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RETRACTED

Correlation between COVID-19 and air pollution: the effects of $PM_{2.5}$ and PM_{10} on COVID-19 outcomes

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Abstract. – OBJECTIVE: Given its effects on long-term illnesses, like heart problems and diabetes, air pollution may be among the reasons that led COVID-19 to get worse and kill a larger number of people. Experiments have shown that breathing in polluted air weakens the immune system, making it easier for viruses to enter th[illegible] and grow. Viruses may be able to surviv[illegible] air by interacting in complex ways with pa[illegible]es and gases. These interactions depend on the[illegible] chemical makeup, the particles' electric charg[illegible] and environmental conditions like humidity, [illegible] light, and temperature. Moreo[illegible]posure t[illegible] UV rays and air pollution ma[illegible] organism's production of antimic[illegible] mole[illegible]es, thus supporting viral infection[illegible]re epid[illegible]logical studies are needed to d[illegible]e wh[illegible] pollution has on COV[illegible]19. [illegible]ew, we will discuss how air poll[illegible]s suc[illegible]$_{2.5}$ and PM_{10} contribute to the tr[illegible]nission of [illegible]19.

MATERIALS [illegible] METHODS: W[illegible] used nine target cit[illegible]uscany regi[illegible] to verify this certai[illegible] and [illegible]hese cases, the air pollution f[illegible]tors were fo[illegible] be strongly correlated w[illegible]COVID-19 case[illegible] each city, we applied [illegible]ultivariate analysis [illegible]d found an appropr[illegible] model [illegible] better fits the data.

R[illegible]LTS: T[illegible] review underlines that both sho[illegible] a[illegible]ong-te[illegible]exposure to air pollution [illegible] crucia[illegible]asperating factors for [illegible]S-Co[illegible]smi[illegible]n and COVID-19 severity [illegible]hality[illegible]istical analysis concludes tha[illegible] pollutio[illegible]ould be accounted for as a pos[illegible] risk facto[illegible] in future COVID-19 investigatio[illegible]ld be avoided as much as poss[illegible]by t[illegible]eral population.

[illegible]ONCLUSIONS: Our research highlighted the [illegible]lation between COVID-19 and air pollution. R[illegible]g air pollution exposure should be one of th[illegible]st measures against COVID-19 spread.

[illegible]Words:
[illegible]OVID-19, Air[illegible]lution, $PM_{2.5}$, PM_{10}, UV light, [illegible]ivariate analy[illegible]

Introduction

[illegible]OVID-19 pandemic has spread worl[illegible]ide, [illegible]ith hundreds of millions of confirmed cases and millions of deaths. Several treatments have been proposed for people infected with the virus, such as antiviral drugs and monoclonal antibodies. Among many others, the development of the so-called "long COVID" syndrome is a crucial consequence of COVID-19 infection. People affected by this condition continue to have COVID-like symptoms (such as fatigue, brain fog, and shortness of breath) even after getting over the virus[1].

COVID-19 transmission modalities have recently been identified[2,3] as direct and indirect. Direct pathways of SARS-CoV-2 bioaerosol transmission can be droplet nuclei and other physiological fluids floating in the interior atmosphere, as well as maternal-to-infant transmission. The indirect method is via fomites, contaminated surfaces on surrounding furniture, and fixtures that cause an infected person to get ill[2]. The nasal epithelial cells have been identified as the main entry for SARS-CoV-2, via the spike protein of the virus being cleaved by proteases. Then, SARS-CoV-2 spike protein attaches to the angiotensin-converting enzyme-2 (ACE2) receptors on the cellular membrane, thus gaining access to the host cells in the nasal and upper airway passages[3].

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Several studies[4-8] support the effects of air pollution in decreasing the antimicrobial defenses of the organism, increasing general inflammation and oxidation, and boosting the possibility of viral infections. Moreover, many viral infections, among which COVID-19, have been correlated to air pollution: for example, increased $PM_{2.5}$ concentrations have been associated with higher rates of respiratory virus transmission – including influenza, swine flu, and measles[9]. Moreover, it has been proved[10] that individuals living in air-polluted areas have an increased viral infection mortality risk. Exposure to polluted air also increases the prevalence of lower respiratory tract infections and also exacerbates respiratory virus symptoms[10]. Coal use, and thus fine and ultrafine particles, seem highly detrimental in increasing viral infection mortality[11].

