PM$_{2.5}$, NO$_2$, wildfires, and other environmental exposures are linked to higher Covid 19 incidence, severity, and death rates

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Abstract
Numerous studies have linked outdoor levels of PM$_{2.5}$, PM$_{10}$, NO$_2$, O$_3$, SO$_2$, and other air pollutants to significantly higher rates of Covid 19 morbidity and mortality, although the rate in which specific concentrations of pollutants increase Covid 19 morbidity and mortality varies widely by specific country and study. As little as a 1-$\mu$g/m$^3$ increase in outdoor PM$_{2.5}$ is estimated to increase rates of Covid 19 by as much as 0.22 to 8%. Two California studies have strongly linked heavy wildfire burning periods with significantly higher outdoor levels of PM$_{2.5}$ and CO as well as significantly higher rates of Covid 19 cases and deaths. Active smoking has also been strongly linked significantly increased risk of Covid 19 severity and death. Other exposures possibly related to greater risk of Covid 19 morbidity and mortality include incense, pesticides, heavy metals, dust/sand, toxic waste sites, and volcanic emissions. The exact mechanisms in which air pollutants increase Covid 19 infections are not fully understood, but are probably related to pollutant-related oxidation and inflammation of the lungs and other tissues and to the pollutant-driven alternation of the angiotensin-converting enzyme 2 in respiratory and other cells.

Keywords  PM$_{2.5}$ · PM$_{10}$ · Nitrogen dioxide (NO$_2$) · Ozone (O$_3$) · Wildfires · Smoking · Covid 19 · SARS Cov 2

Introduction
Covid 19 (CoronaVIrus Disease 2019) is caused by SARS2 Cov 2 (severe acute respiratory syndrome coronavirus 2), which is a RNA respiratory virus which is believed to be transmitted mostly by droplet nuclei in the air (Brandt and Mersha 2021). Covid 19 is especially dangerous to older humans as death rates for those over 70 years of age is more than 10%, while less than 0.1% for children and young adults (Signorelli and Odone 2020). Covid 19 infection rates in the USA are also significantly higher in African Americans as compared to the population as a whole (Brandt et al. 2020; Phillips et al. 2020).

Many papers and reviews have reported that exposure to air pollutants such as PM$_{2.5}$, NO$_2$, and O$_3$ are associated with higher rates of Covid 19 incidence, severity, or mortality (Brandt and Mersha 2021; Copat et al. 2020). In addition, other pollutant sources such as wildfires and smoking have also been associated with greater risks of Covid 19 infection and mortality (Meo et al. 2020; Salah et al. 2020). This review will attempt to review the published data on environmental factors and Covid 19 on papers published up to March 21, 2021. This review will also briefly discuss possible mechanisms in which environmental factors may affect Covid 19 morbidity and mortality.

Materials and methods
Databases such as PubMed, MEDLINE, Google Scholar, and Scopus were searched for articles. Search terms used included Covid 19, SARS Cov-2, influenza, PM$_{2.5}$, PM$_{10}$, ozone, nitrogen oxides, sulfur oxides, traffic, wildfires, wood burning, biomass burning, forest fires, traffic, pesticides, incense, solvents, sand, sandstorms, and volcanoes. Publications were searched up to March 21, 2021.

For papers relating outdoor air pollutants (“Introduction” section and Table), 31 papers were found that examined the following pollutants and their effects on Covid 19 morbidity and mortality: 29 papers for PM$_{2.5}$, 14 papers for PM$_{10}$. 2 that measured AQI (Air Quality Index), 13 papers for NO$_2$, 8...
papers which measured O₃, 5 papers which measured SO₂, 5 papers which measured CO₂, and 1 paper each for NH₃, methane, lead, total volatile organics, and non-methane volatile organics. Table 1 is sorted first by various pollutants (PM₂.₅, PM₁₀, NO₂, etc.), then it is arranged with the papers which reported quantitative relationships between pollutant levels and rates of Covid 19 morbidity and mortality first, studies which calculated R₀ (the basic reproduction ratio for Covid 19 values) are listed last, and other papers in the middle sections. Because many papers do not report social distancing measures, it was decided not to include social distancing measures in Table 1. Forest plots were also presented in Figs. 1, 2, and 3 to summarize the estimated relationships (in 4 or more studies cited—for the other pollutants, there were less than 4 studies and were presented in the text but not in the forest plots) between a 1 μg/m³ increases in ambient PM₂.₅, PM₁₀, and NO₂ and % increases in Covid 19 cases.

In “Material and methods” section, a brief review was conducted of selected papers which measured changes in outdoor air quality as a result of the Covid 19 crises and lockdown. To save space, not all papers which measured changes in ambient air pollutants during the Covid 19 era were reported. Two papers measured the effects of wildfires on Covid 19 were reported (both from California, USA) (“Results” section). Four meta-analysis examining the effects of smoking on Covid 19 are reported in “Results” section, as well as some studies reporting the effects of smoking on other respiratory infections. To save space, not all individual smoking studies were reported. In “Results” section, some papers examining possible links with Covid 19 and environmental exposures such as pesticides, heavy metals, dust storms, incense, sewage, forested areas, and volcanoes. Section 6 examines possible links between airborne dust and respiratory infections. Section 7 summarizes possible physiological and biochemical mechanisms in which air pollutants may increase Covid 19 morbidity and mortality, including lung inflammation, oxidation, and altered expression of the ACE2 receptors.

Results

Outdoor PM₂.₅ and other air pollutants increase Covid 19 morbidity and mortality

Key points

- Most studies have reported that higher outdoor levels of PM₂.₅, PM₁₀, NO₂, O₃, SO₂, and other pollutants are associated with significantly higher rates of Covid 19 Morbidity and Mortality.
- Two studies have reported that increasing outdoor levels of PM₂.₅ and NO₂ are associated with significantly higher R₀—reproduction rate for Covid 19.
- Other studies have reported that higher levels of air pollutants are associated with significantly higher infection rates for influenza and other respiratory viruses.

A number of studies have reported that exposure to PM₂.₅, PM₁₀, ozone, SO₂, and NO₂ are associated with higher rates of Covid 19 cases and mortality. Please see the following paragraphs and Table 1 for a summary of these studies. Some of these studies have estimated relationships between increased air pollution levels and increased (or decreased) rates of Covid 19 cases and mortality. For forest plots of the relationships between PM₂.₅, PM₁₀, and NO₂ and increases in Covid 19 cases, please see Figs 1, 2, and 3 (data expressed as mean and 95% confidence intervals). Nine studies estimated that a 1-μg/m³ increase in outdoor PM₂.₅ increased case rates or death rates of Covid 19 by as much as 0.22 to 8%, with an unweighted average of a 2.74% increase per 1 μg/m³ PM₂.₅ (de Angelis et al. 2021, López-Feldman et al. 2021, Meo et al. 2021a, b, Sahoo 2021, Solomini et al. 2021, Stieb et al. 2020, Wu et al. 2020, Zheng et al. 2021, Zhu et al. 2020). Four published studies reported that a 10-μg/m³ increase in ambient NO₂ was associated with a 4.56 to 37.8% increase in Covid 19 cases (Sahoo 2021; Zheng et al. 2021; Zhu et al. 2020) or a 7% decrease in Covid 19 cases (de Angelis et al. 2021). The average unweighted increase in Covid 19 cases per 10 μg/m³ NO₂ was 10.57%.

Sharma’s study in 10 nations reported that temperature and pressure are negatively associated with Covid 19 cases, while ambient PM₂.₅ are significantly associated with more Covid 19 cases and deaths (Sharma et al. 2021). Solomini’s large study of 237,749 Covid-19 cases from 63 countries and 5 continents reported that a 10-μg/m³ increase in PM₂.₅ was associated with an 8.1% (95% CI 5.4 to 10.5%) increase in Covid 19 cases in a 14-day window (Solomini et al. 2021). Barnett reported that both ambient PM₂.₅ and nitrogen oxides were associated with significantly increased rates of both Covid 19 morbidity and mortality in 32 OECD countries (Barnett-Itzhaki and Levi 2021). De Angelis reported that a 10-μg/m³ increase in ambient PM₂.₅ was associated with a 58% increased risk of Covid 19 incidence in 1439 Lombardy Italian municipalities (95% CI 1.31–1.90, p < 0.01) (de Angelis et al. 2021).

A large US study of 3000 US counties (comprising 98% of the population) up to April 22, 2020 reported that only a 1-μg/m³ increase in PM₂.₅ was associated with an 8% increase in Covid 19 deaths (95% CI 2–15%) (Wu et al. 2020).

A study of 120 Chinese cities reported that an 10-μg/m³ increase in PM₂.₅ was associated with a 2.24% increase in Covid 19 mortality (95% CI 1.012 to 3.46) (Zhu et al. 2020). A 2021 study reported that an increase of 1 μg/m³ of PM₂.₅ was associated with a 7.4% increased risk of Covid 19 death in Mexico City (López-Feldman et al. 2021). Several Italian studies have also reported a significant association...
Table 1 Air pollutants and their associations with Covid 19 morbidity and mortality

| Pollutant | Study reference | Location | Sample size and demographics | Time period of study | Covid 19 outcomes with increased pollutant |
|-----------|----------------|----------|------------------------------|---------------------|---------------------------------------------|
| PM$_{2.5}$ | (Solimini et al. 2021) | 63 nations 730 regions 5 continents | 237,749 Covid 19 cases | Begun when 10+ Covid 19 cases obtained in 1 region until 5/20/20 | A 10-μg/m$^3$ PM$_{2.5}$ increase is associated with a 8.1% increase cases (95% CI 5.4 to 10.5%) over 14-day lag |
| PM$_{2.5}$ | (de Angelis et al. 2021) | Lombardy Italy, 1439 out of 1507 municipalities | 61,377 Covid 19 cases 3/1/20 to 4/30/20 | | A 10-μg/m$^3$ PM$_{2.5}$ increase is associated with a 58% increase cases (IRR 1.58, 95% CI 1.31–19.90, p < 0.01) |
| PM$_{2.5}$ | (Wu et al. 2020) | USA 3087 counties representing 98% population. 1288 counties reporting Covid 19 deaths up to 4/22/20 | 1/2020 to 4/22/20 | A 1-μg/m$^3$ PM$_{2.5}$ increase is associated with a 8% increase in Covid 19 death rates (95% CI 2 to 15%). Death rates adjusted for 20 covariate factors including population size/density, age distribution, time of start and stay at home orders, weather, Covid 19 testing, smoking, obesity, and socioeconomic factors |
| PM$_{2.5}$ | (Stieb et al. 2020) | Canada 111 regions covering most of country | 73,390 cases average rate 208 cases/100,000—case rates highest in Quebec (489/100,000) and lowest in Nunavut (0/100,000) and NW Territories (12/100,00) | Up to 5/13/20 | A 1-μg/m$^3$ increase is associated with 7% more Covid 19 cases (95% CI 0.97–1.18) adjusted for a number of factors including weather, % Black population, age distribution, and economic and medical factors |
| PM$_{2.5}$ | (Zhu et al. 2020) | 120 cities all over China | Over 58,000 cases in 120 cities comprising about 70% China’s population | 1/23/20 to 2/29/20 | A 10-μg/m$^3$ PM$_{2.5}$ increase is associated with 2.24% increase cases (95% CI 1.02 to 3.46%), 0–14-day lag |
| PM$_{2.5}$ | (Sahoo 2021) | 288 districts in India covering 65% India’s total Covid 19 cases | 21,700 cases India to 4/23/20 with about 65% in study region | 1/23/20 to 4/23/20 | A 10-μg/m$^3$ increase is associated with a 2.21% more cases (95% CI 1.13 to 3.29) |
| PM$_{2.5}$ | (Meo et al. 2021b) | London, England—not clear whether it means central London or metro area | Median 168 cases and 4 deaths per day over a 253 day period | 2/24/20 to 11/2/20 | A 1-μg/m$^3$ PM$_{2.5}$ increase is associated with 1.1% increase in Covid 19 cases and 2.3% increase in Covid 19 deaths (p < 0.001, both cases) |
| PM$_{2.5}$ | (Zheng et al. 2021) | China | 81,132 Covid 19 cases 50,783 cases in Wuhan | 12/31/19 to 3/6/20 | A 10-μg/m$^3$ PM$_{2.5}$ increase is associated with 32.3% increase in Covid 19 cases (95% CI 22.4–42.4%) adjusted for socioeconomic and social mobility factors |
| PM$_{2.5}$ | (López-Feldman et al. 2021) | Mexico City 14 out of 16 municipalities | 21,000+ Covid 19 deaths Mexico City up to 10/28/20 | Up till 10/28/20 | Increasing PM$_{10}$ by 1 μg/m$^3$ is associated with an 7.4% increase in Covid 19 deaths. Data adjusted for factors such as population density, health care factors, and smoking |
| PM$_{2.5}$ | (Fiasca et al. 2020) | Italy | | | |
| Pollutant | Study reference | Location | Sample size and demographics | Time period of study | Covid 19 outcomes with increased pollutant |
|-----------|-----------------|----------|-----------------------------|----------------------|------------------------------------------|
| PM$_{2.5}$ | (Sharma et al. 2021) | