown in Fig. 4; the inclusion probabilities for the other variables are presented in the SI (Tables A3–A4). Fig. 4 shows, for example, that the posterior inclusion probability for NO_2 in modelling the admission to ICU during the 1st wave is 0.89, suggesting that NO_2 was included in 89% of all possible models (around half a billion models) generated from our predictors.

Bayesian variable selection indicates similarities between the estimated inclusion probabilities for some of the variables (Tables A3–A4 in SI). In particular, sex, age, comorbidities, and language of the region play an important role in modelling both outcomes for both study periods. However, a few other variables are important when analyzing only the first period and are not important during the entire study period, and vice versa. Thus, the number of hospital beds, the elapsing

Table 1
Estimates of the univariate associations between the risks of admission to the intensive care unit (ICU) or death and individual level characteristics of the patients based on logistic regression. OR – odds ratio; BCI – Bayesian credible intervals.

Variable	Category	Total	ICU	ICU OR [95% BCI]	Deaths	Deaths OR [95% BCI]
Age(years)	≤39	1862(6.5%)	75(4%)	1.00	13(0.7%)	1.00
	40–59	5362(18.8%)	439(8.2%)	2.12 [1.65, 2.73]	186(3.5%)	5.11 [2.91, 8.99]
	60–79	12103(42.4%)	2470(20.4%)	6.11 [4.83, 7.73]	2025(16.7%)	28.58 [16.53, 49.41]
	80+	9213(32.3%)	2865(31.1%)	10.75 [8.5, 13.6]	3010(32.7%)	69.02 [39.93, 119.29]
Sex	Male	16357(57.3%)	3885(23.8%)	1.00	3401(20.8%)	1.00
	Female	12180(42.7%)	1963(16.1%)	0.62 [0.58, 0.66]	1833(15%)	0.67 [0.63, 0.72]
Diabetes	Unknown	22081(77.4%)	3994(18.1%)	1.00	3566(16.1%)	1.00
	Yes	6459(22.6%)	1855(28.7%)	1.82 [1.71, 1.94]	1668(25.8%)	1.81 [1.69, 1.93]
Cardio	Unknown	18216(63.8%)	2464(13.5%)	1.00	1907(10.5%)	1.00
	Yes	10324(36.2%)	3385(32.8%)	3.12 [2.94, 3.31]	3327(32.2%)	4.07 [3.82, 4.33]
Hypertension	Unknown	15362(53.8%)	2203(14.3%)	1.00	1842(12%)	1.00
	Yes	13178(46.2%)	3646(27.7%)	2.28 [2.15, 2.42]	3392(25.7%)	2.54 [2.39, 2.71]
Chronic Respiratory Disease	Unknown	24314(85.2%)	4517(18.6%)	1.00	3978(16.4%)	1.00
	Yes	4226(14.8%)	1332(31.5%)	2.02 [1.88, 2.17]	1256(29.7%)	2.16 [2.01, 2.33]
Cancer	Unknown	25669(89.9%)	4794(18.7%)	1.00	4181(16.3%)	1.00
	Yes	2871(10.1%)	1055(36.7%)	2.53 [2.33, 2.75]	1053(36.7%)	2.98 [2.74, 3.23]
Immunosuppression	Unknown	27196(95.3%)	5412(19.9%)	1.00	4813(17.7%)	1.00
	Yes	1344(4.7%)	437(32.5%)	1.94 [1.72, 2.18]	421(31.3%)	2.12 [1.88, 2.39]
Adiposity	Unknown	26291(92.1%)	5262(20%)	1.00	4731(18%)	1.00
	Yes	2249(7.9%)	587(26.1%)	1.41 [1.28, 1.56]	503(22.4%)	1.31 [1.18, 1.46]
Chronic Kidney Disease	Unknown	24218(84.9%)	4255(17.6%)	1.00	3613(14.9%)	1.00
	Yes	4322(15.1%)	1594(36.9%)	2.74 [2.56, 2.94]	1621(37.5%)	3.42 [3.19, 3.67]
Other Disease	Unknown	21784(76.3%)	3886(17.8%)	1.00	3408(15.6%)	1.00
	Yes	6756(23.7%)	1963(29.1%)	1.89 [1.77, 2.01]	1826(27%)	2.00 [1.87, 2.13]
No Disease	Unknown	24717(86.6%)	5538(22.4%)	1.00	5035(20.4%)	1.00
	Yes	3823(13.4%)	311(8.1%)	0.31 [0.27, 0.35]	199(5.2%)	0.21 [0.19, 0.25]
Smoking	No	10883(85.1%)	1480(13.6%)	1.00	1242(11.4%)	1.00
	Yes	1907(14.9%)	303(15.9%)	1.20 [1.05, 1.37]	246(12.9%)	1.15 [0.99, 1.33]

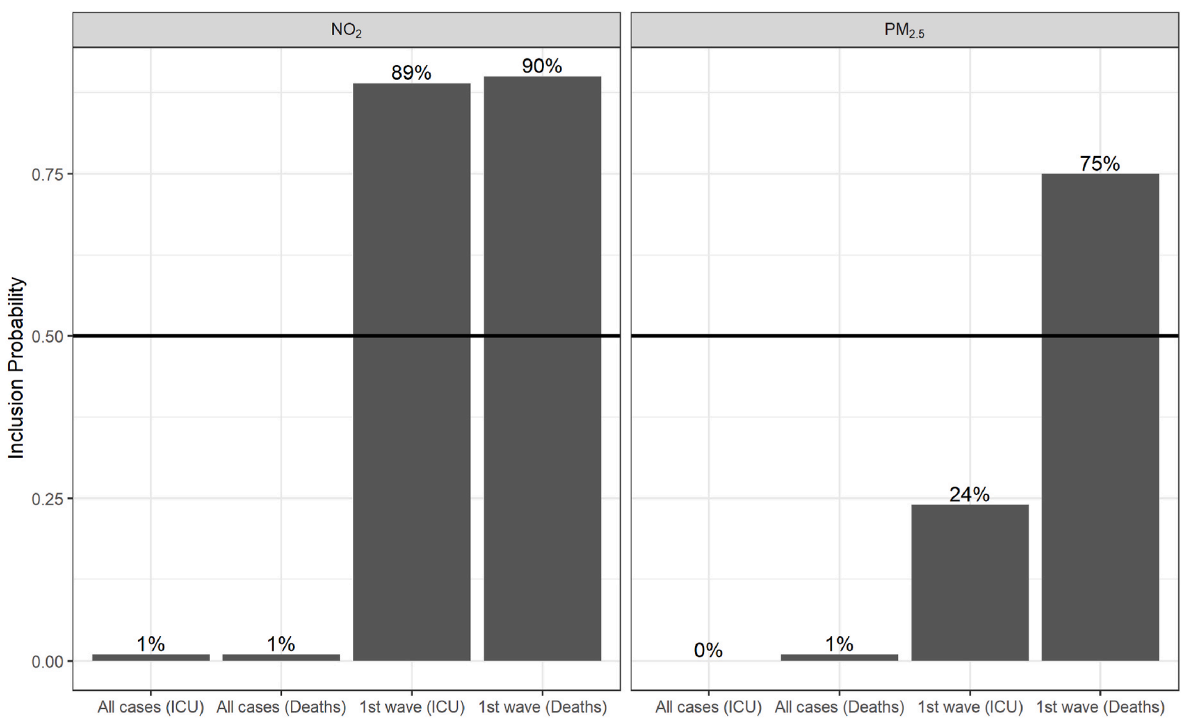

Fig. 4. Probability of inclusion for NO_2 and $PM_{2.5}$ variables based on the Bayesian variable selection process in modelling the admission to the intensive care unit (ICU) and death during the 1st wave of the pandemic and during the entire study period. The solid horizontal line corresponds to a probability of inclusion of 50%.

time, and the number of spitex staff are important variables in modelling both outcomes only when analyzing all cases, i.e., during the entire study period. Similarly, the number of nursing home staff is selected to be important in modelling deaths only during the entire study period. On the other hand, the climatic and air pollution variables do not seem important when analyzing all cases, as indicated by the low inclusion probability; however, the BVS reveals their importance when modelling the data covering only the first period. In particular, both NO_2 and air temperature were selected as important predictors for ICU and Deaths, whereas the $PM_{2.5}$ variable had high probability of inclusion when modelling the mortality risk.

Most socio-economic variables, besides the language of the region, are not statistically important (Tables A3–A4 in SI). From the indices related to the distribution of the population, the urbanization status, and the economic indicators across municipalities, only the variable indicating the share of households with five or more people in total private households appears to have an inclusion probability higher than 50% when modelling admission to ICU.

A total of 16 distinct models were fitted, corresponding to the combination of two pollutants, two temporal scales of the analysis, two outcomes, and two types of models (independent and spatial) with predictors selected via BVS. The results of the spatial BYM models are shown in Tables 2 and 3, for models including either the NO_2, or $PM_{2.5}$ predictor, respectively. The results of the independent (i.e., the non-spatial model) formulations are presented in the SI (Tables A5–A6). As indicated by the lower DIC values, all the spatial models outperform the independent formulations.

The inferences on the individual level characteristics in the multivariate spatial conditional autoregressive models are similar to the univariate analysis. Thus, in each model, irrespective of the temporal scale or the included pollutant, the male sex and the higher age of the patients indicate increased odds of entering the intensive care unit and of dying after contacting coronavirus infection (Tables 2 and 3). Furthermore, the same tables show that the higher the number of comorbidities, the higher the risks, as indicated by a gradual increase in the odds ratios for 1, 2, and 3 or more comorbidities when compared to none. The odds ratios in the French regions are higher than in the German part of Switzerland, whereas the differences with the Italian region are not statistically important.

As already mentioned above, the other factors, selected as important in the BVS models, differ between the analyses of only the 1st wave of the pandemic and the entire time series. Thus, higher NO_2 concentrations increase the odds of being in the ICU and of dying during the first study period, whereas increased $PM_{2.5}$ levels increase only the mortality risks. The magnitude of the air pollution-related regression coefficients is lower than that of the individual risk factors. The analyses based on the data covering only the first wave of COVID-19 show that higher air temperature leads to decreased risks of both outcomes and that in municipalities where the share of households with five or more people in total private households is high, the odds of ICU stay increase. On the other hand, the models for the entire time series show the important associations with the health-system factors. In particular, the higher the elapsing time and the number of hospital beds in a particular canton, the higher the odds of ICU stay and mortality, whereas there is a negative association between the number of employees in spitex and in nursing homes with the odds of the above outcomes (Tables 2 and 3).

Table 2
The parameter estimates (posterior medians and 95% Bayesian credible intervals of odds ratios) of the BYM models fitted to the intensive care unit (ICU) and death data during the first study period (i.e., 1st wave of the pandemic) and during the entire study period, based on the Bayesian variable selection performed with the inclusion of the NO_2 covariate. Ref – reference value; DIC – deviance information criteria.

Variable	All cases (ICU)	All cases (Deaths)	1st wave (ICU)	1st wave (Deaths)
Number of hospital beds (in canton of residence)	1.09 (1.02, 1.16)	1.08 (1.00, 1.16)		
Average length of hospital stay (in canton of residence)	1.13 (1.02, 1.25)			
Number of nursing home staff employees (in canton of residence)		0.95 (0.87, 1.04)		
Number of spitex staff employees (in canton of residence)	0.89 (0.80, 0.99)	0.98 (0.88, 1.10)		
Elapsing time between the case date and the hospitalization	1.07 (1.04, 1.11)	1.09 (1.05, 1.12)		
Share of households with five or more people in total private households (in municipality of residence)			1.17 (1.06, 1.29)	
Average air temperature during hospitalization (in residence municipality)			0.75 (0.69, 0.82)	0.71 (0.64, 0.78)
Average NO_2 exposure during 2014–2019 (in residence municipality)			1.17 (1.05, 1.30)	1.15 (1.03, 1.27)
Sex: Male	1.75 (1.63, 1.87)	1.67 (1.55, 1.79)	1.87 (1.60, 2.19)	1.68 (1.41, 2.00)
Age groups:	Ref (Age ≤ 40)			
40–59	1.51 (1.16, 1.99)	2.91 (1.72, 5.41)	1.70 (1.09, 2.78)	1.56 (0.67, 4.50)
60–79	2.88 (2.25, 3.75)	10.30 (6.22, 18.85)	2.75 (1.79, 4.42)	5.52 (2.49, 15.31)
80+	4.78 (3.73, 6.25)	24.16 (14.58, 44.23)	4.12 (2.66, 6.68)	14.54 (6.54, 40.41)
Number of comorbidities:	Ref (Comorbidities = 0)			
1	1.69 (1.48, 1.94)	2.10 (1.77, 2.50)	1.48 (1.14, 1.94)	2.91 (1.92, 4.59)
2	2.57 (2.26, 2.94)	3.43 (2.92, 4.07)	2.42 (1.86, 3.17)	5.64 (3.76, 8.82)
3 or more	5.51 (4.86, 6.26)	7.91 (6.76, 9.32)	5.51 (4.25, 7.21)	13.14 (8.82, 20.48)
Main language of the residence municipality:	Ref (Language = German)			
French	1.63 (1.28, 2.08)	1.67 (1.25, 2.22)	1.32 (1.01, 1.77)	1.35 (1.02, 1.70)
Italian	1.04 (0.62, 1.72)	1.18 (0.64, 2.16)	1.00 (0.63, 1.42)	1.05 (0.72, 1.40)
DIC	23530.98	20627.46	4439.24	3534.78

4. Discussion

The present study assesses the relationship between the long-term exposure to air pollution and the morbidity and mortality risk of the COVID-19 infection in Switzerland. The country represents a low-level air pollution setting and has low population density, which may affect the pandemic impact. Analyzing individual level data, we quantify the effects of air pollution during different waves of the pandemic, taking into account individual-level risk factors and climatic, socio-economic, and health system determinants. The results indicate that the long-term exposure to $PM_{2.5}$ and NO_2 was related to the severity of the disease only during the first major wave of the infection when the national health system was not fully prepared to face the pandemic.

Bayesian variable selection, performed separately for each outcome, pollutant and study period, identified predictors that are associated with the severity of the disease in each case. The individual-level characteristics are important factors related to the COVID-19 morbidity and mortality in all the models. In particular, consistently with the other studies worldwide (Bourdrel et al., 2021), we estimated a gradual increase in the odds of entering the intensive care unit after contacting coronavirus infection and the odds of dying, with the increasing age of the patients; being male also increases these odds. The analysis of the comorbidities reveals that there is a significant increase in the odds ratios of both ICU and death when the patient has at least one disease, whereas the multivariate models show that the higher the number of comorbidities, the higher the odds of COVID-19 severity.

In contrast to the effects of the individual level characteristics, which are statistically important in all the tested models, the other predictors are related to the severity and the lethality of the disease differently during various time points. In particular, long-term exposure to air

Table 3
The parameter estimates (posterior medians and 95% Bayesian credible intervals of odds ratios) of the BYM models fitted to the intensive care unit (ICU) and death data during the first study period (i.e., 1st wave of the pandemic) and during the entire study period, based on the Bayesian variable selection performed with the inclusion of the $PM_{2.5}$ covariate. Ref – reference value; DIC – deviance information criteria.

Variable	All cases (ICU)	All cases (Deaths)	1st wave (ICU)	1st wave (Deaths)
Number of hospital beds (in canton of residence)	1.08 (1.02, 1.15)	1.08 (1.00, 1.16)		
Number of nursing home staff employees (in canton of residence)		0.95 (0.87, 1.04)		
Number of spitex staff employees (in canton of residence)	0.93 (0.85, 1.03)	0.98 (0.88, 1.10)		
Density of doctors in the outpatient sector (in canton of residence)			1.07 (0.92, 1.22)	
Elapsing time between the case date and the hospitalization	1.07 (1.04, 1.11)	1.09 (1.05, 1.12)		
Share of households with five or more people in total private households (in municipality of residence)	1.03 (0.98, 1.08)		1.12 (1.01, 1.23)	
Average air temperature during hospitalization (in residence municipality)			0.78 (0.71, 0.84)	0.70 (0.63, 0.77)
Average $PM_{2.5}$ exposure during 2014–2019 (in residence municipality)				1.16 (1.04, 1.28)
Sex: Male	1.74 (1.63, 1.87)	1.67 (1.55, 1.79)	1.88 (1.61, 2.20)	1.68 (1.41, 2.00)
Age groups:	Ref (Age $\leq$ 40)			
40–59	1.51 (1.16, 1.99)	2.91 (1.72, 5.41)	1.72 (1.10, 2.80)	1.55 (0.66, 4.47)
60–79	2.88 (2.25, 3.75)	10.30 (6.22, 18.85)	2.75 (1.79, 4.42)	5.49 (2.48, 15.24)
80+	4.79 (3.73, 6.26)	24.16 (14.58, 44.23)	4.12 (2.66, 6.68)	14.45 (6.50, 40.16)
Number of comorbidities:	Ref (Comorbidities = 0)			
1	1.69 (1.48, 1.94)	2.10 (1.77, 2.50)	1.50 (1.15, 1.96)	2.93 (1.93, 4.62)
2	2.57 (2.26, 2.94)	3.43 (2.92, 4.07)	2.44 (1.87, 3.20)	5.66 (3.78, 8.86)
3 or more	5.50 (4.86, 6.26)	7.91 (6.76, 9.32)	5.51 (4.25, 7.22)	13.21 (8.86, 20.58)
Main language of the residence municipality:	Ref (Language = German)			
French	1.70 (1.33, 2.15)	1.67 (1.25, 2.22)	1.27 (0.95, 1.82)	1.29 (0.99, 1.62)
Italian	1.24 (0.77, 1.99)	1.18 (0.64, 2.16)	0.90 (0.53, 1.37)	0.94 (0.67, 1.27)
DIC	23536.84	20627.46	4442.47	3533.90

pollution appears to be an important risk factor for the severity of the disease only when analyzing data during the first major wave of infection in Switzerland (i.e., before October 2020), as indicated by the high inclusion probabilities estimated using Bayesian variable selection models only during this period. Multivariate BYM spatial models indicate that long-term exposure to both NO_2 and $PM_{2.5}$ is associated with an increased risk of dying after contracting COVID-19, while exposure to NO_2 also increases the odds of entering ICU. On the other hand, the BYM models indicate that during the first wave, the increase in the surface air temperature decreases the odds of both ICU and death. However, the magnitude of air pollution and climate effects is lower than that of known individual risk factors. For $PM_{2.5}$ the result is consistent with findings put forth in the study based on individual-level data in Mexico City (López-Feldman et al., 2021), which estimated a positive relationship between $PM_{2.5}$ and the probability of dying from COVID-19 adjusting for individual- and municipal-level characteristics. Nonetheless, the study conducted in Catalan hospitals discovered that long-term exposure to PM_{10} is a more important predictor of COVID-19 severity and mortality than some of the comorbidities, such as COPD/asthma, diabetes, or obesity (Marquès et al., 2022). As for the ambient temperature, a significant negative association between the increased temperature levels and the subsequent COVID-19 mortality was also previously estimated in China (Zhu et al., 2021) and the US (Christophi et al., 2021).

The inference regarding the important associations with the air pollution and the air temperature when modelling the entire time series (i.e., February 2020–April 2021) is different to the one discussed in the previous paragraph. The results of the variable selection have shown that, when modelling both major waves of the pandemic in Switzerland, these important associations are attenuated. In this case, the BVS has indicated a higher inclusion probability in the models of the parameters related to the health-system of the country. In particular, we estimated higher odds of ICU stay or dying in cantons with a higher number of hospital beds; a plausible explanation is that some specific hospitals were designated to treat patients infected with the coronavirus infection. On the other hand, the cantons with more employees in the spitex and in the nursing homes appear to be associated with lower odds of both outcomes. This may be explained by the fact that, in this case, people were dying in these facilities without being hospitalized, and therefore they were not included in our analyzed dataset. Additionally, we found that an increase in the elapsing time, which on average was higher during the entire study period, increased the risks of ICU and mortality, an association that was not found important when modelling only the 1st wave of the pandemic. These findings suggest that changes in disease management during the second wave of the pandemic, including changes in notification and testing criteria, in the probability of getting diagnosed and hospitalized, or in people's health seeking, are likely to confound the effects of climate or air pollution on the severity of COVID-19. Interestingly, the estimated odds ratios for the individual level characteristics remained stable during the two study periods. Non-significant association between the NO_x, $PM_{2.5}$ or PM_{10} and the risk of the COVID-19 deaths, when adjusting for other patient characteristics, was estimated in the individual-level analysis of the UK Biobank cohort (Elliott et al., 2021).

Similarly to our estimates, Roelens et al. (2021) found that the overall COVID-19 in-hospital mortality in Switzerland was lower during the second wave than in the first wave, a decrease that was not explained by changes in the demographic characteristics of the patients. The authors attributed these temporal differences to the development of case management, treatment strategy, hospital burden, and non-pharmaceutical interventions in the country (Roelens et al., 2021).

Our results suggest that very few socio-economic factors at the municipality level are important in modelling the severity of the COVID-19 infection. A possible explanation is that assigning the municipality level averages to each individual living in this municipality may not reflect the true status of the particular patient. In fact, of the indices related to the distribution of the population, the urbanization status, and the economic indicators, only the variable quantifying the share of households with five or more people in total private households is statistically important when modelling admission to ICU. Besides that, the language of the region is related to both outcomes. Thus, in the French region of Switzerland, the odds of dying or ending up in ICU after hospitalization with COVID-19 are higher than in the German part. Different language regions in Switzerland reflect cultural and lifestyle differences and have been shown to be related to the geographical variation of other health outcomes in the country, including cancer (Jürgens et al., 2013) and other cause-specific mortality (Chammartin et al., 2016). Another plausible explanation is that people in the French-speaking part were more likely to die at the hospital rather than at the nursing home.

The analyses performed here are based only on the individuals that were hospitalized. Many COVID-19 deaths in Switzerland occurred either at home or at nursing homes and were not included in the current analyses. To investigate potential selection bias due to missing deaths, we assessed the relationship between the geographical distribution of the proportion of deaths outside the hospital and the distribution of NO_2 and $PM_{2.5}$ concentrations. This analysis was only possible during the 1st major wave because there is almost a 2-year delay in the publication of the cause-specific mortality data in Switzerland. For each municipality, we used the total number of COVID-19 deaths from the FSO database and removed the deaths in the hospital (from the hospital database) to calculate the proportion of deaths outside the hospital. Logistic regression models were fitted to the above proportion, with independent variables being the average concentrations (at municipality level) of NO_2, $PM_{2.5}$, or both pollutants together. The findings show that during the 1st wave of the pandemic, approximately 46.7% of people died in hospitals; however, the distribution of the excluded deaths is unrelated to the distribution of the exposure(s), and thus should not lead to any selection bias (Table A7 in SI).

A comparison between the statistical models with and without the structured spatial random effect revealed that all the spatial models outperformed (in terms of DIC) the corresponding independent formulations. When analyzing spatially varying exposures that do not have replicates over time, incorporation of the spatial random effect could generally bias the fixed effects of interest (Hodges and Reich, 2010). Several methods have been proposed to address this so-called spatial confounding, such as the restricted geostatistical regression (Hanks et al., 2015) or the spatial orthogonal centroid “k”orrection model (Prates et al., 2019). However, in our case, the regression coefficients estimated using the spatial models (Tables 2 and 3) were very similar to the ones estimated using the models without the spatial random effects (Tables A5 and A6 in SI) for both $PM_{2.5}$ and NO_2 concentrations, indicating no evidence of spatial confounding.

Many variable selection methods, including some spike and slab approaches, may under select covariates that are correlated with each other (Delattre et al., 2022). Following up on a suggestion made by a reviewer, we have fitted additional models, that included all the covariates (full models) and compared them to the results obtained using BVS. We focused on the deaths and ICU outcomes during the first wave, where a non-zero effect of pollutants was estimated. The results have shown that, indeed, there was some under selection of the covariates. In particular, NO_2 models fitted to the death outcome identified three statistically important covariates (i.e., the 95% BCIs did not include zero) in the full formulation that were not selected by BVS, namely: (1) number of employees in the 1st economic sector; (2) proportion of the permanent foreign population in the total permanent resident population; and (3) social assistance rate. The first two had an important positive association with the probability of dying from COVID-19, and the third one had a negative association (i.e., a protective effect). To ensure that no statistically important covariate was excluded from the final models, we fitted a third set of models that incorporated variables selected through BVS and the ones identified by the full model (as mentioned above). The results (Table A8 in SI) have shown that, despite the fact that DIC slightly improved when compared to BVS analysis (3530.7 vs. 3534.8), out of these three additional covariates, only one (the social assistance rate) maintained a statistically important effect. Furthermore, the average effect of NO_2 (and most of the other variables) did not change, but only the uncertainty increased (i.e., wider 95% BCIs), as more parameters were used to estimate the effect. Very similar results were observed in the NO_2 models fitted to the ICU outcome (Table A9 in SI), and in the $PM_{2.5}$ models fitted to both death (Table A10 in SI) and ICU (Table A11 in SI) outcomes during the 1st wave of COVID-19.

It is important to note that the individual-level demographic, social, and biological characteristics, which are typically available in cohort data analyses (Elliott et al., 2021), were not recorded in the current COVID-19 dataset. In addition, due to the lack of information on patients' home addresses, we have assigned to each individual the average air pollution exposure in the reported municipality of residence during the 6 years preceding the pandemic. This is a strong limitation since we do not know whether the patient was living in that municipality during all this time. Furthermore, here we looked at the long-term air pollution exposure preceding the pandemic and ignored the short-term exposure, which has a clear seasonal pattern in Europe, both before and during the pandemic (Beloconi et al., 2021; Barré et al., 2021). It was previously shown that COVID-19 exhibits seasonal behavior and that both air pollution and climate can influence the transmission of the disease (Coccia, 2022). Nonetheless, in the absence of individual exposures, this is among the very few studies that assess the association of COVID-19 severity and air pollution using individual information on the infection course, demographic characteristics, and comorbidities.

In conclusion, our study of the ongoing COVID-19 epidemic identified differences in the associations between the severity of the disease and various risk factors during the first wave. The findings suggest that air pollution burden has increased the risks of COVID-19 in the beginning of the pandemic but not during the whole period, which is influenced by the second wave, when the national health system was better prepared to treat the patients. The results of this work can lead to an improved understanding of the effect of air pollution exposure on COVID-19 morbidity and mortality in Switzerland and beyond.

Declaration of competing interest

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

Data availability

The authors do not have permission to share data.

Acknowledgments

This study was funded by the Swiss Federal Office for the Environment (FOEN) [Contract no. 17.0094.PJ/5666BF610]. We are grateful to Lara Milena Lüthi, Richard Ballaman, Rudolf Weber and other colleagues from FOEN for their valuable inputs during conceptualization of the work, performance of the analysis and interpretation of the results. We are thankful to the Federal Office of Public Health (FOPH), in particular Damir Perisa, Bettina Ley and Mirjam Mäusezahl, for providing the COVID-19 dataset and for their helpful comments to the manuscript. We would also like to thank Nicole Probst-Hensch, Meltem Kutlar Joss and Ron Kappeler for critically reviewing the manuscript.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envres.2022.114481.

References

Aloisi, V., Gatto, A., Accarino, G., Donato, F., Aloisio, G., 2022. The effect of known and unknown confounders on the relationship between air pollution and Covid-19 mortality in Italy: a sensitivity analysis of an ecological study based on the E-value. Environ. Res. 207, 112131 https://doi.org/10.1016/j.envres.2021.112131.

Amy McNally NASA/GSFC/HSL, 2018. FLDAS Noah Land Surface Model L4 Global Monthly 0.1 X 0.1 Degree (MERRA-2 and CHIRPS), Greenbelt, MD, USA. Goddard

Earth Sciences Data and Information Services Center (GES DISC). https://doi.org/10.5067/5NHC22T9375G. (Accessed 1 July 2021). Accessed:
Barré, J., Petetin, H., Colette, A., Guevara, M., Peuch, V.H., Rouil, L., et al., 2021. Estimating lockdown-induced European NO2 changes using satellite and surface observations and air quality models. Atmos. Chem. Phys. 21 (9), 7373–7394. https://doi.org/10.5194/acp-21-7373-2021.
Bashir, M.F., Jiang, B., Komal, B., Bashir, M.A., Farooq, T.H., Iqbal, N., Bashir, M., 2020. Correlation between environmental pollution indicators and COVID-19 pandemic: a brief study in Californian context. Environ. Res. 187, 109652 https://doi.org/10.1016/j. envpol.2020.114732.
Beloconi, A., Vounatsou, P., 2020. Bayesian geostatistical modelling of high-resolution NO2 exposure in Europe combining data from monitors, satellites and chemical transport models. Environ. Int. 138, 105578 https://doi.org/10.1016/j.envint.2020.105578.
Beloconi, A., Vounatsou, P., 2021. Substantial reduction in particulate matter air pollution across Europe during 2006-2019: a spatiotemporal modeling analysis. Environ. Sci. Technol. https://doi.org/10.1021/acs.est.1c03748.
Beloconi, A., Chrysoulakis, N., Lyapustin, A., Utzinger, J., Vounatsou, P., 2018. Bayesian geostatistical modelling of PM10 and PM2.5 surface level concentrations in Europe using high-resolution satellite-derived products. Eniron. Int. 121, 57–70. https://doi.org/10.1016/j.envint.2018.08.041.
Beloconi, A., Probst-Hensch, N.M., Vounatsou, P., 2021. Spatio-temporal modelling of changes in air pollution exposure associated to the COVID-19 lockdown measures across Europe. Sci. Total Environ. 787, 147607 https://doi.org/10.1016/j.scitotenv.2021.147607.
Besag, J., York, J., Mollié, A., 1991. Bayesian image restoration, with two applications in spatial statistics. Ann. Inst. Stat. Math. 43 (1), 1–20. https://doi.org/10.1007/BF00116466.
Bourdrel, T., Annesi-Maesano, I., Alahmad, B., Maesano, C.N., Bind, M.A., 2021. The impact of outdoor air pollution on COVID-19: a review of evidence from in vitro, animal, and human studies. Eur. Respir. Rev. 30, 159. https://doi.org/10.1183/16000617.0242-2020.
Brunekreef, B., Downward, G., Forastiere, F., Gehring, U., Heederik, D.J.J., Hoek, G., Koopmans, M.P.G., Smit, L.A.M., Vermeulen, R.C.H., 2021. Air Pollution and COVID-19. Including Elements of Air Pollution in Rural Areas, Indoor Air Pollution and Vulnerability and Resilience Aspects of Our Society against Respiratory Disease, Social Inequality Stemming from Air Pollution. Study for the Committee on Environment, Public Health and Food Safety. Policy Department for Economic, Scientific and Quality of Life Policies, European Parliament, Luxembourg.
Chammartin, F., Hürlimann, E., Raso, G., N'Goran, E.K., Utzinger, J., Vounatsou, P., 2013. Statistical methodological issues in mapping historical schistosomiasis survey data. Acta Trop. 128, 345–352. https://doi.org/10.1016/j.actatropica.2013.04.012.
Chammartin, F., Probst-Hensch, N., Utzinger, J., Vounatsou, P., 2016. Mortality atlas of the main causes of death in Switzerland. Swiss Med. Wkly. 146, w14280 https://doi.org/10.4414/smw.2016.14280, 2008-2012.
Chen, J.C., Schwartz, J., 2008. Metabolic syndrome and inflammatory responses to long-term particulate air pollutants. Environ. Health Perspect. 116 (5), 612–617. https://doi.org/10.1289/ehp.10565, 2008.
Christophi, C.A., Sotos-Prieto, M., Lan, F.Y., Delgado-Velandia, M., Efthymiou, V., Gaviola, G.C., et al., 2021. Ambient temperature and subsequent COVID-19 mortality in the OECD countries and individual United States. Sci. Rep. 11 (1), 1–9. https://doi.org/10.1038/s41598-021-87803-w.
Coccia, M., 2020. Factors determining the diffusion of COVID-19 and suggested strategy to prevent future accelerated viral infectivity similar to COVID. Sci. Total Environ. 729, 138474 https://doi.org/10.1016/j.scitotenv.2020.138474.
Coccia, M., 2022. COVID-19 pandemic over 2020 (with lockdowns) and 2021 (with vaccinations): similar effects for seasonality and environmental factors. Environ. Res. 208, 112711 https://doi.org/10.1016/j.envres.2022.112711.
Cohen, A.J., Brauer, M., Burnett, R., Anderson, H.R., Frostad, J., et al., 2017. Estimates and 25-year trends of the global burden of disease attributable to ambient air pollution: an analysis of data from the Global Burden of Diseases Study 2015. Lancet 389 (10082), 1907–1918. https://doi.org/10.1016/S0140-6736(17)30505-6.
Copat, C., Cristaldi, A., Fiore, M., Grasso, A., Zuccarello, P., Santo Signorelli, S., et al., 2020. The role of air pollution (PM and NO2) in COVID-19 spread and lethality: a systematic review. Environ. Res. 191, 110129 https://doi.org/10.1016/j.envres.2020.110129.
Daes, R., Blanco-Vidal, C., Romero-Meza, R., Schoen, S., Lukina, A., Cakmak, S., 2021. The association between air pollution and COVID-19 related mortality in Santiago, Chile: a daily time series analysis. Environ. Res. 198, 111284 https://doi.org/10.1016/j.envres.2021.111284.
De Angelis, E., Renzetti, S., Volta, M., Donato, F., Calza, S., Placidi, D., et al., 2021. COVID-19 incidence and mortality in Lombardy, Italy: an ecological study on the role of air pollution, meteorological factors, demographic and socioeconomic variables. Environ. Res. 195, 110777 https://doi.org/10.1016/j.envres.2021.110777.
Delattre, M., King, G.K.K., Naveau, M., Sansonnet, L., 2022. Bayesian High-Dimensional Covariate Selection in Non-linear Mixed-Effects Models Using the SAEM Algorithm. https://doi.org/10.48550/arXiv.2206.01012 arXiv preprint.
Elliott, J., Bodinier, B., Whitaker, M., Delpierre, C., Vermeulen, R., Tzoulaki, I., et al., 2021. COVID-19 mortality in the UK Biobank cohort: revisiting and evaluating risk factors. Eur. J. Epidemiol. 36 (3), 299–309. https://doi.org/10.1007/s10654-021-00722-y.
Fatorini, D., Regoli, F., 2020. Role of the chronic air pollution levels in the Covid-19 outbreak risk in Italy. Environ. Pollut. 264, 114732 https://doi.org/10.1016/j.envpol.2020.114732.
Funk, C., Peterson, P., Landsfeld, M., Pedreros, D., Verdin, J., Shukla, S., et al., 2015. The climate hazards infrared precipitation with stations—a new environmental record for monitoring extremes. Sci. Data 2, 150066. https://doi.org/10.1038/sdata.2015.66.
George, E.I., McCulloch, R.E., 1996. Stochastic search variable selection. In: Markov Chain Monte Carlo in Practice. Springer, pp. 203–214.
Gorelick, N., Hancher, M., Dixon, M., Ilyushchenko, S., Thau, D., Moore, R., 2017. Google Earth engine: planetary-scale geospatial analysis for everyone. Remote Sens. Environ. 202, 18–27. https://doi.org/10.1016/j.rse.2017.06.031.
Guan, W.J., Liang, W.H., Zhao, Y., Liang, H.R., Chen, Z.S., Li, Y.M., et al., 2020. Comorbidity and its impact on 1590 patients with Covid-19 in China: a nationwide analysis. Eur. Respir. J. 55, 2000547 https://doi.org/10.1183/13993003.00547-2020, 2020.
Hanks, E.M., Schliep, E.M., Hooten, M.B., Hoeting, J.A., 2015. Restricted spatial regression in practice: geostatistical models, confounding, and robustness under model misspecification. Environmetrics 26 (4), 243–254. https://doi.org/10.1002/env.2331.
Hodges, J.S., Reich, B.J., 2010. Adding spatially-correlated errors can mess up the fixed effect you love. Am. Statistician 64 (4), 325–334. https://doi.org/10.1198/tast.2010.10052.
Jiang, Y., Wu, X.J., Guan, Y.J., 2020. Effect of ambient air pollutants and meteorological variables on COVID-19 incidence. Infect. Control Hosp. Epidemiol. 41 (9), 1011–1015. https://doi.org/10.1017/ice.2020.222.
Jürgens, V., Ess, S., Phuleria, H.C., Früh, M., Schwenkglenks, M., Frick, H., et al., 2013. Bayesian spatio-temporal modelling of tobacco-related cancer mortality in Switzerland. Geospatial Health 7 (2), 219–236. https://doi.org/10.4081/gh.2013.82.
Konstantinoudis, G., Padellini, T., Bennett, J., Davies, B., Ezzati, M., Blangiardo, M., 2021. Long-term exposure to air-pollution and COVID-19 mortality in England: a hierarchical spatial analysis. Environ. Int. 146, 106316 https://doi.org/10.1016/j.envint.2020.106316.
Li, H., Xu, X., Dai, D., Huang, Z., Ma, Z., Guan, Y., 2020. Air pollution and temperature are associated with increased COVID-19 incidence: a time series study. Int. J. Infect. Dis. 97, 278–282. https://doi.org/10.1016/j.ijid.2020.05.076.
Lindgren, F., Rue, H., Lindström, J., 2011. An explicit link between Gaussian fields and Gaussian Markov random fields: the stochastic partial differential equation approach. J. R. Stat. Soc. Ser. B Methodol. 73 (4), 423–498. https://doi.org/10.1111/j.1467-9868.2011.00777.x.
López-Feldman, A., Heres, D., Marquez-Padilla, F., 2021. Air pollution exposure and COVID-19: a look at mortality in Mexico City using individual-level data. Sci. Total Environ. 756, 143929 https://doi.org/10.1016/j.scitotenv.2020.143929.
Marquès, M., Domingo, J.L., 2022. Positive association between outdoor air pollution and the incidence and severity of COVID-19. A review of the recent scientific evidences. Environ. Res. 203, 111930 https://doi.org/10.1016/j.envres.2021.111930.
Marquès, M., Correig, E., Ibarretxe, D., Anoro, E., Antonio Arroyo, J., Jericó, C., Borrallo, R.M., Miret, M., Näf, S., Pardo, A., Perea, V., Pérez-Bernalte, R., Ramírez-Montesinos, R., Royuela, M., Soler, C., Urquizu-Padilla, M., Zamora, A., Pedro-Botet, J., , STACOV-XULA research group, Masana, L., Domingo, J.L., 2022. Long-term exposure to PM10 above WHO guidelines exacerbates COVID-19 severity and mortality. Environ. Int. 158, 106930.
McNally, A., Arsenault, K., Kumar, S., Shukla, S., Peterson, P., Wang, S., Funk, C., Peters-Lidard, C.D., Verdin, J.P., 2017. A land data assimilation system for sub-Saharan Africa food and water security applications. Sci. Data 4, 170012. https://doi.org/10.1038/sdata.2017.12.
Mostafavi, N., Jeong, A., Vlaanderen, J., Imboden, M., Vineis, P., Jarvis, D., Kogevinas, M., Probst-Hensch, N., Vermeulen, R., 2019. The mediating effect of immune markers on the association between ambient air pollution and adult-onset asthma. Sci. Rep. 9, 8818. https://doi.org/10.1038/s41598-019-45327-4.
Pegoraro, V., Heiman, F., Levante, A., Urbinati, D., Peduto, I., 2021. An Italian individual-level data study investigating on the association between air pollution exposure and Covid-19 severity in primary-care setting. BMC Publ. Health 21 (1), 1–11. https://doi.org/10.1186/s12889-021-10949-9.
Plummer, M., 2003. JAGS: A Program for Analysis of Bayesian Graphical Models Using Gibbs Sampling. (Proceedings of the 3rd International Workshop on Distributed Statistical Computing. Vienna, Austria. In: https://www.r-project.org/conferences/DSC-2003/Proceedings/Plummer.pdf.
Prates, M.O., Assunção, R.M., Rodrigues, E.C., 2019. Alleviating spatial confounding for areal data problems by displacing the geographical centroids. Bayesian Anal 14 (2), 623–647. https://doi.org/10.1214/18-BA1123.
R Core Team, 2021. R: A Language and Environment for Statistical Computing. R Foundation for Statistical Computing, Vienna, Austria. http://www.R-project.org/.
Roelens, M., Martin, A., Friker, B., Sousa, F.M., Thiabaud, A., Vidondo, B., et al., 2021. Evolution of COVID-19 mortality over time: results from the Swiss hospital surveillance system (CH-SUR). Swiss Med. Wkly. 151, w30105 https://doi.org/10.4414/smw.2021.w30105.
Rue, H., Martino, S., Chopin, N., 2009. Approximate Bayesian inference for latent Gaussian models by using integrated nested Laplace approximations. J. R. Stat. Soc. Ser. B Methodol. 71 (2), 319–392. https://doi.org/10.1111/j.1467-9868.2008.00700.x.
Rue, H., Martino, S., Lindgren, F., Simpson, D., Riebler, A., 2013. R-INLA: Approximate Bayesian Inference Using Integrated Nested Laplace Approximations. Trondheim, Norway. http://www.r-inla.org.
Scheipl, F., Fahrmeir, L., Kneib, T., 2012. Spike-and-slab priors for function selection in structured additive regression models. J. Am. Stat. Assoc. 107 (500), 1518–1532. https://doi.org/10.1080/01621459.2012.737742.

Zoran, M.A., Savastru, R.S., Savastru, D.M., Tautan, M.N., 2020a. Assessing the relationship between surface levels of PM2.5 and PM10 particulate matter impact on COVID-19 in Milan, Italy. Sci. Total Environ. 738, 139825 https://doi.org/10.1016/j.scitotenv.2020.139825.

Zoran, M.A., Savastru, R.S., Savastru, D.M., Tautan, M.N., 2020b. Assessing the relationship between ground levels of ozone (O3) and nitrogen dioxide (NO2) with coronavirus (COVID-19) in Milan, Italy. Sci. Total Environ. 740, 140005 https://doi.org/10.1016/j.scitotenv.2020.140005.

Swiss Federal office of statistics. Statistical Atlas of Switzerland. https://www.bfs.admin.ch/bfs/en/home/statistics/regional-statistics/atlases/interactive-statistical-atlas-switzerland.html.

Telo-Leal, E., Macías-Hernandez, B., 2021. Association of environmental and meteorological factors on the spread of COVID-19 in Victoria, Mexico, and air quality during the lockdown. Environ. Res. 196, 110442 https://doi.org/10.1016/j.envres.2020.110442.

Villeneuve, P.J., Goldberg, M.S., 2020. Methodological considerations for epidemiological studies of air pollution and the SARS and COVID-19 coronavirus outbreaks. Environ. Health Perspect. 128 (9), 095001 https://doi.org/10.1289/EHP7411.

Wakefield, J., 2008. Ecologic studies revisited. Annu. Rev. Publ. Health 29, 75–90. https://doi.org/10.1146/annurev.publhealth.29.020907.090821.

Wu, X., Nethery, R.C., Sabath, M.B., Braun, D., Dominici, F., 2020. Air pollution and COVID-19 mortality in the United States: strengths and limitations of an ecological regression analysis. Sci. Adv. 6 (45), eabd4049 https://doi.org/10.1126/sciadv.abd4049.

Zhu, N., Zhang, D., Wang, W., Li, X., Yang, B., Song, J., et al., 2020a. A novel coronavirus from patients with pneumonia in China. N. Engl. J. Med. 382, 727–733. https://doi.org/10.1056/NEJMoa2001017.

Zhu, Y., Xie, J., Huang, F., Cao, L., 2020b. Association between short-term exposure to air pollution and COVID-19 infection: evidence from China. Sci. Total Environ. 727, 138704 https://doi.org/10.1016/j.scitotenv.2020.138704.

Zhu, G., Zhu, Y., Wang, Z., Meng, W., Wang, X., Feng, J., et al., 2021. The association between ambient temperature and mortality of the coronavirus disease 2019 (COVID-19) in Wuhan, China: a time-series analysis. BMC Publ. Health 21 (1), 1–10. https://doi.org/10.1186/s12889-020-10131-7.