Among the different air pollutants, some specific ones have been correlated to viral infections, such as particulate matter (PM), with a 50% cut-off aerodynamic diameter of 10 m (PM_{10}), tiny particles ($PM_{2.5}$) and ultrafine particles (0.1 m in diameter). PM size substantially affects its ability to be transported and to reach its destination within the respiratory system and bloodstre[illegible] composition of particulate matter may va[illegible] depending on its source[12]. Moreover, another ty[illegible] air pollutant with widespread toxic effects is N[illegible]. It is a significant air pollutant in cities, main[illegible] owing to traffic (especially fr[illegible] automobiles), and has been linked[illegible] asth[illegible], COPD, bronchiolitis, and cardiova[illegible]ar dise[illegible]

Materia[illegible]nd M[illegible]s

This scoping [illegible] followed PR[illegible]A guidelines[14] for [illegible]. This article starts with a revi[illegible] of existing [illegible]ture that focuses on SARS[illegible]-2 and the eff[illegible] air pollution, PM_{10}, a[illegible] $PM_{2.5}$. To do this, we selected original and r[illegible] articles from online databases such as Pu[illegible] and [illegible]us, using the following strings: (SAR[illegible] [Text W[illegible]]) AND (air pollution [Text W[illegible] OR P[illegible] [Text Word] OR $PM_{2.5}$ [illegible] Word]) [illegible]icles published in English were included. [illegible], we followed a pipeline of statistical methods in order to study the correlation [illegible]9 with air pollution and climate [illegible]rs. In the study, four air pollution factors were taken into consideration: PM_{10}, $PM_{2.5}$, NO_2, and s[illegible] climate factors, namely medium temperature ([illegible]ed_T), minimum temperature (Min_T), maximum temperature (Max_T), dew point (DP), medium wind speed (Med_WS), maxi[illegible] speed (Max_WS), humidity (H); th[illegible]ere w[illegible] 11 factors in total that are involv[illegible] the study. For the analysis, the open-acc[illegible]tasets were taken from the web (available [illegible]://www.arpat.toscana.it/temi-ambie[illegible]li/aria/[illegible]aria/archivio_dati_orari). In [illegible]aset with [illegible]riables, groups of vari[illegible] often move toge[illegible], and as we conside[illegible] 11 fa[illegible], we applied Principal Compone[illegible] (PCA), [illegible]ch is a classical multi[illegible]ate [illegible] techn[illegible] to reduce the dim[illegible]ons. PC[illegible] the most widely used [illegible]niques whe[illegible]ensionality reduction [illegible]. The main pur[illegible]se of PCA is to solve [illegible] probl[illegible] dimensionality reduction, and through it is po[illegible] to capture the 'information [illegible]tained in a d[illegible]t with a smaller set o[illegible] compared to the original one. This [illegible]hod is used w[illegible]n there is a variable that is a [illegible]ction of othe[illegible]riables, and, in consequence, [illegible]ntains redun[illegible]t information; the other case is [illegible] the obs[illegible]d variables are correlated, and a sm[illegible] of new variables could replace them w[illegible] loss of information. The dimensionality reduction allows us to simplify posterior [illegible]d carry out graphical visualization in [illegible]ensions. The PCA is the first step before performing a multivariate analysis.

We applied PCA for nine provinces in the region of Tuscany and chose 3 to 5 principal factors that better explain the original dataset. There are several methods to decide how many components to use; in this study, we used the percentage of explained variability – it is desirable to achieve a relatively high percentage of explained variability (i.e., 70-90%). We also used the Kaiser-Meyer-Olkin (KMO) test, which is a statistical measure to determine how suited data are for factor analysis. The higher the proportion, the higher the KMO value, and the more suited the data is to factor analysis. In the field of statistics, Bartlett's test, attributed to Maurice Stevenson Bartlett, is employed for assessing homoscedasticity. Specifically, it is used to determine whether multiple sets of data originate from populations characterized by comparable variances. Kaiser's criterion excludes those components whose eigenvalues are smaller than the average eigenvalue or others smaller than 1 if they are computed from the correlation matrix[15]. In this work, we used the high percentage of explained variability, Kaiser-Meyer-Olkin (KMO) test, Bartlett's test, and eigenvalues' test for the principal components that we involved in the multivariate analysis. The detailed information and numerical calculation for our dataset are shown in **Supplementary File 1**. With the new variables obtained from the PCA analysis, the multivariate analysis was performed using linear and nonlinear regression.

Results

Multiple studies in literature have shown that increases in air pollutant concentrations relate to an increase in viral respiratory illnesses in children and adults, mainly when the viral infection occurs concurrently with a short-term surge in air pollution exposure[4]. These data prompted research on the potential relationship between pollution and COVID-19. According to several investigations[4], long-term exposure to air pollution, which varies geographically and temporally, may increase the likelihood of COVID-19 causing severe consequences. COVID-19 cases have indeed been related to fine particle levels, showing that $PM_{2.5}$ has a greater impact than PM_{10}. Indeed, $PM_{2.5}$ and PM_{10} seem to have a positive rel[illegible]ship with SARS-CoV-2[14,16,17], and recent r[illegible] has shown that COVID-19 mortality has [illegible]st doubled in places with high $PM_{2.5}$ levels[illegible]trogen oxides (NO_2) and ozone (O_3), two ty[illegible] of gaseous pollution, have also been linked [illegible] COVID-19 and other respirato[illegible] Indeed, NO_2 levels have been positi[illegible] con[illegible]ed[16,17] to the spread of COVID-19[illegible]ally, a[illegible]ollution may enhance ACE-2 (an[illegible]sin-c[illegible]zyme 2) synthesis in [illegible]lmo[illegible]helial cells, thus increasing SA[illegible]oV-2 i[illegible]ity[2].

This study monitored the air pollution and climate factors with respect to the respo[illegible] COVID-19 cases for a time interval [illegible] days [illegible] the period 25.02.2020 – 08.03.20[illegible] We decided to choose this period of time [illegible] it was the first month of the spread of the [illegible]mic, and there were no vaccinations[illegible]

Table I shows the new [illegible]bles perform[illegible] the PCA analysis and [illegible] which [illegible]riginal fa[illegible] they are composed, [illegible]luding [illegible] cities where the air pollution fac[illegible] in [illegible] fourth [illegible] fifth PC, in the other [illegible]s, [illegible]llution [illegible]ors are present in the [illegible] second, [illegible]ird[illegible]

The num[illegible] of PCs presen[illegible]able I was obtained [illegible] high percen[illegible]e of explained var[illegible]ty, K[illegible]Meyer-Olkin (KMO) test, Bartlett's test, and e[illegible]ues' test, while Table II s[illegible]e percentage [illegible]iance explained for e[illegible]ncipal component. We noticed that for the [illegible] provinces, th[illegible] total variance explained was [illegible]r 80%. The c[illegible]lete information for the other [illegible]rovinces is [illegible]n in **Supplementary File 2**. [illegible] first p[illegible]nted province is Florence, beca[illegible] largest one with respect to population, the second one is Pistoia, and it [illegible] the specification that the four air pollution [illegible] the first and second principal com[illegible]ne[illegible], the third province is Siena, because the composite factors of the first component are quite common with five cites.

In the following equation, we are giving the Linear Multiple Regression of the COVID-19 cases with respect to the first and second principal components, where the first principal component is related to the original variables NO_2, O_3, H, Med_WS, Max_WS, and the second principal

Table I. The pri[illegible] c[illegible]ts (PCs) of each city which explain the model. The factors are written in decreasing order for the percentage c[illegible]bution i[illegible]pective PC.

City	[illegible]t PC	Second PC	Third PC	Fourth PC	Fifth PC
Flor[illegible]	NO_2, O[illegible] Med_WS, Max_WS	$PM_{2.5}$, PM_{10}, Med_T., Max_T., Med_WS.	Med_T., Min_T, DP.		
L[illegible]	PM[illegible]$_{2.5}$, Max[illegible]Med_WS,.	Med_T., Min_T, DP.	NO_2, O_3, H.		
Gro[illegible]	[illegible]VS, Max[illegible]	Min_T, DP, H.	Med_Tp., Max_Tp.,	$PM_{2.5}$, NO_2, O_3,	PM_{10}
Massa	[illegible]Med_W[illegible]ax_WS	Min_T, DP, H..	Med_T., Max_T.,	PM_{10}, $PM_{2.5}$.	
[illegible]a	PM[illegible], H., Med_WS, Max_W[illegible]	$PM_{2.5}$, PM_{10}, Med_T., Max_T., Max_WS.	Med_T., Min_T., DP, H.		
Pi[illegible]	PM[illegible] $PM_{2.5}$, Max_T., Med_WS, [illegible]S	Med_T., Min_T., Dew point.	NO_2, O_3 , H		
[illegible]a	NO_2, Med_WS, Max_WS,	PM_{10}, $PM_{2.5}$, Med_T., Max_T., Min_T., DP, H.	Med_T., Min_T., DP, H.		
[illegible]	NO_2, Med_WS, Max_WS, H.	Med_T., Min_T., DP, H.	Med_T., Max_T.	PM_{10}, $PM_{2.5}$.	
[illegible]	NO_2, H., Med_WS, Max_WS.	Med_T., Min_T., DP, H.	PM_{10}, $PM_{2.5}$.	O_3, Max_T.	

component is related to the original variables $PM_{2.5}$, PM_{10}, Med_T, Max_T, Med_WS.

$$y = 479.116 + 417.57x_1 + 145.74x_2$$

Figure 1 shows the graphical visualization of the plane that fits the data for Florence. In this model, we observed that the four considered air pollution factors among the climate factors were present, with humidity (H.), wind speed (Med_WS, Max_WS), and temperature (Med_T., Max_T.) being the most important. For this model, the p-value corresponded to $4.4517e^{-7}$, meaning that it is statistically significant, giving a good approximation for the data.

The second model is constructed with respect to the second and third principal components. The second principal component is related to the original variables $PM_{2.5}$, PM_{10}, Med_T., Max_T., and Med_WS, and the third principal component is related to the original variables Med_T., Min_T, and Dew Point (DP).

$$y = 531.02 + 151.11x_1 - 182.43x_2$$

From the visualization of the model, we [illegible] that the fitting is not good, meaning that [illegible]ng more climate factors, such as the Dew Point, [illegible] not increase the accuracy of the approximation[illegible]

For the lack of accuracy, we find the nonl[illegible]near multiple regression o[illegible]VID-19 case with respect to the fi[illegible]nd se[illegible]d principal components, show[illegible] the rig[illegible]raph of Figure 2. This model h[illegible]tatisti[illegible]cance as p-value = [illegible]382[illegible]ng a good approximation of t[illegible]ataset.

$$y = 479.06 + [illegible] + 141.79x^1 + [illegible]x^1x^2$$

The line[illegible] multiple re[illegible]n with three factors is gi[illegible] with the follow[illegible]ation, and the p-value [illegible].47e^{-8}, increasing the statistical significan[illegible] compar[illegible] with the previous nonlinear mu[illegible] regre[illegible]n with [illegible]ly two factors.

$$y = 47[illegible] 416.9[illegible] + 150.89x^2 - 181.12x^3$$

A[illegible]e could [illegible] represent this model in a thre[illegible]mensional space, Figure 3 shows the ad[illegible]h respect to the fitted line with a [illegible]dence interval of 95%.

The linear multiple regression with the first a[illegible]ond principal components for Pistoia is give[illegible]ith the following equation:

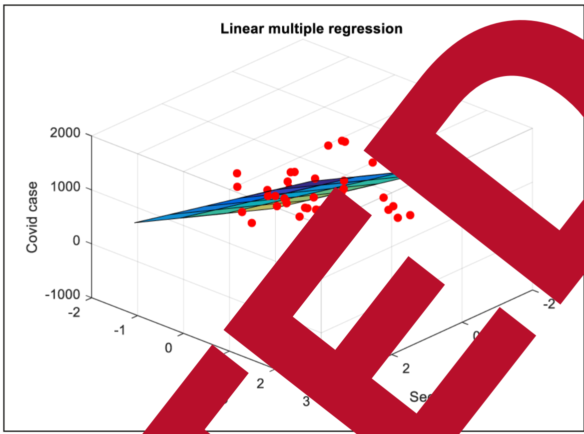

Figure 1. Li[illegible]iple regression [illegible]rence with the first and se[illegible] PC[illegible]

$$y = [illegible]4 - 113.80x^1 + [illegible]8x^2$$

[illegible]igure 4 show[illegible] the visualization of the linear multiple regr[illegible]on with respect to the CO[illegible]-19 cases. F[illegible] the purpose of comparison,

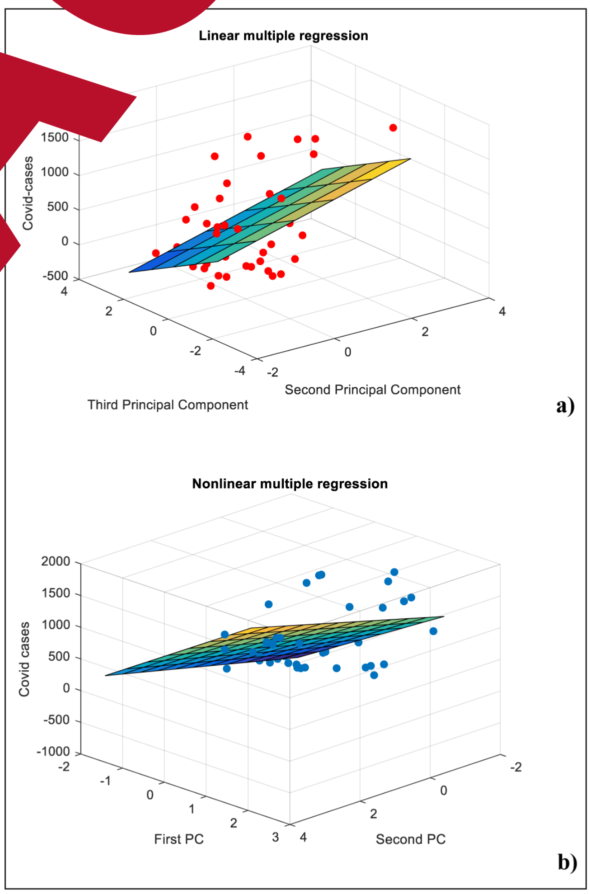

Figure 2. **a**, Linear multiple regression for Florence with the second and third PCs. **b**, Nonlinear multiple regression for Florence with the first and second PCs.

we constructed the nonlinear multiple regression with the first and second principal components.

$$y= 143.98 - 110.11x^1 + 41.84x^2 + 11.76x^1x^2$$

The accuracy for both models using the first and second principal components is very good, and the statistical significance of them is of the order p-value = e^{-9}.

Referring to the results of Table II, the original dataset for Pistoia is explained as 82% with three principal components. The following equation shows the linear multiple regression with all the principal components. The approximation is satisfactory, and the statistical significance is increased up to p-value = 6.34^{e-10}.

$$y = 143.42 - 113.64x^1 + 35.677x^2 - 40.503x^3$$

Figure 5 presents the visualization of nonlinear multiple regression for Pistoia. Siena is the third

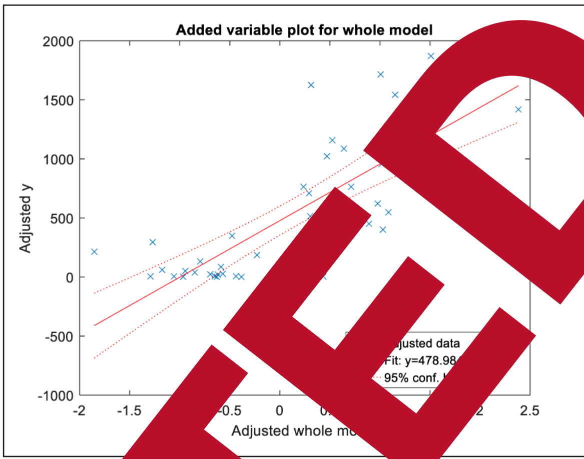

Figure 3 [illegible] ...le regression for Florence with three prin[illegible] compo[illegible]

p[illegible]ce we have extracted to present in this [illegible]k, and it model[illegible] the linear multiple regression

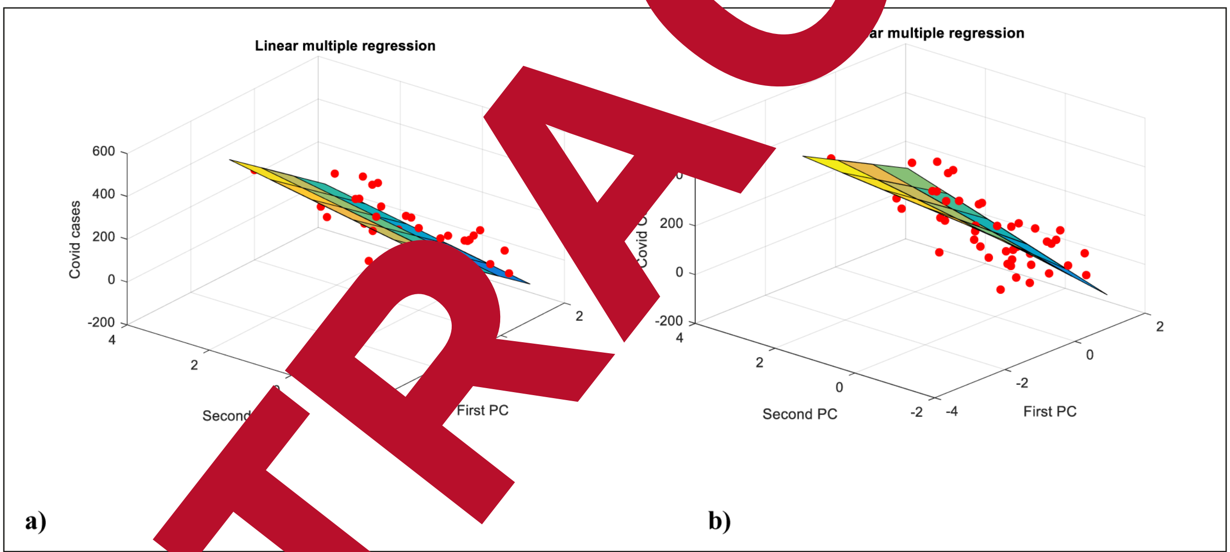

Figure 4. a[illegible]ear multiple re[illegible] for Pistoria with the first and second PCs. **b**, Nonlinear multiple regression for Pistoria with the fi[illegible] second PCs.

Tab[illegible] The per[illegible]ge of va[illegible]iance explained from each principal component (PC).

City	First PC	Second PC	Third PC	Fourth PC	Fifth PC	Total variance explained
[illegible]nce	[illegible]	23%	18%			82%
[illegible]	[illegible]	24%	14%			81%
Gr[illegible]to	3[illegible]	21%	15%	10%	5%	90%
M[illegible]	37%	19%	18%	12%		86%
[illegible]	[illegible]4%	22%	17%			82%
[illegible]	44%	25%	12%			81%
[illegible]ena	37%	24%	20%			82%
[illegible]	42%	23%	16%	10%		90%
[illegible]	35%	25%	14%	11%		85%

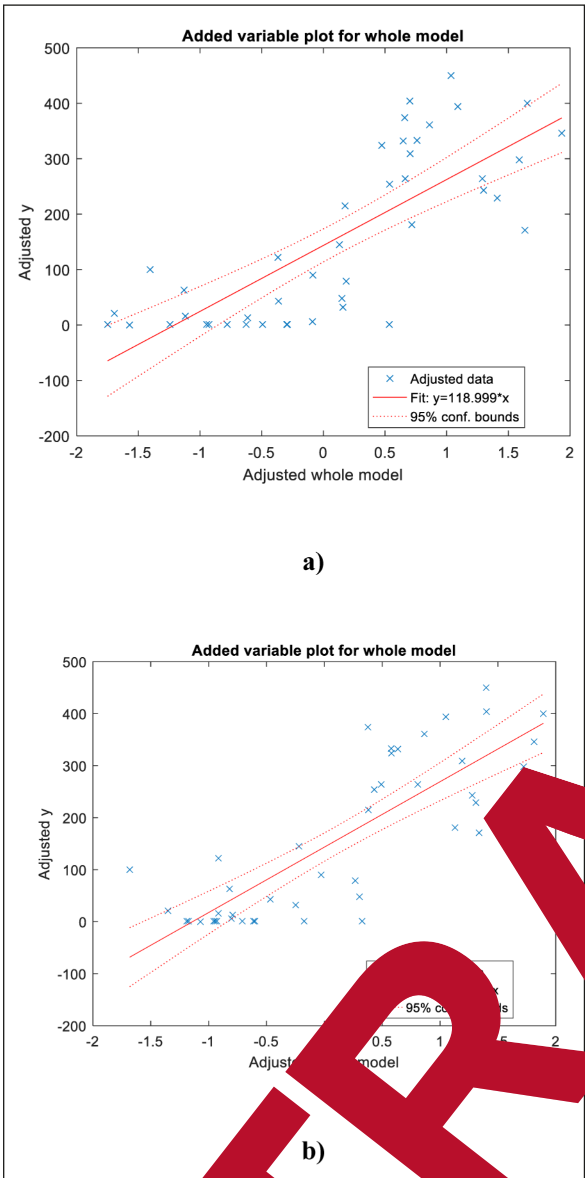

Figure 5. a, Nonl... le regression fo... oria with the first and sec... Cs. ... linear multiple regression for Pistoria with ... first, the ... and the third PCs.

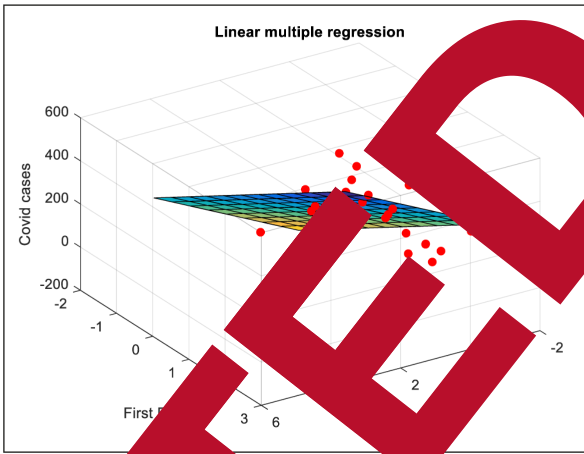

Figure 6. ... regression for ...ena with the first and secon... s.

of the ...VID-1... es with respect to the first and sec... incip... ctors. T... first principal component i... the or... l variables NO_2, Med_WS, Max_... nd th... cond principal component ...ed to ... l variables. The statistical sign...nce is *p*-... = 0.0005654 lower compared with ... previous case but within the allowed limits.

$$... = 129.12 + 69.12x^1 + 37.97x^2$$

...e 6 shows the visualization of the linear mult... regression with respect to Siena with the f... ...cond PCs. The linear model with three ..., according to the results given in Table II, ...lains that 82... f the total variance has sta-...al significan... (*p*-value = 1.35e^{-6}), which is m... tter th... e model with two PCs.

$$y = 12... + 64.065x^1 + 39.449x^2 - 60.078x^3$$

...7 shows the visualization of linear multi...ple re...ession for Siena. In order to find the best fit for the data, we have presented the linear and nonlinear multiple regression with the second and the third principal components presented with the following equations:

$$y = 145.86 + 39.32x^2 - 64.15x^3$$
$$y = 145.22 + 4645x^2 - 60.13x^3 + 20.72x^2x^3$$

The visualization of the linear and nonlinear multiple regressions is given in Figure 8. Linear multiple regression for Siena with the second and third PCs has a statistical significance (*p*-value = 2.2575e^{-4}), and the nonlinear multiple regression for Siena with the second and the third PCs has a statistical significance as *p*-value = 6.015^{e-4}. Comparing the accuracy, we conclude that it is more appropriate to use the linear model with the second and the third PC.

Discussion

Both long-term and short-term/acute exposure to air pollution have adverse effects, contributing to a wide range of chronic disorders[18,19]. Epidemiological studies[20,21] have revealed that exposure to

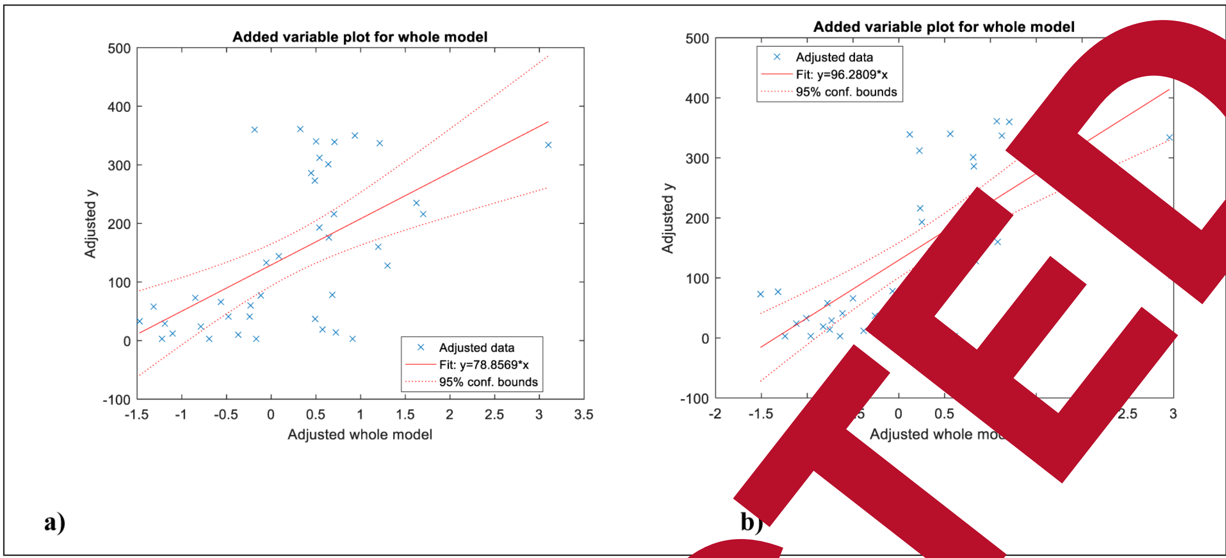

Figure 7. **a**, Linear multiple regression for Siena with the first and second PCs. **b**, Linear multiple regression for Siena with the first, the second, and the third PCs.

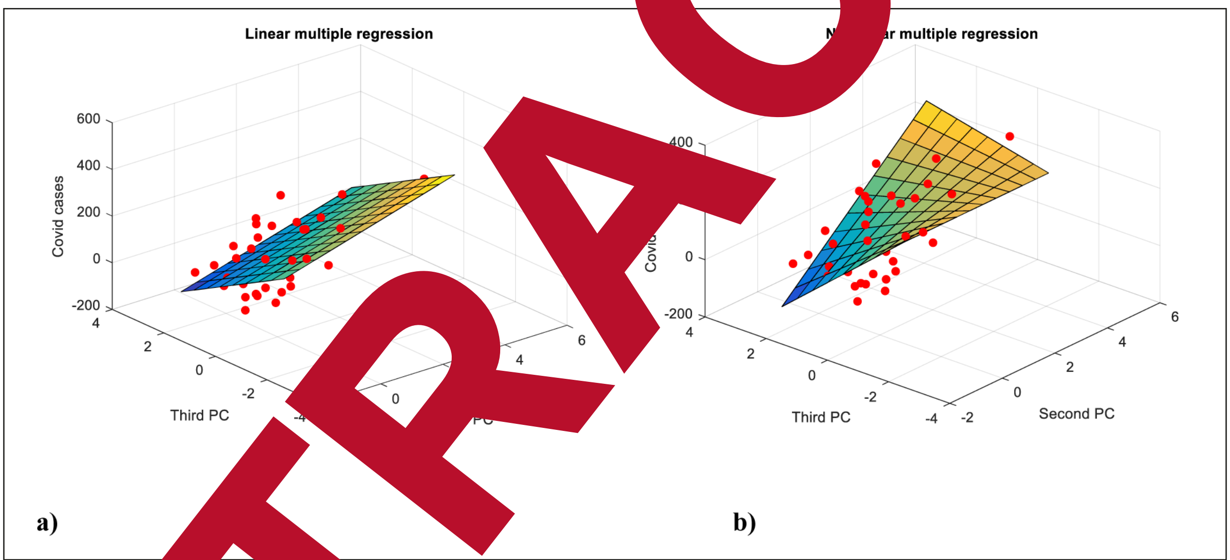

Figure 8. **a**, Linear multiple regression for Siena with the second and third PCs. **b**, Nonlinear multiple regression for Siena with the second and the third PCs.

air pollution may indirectly predispose people to severe and potentially fatal types of COVID-19. Indeed, the respiratory system, apart from being highly impacted by air pollution, is also the bodily part that is most affected by the symptoms of SARS-CoV-2, going from moderate upper airway sickness to severe pneumonia and abrupt respiratory distress syndrome (ARDS). Short-term and long-term impacts on obstructive airway disorders (like asthma and COPD) and restrictive lung parenchyma diseases (e.g., fibrosis) are caused by the inflammation and oxidative stress air pollution causes in the lungs. Children exposed to high NO_2 concentrations are more likely to develop severe types of virus-induced asthma, suggesting that air pollution may exacerbate the severity of SARS-CoV-2 pneumonia by weakening the respiratory system[22]. Chronic rhinitis and rhinosinusitis, which have been linked to air pollution, may enhance airway mucosal permeability, thus making SARS-CoV-2 infections more likely[3].

Meteorological conditions represent another factor influencing air pollution and viruses' vitality. Pollutants and respiratory viruses have intricate interactions in the environment; for example, PM is known to contain microbes like viruses, and SARS-CoV-2 RNA was indeed discovered in PM. However, how long this virus stays infectious in ambient air and whether the tiny amount of virus in the aerosol is enough to cause infection are still open questions[23]. Weather elements, like ultraviolet light and relative humidity, all play a role in the complicated interactions between gases and viruses in the atmosphere. Air pollution may have a role in the immune response to viral infections by lowering vitamin D production and decreasing UV radiations (which have antiviral action), contributing to viral persistence in ambient air[24].

This review underlines that both short-term and long-term exposure to air pollution may be crucial exasperating factors for SARS-CoV-2 transmission and COVID-19 severity and lethality through multiple mechanisms. Considering the numerical results obtained for nine provinces, we conclude that air pollution should be accounted for as a possible risk factor in future COVID-19 investigations, and it should be avoided as much as possible by the general popu[illegible]. Reducing outdoor and indoor air poll[illegible] cities or nations may have immediate and [illegible]nificant health benefits, which may conside[illegible] exceed the costs; moreover, strict control of [illegible] pollutants could decrease the incidence of ma[illegible] disorders, among which COV[illegible]

Conc[illegible]s

Air pollution ha[illegible]en co[illegible] with COVID-19 onset si[illegible] affects the [illegible]ism by increasing infl[illegible] and oxida[illegible] stress and decreasi[illegible] the [illegible]crobial defenses of the organis[illegible] Indeed, m[illegible] pollutants, such as PM_{2}[illegible]$_{10}$, and NO_2, h[illegible]en correlated to high[illegible]ates of SARS-CoV-2 infectivity and mort[illegible]. In th[illegible]rget provinces that we studie[illegible] air [illegible]tants [illegible]$_{5}$, PM_{10}, and NO_2 are prese[illegible]rst and [illegible]ond principal components wi[illegible]gh p[illegible]tage of variance expla[illegible] The [illegible]e constructed have a very goo[illegible]curacy a[illegible]show high statistical significan[illegible]he aim of this paper is to highlight the ne[illegible] of air pollution combined with [illegible]ate factors on the spread of COVID-19 and, [illegible]eneral, in all respiratory diseases. Reducing a[illegible]tion exposure should be one of the first mea[illegible]s against COVID-19 spread.

Informed Consent

The participants and their families pro[illegible] informed consent.

Ethics Approval

The Ethics Committee of the C[illegible]il Fray [illegible] Alcalde Hospital approved the prot[illegible] with the o[illegible] HCG/ CEI-2028/21. The pro[illegible] was performed [illegible] dance with the Declaration [illegible]elsinki.

Availability of D[illegible]a a[illegible]rials

All data associate[illegible]n this p[illegible]e ava[illegible] from the corresponding a[illegible] upon reason[illegible]

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This research was funde[illegible]e Provincia Autonoma di Bolz[illegible]e framework o[illegible]2006.

[illegible]thors' Contr[illegible]ions

[illegible]ceptualization, [illegible] and E.K.; Methodology, E.K.; In[illegible]ation, E.K., K[illegible] I.A., X.D., G.M., and M.B.; Writi[illegible]inal draf[illegible]paration, E.K., K.B., I.A., X.D., and G.B.,[illegible] and editing, K.D., G.M., C.M., G.B, C.Z., G.[illegible]M.B.; Project administration, E.K., and M.B.; Funding acquisition, E.K., and M.B. All authors have [illegible]nd agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

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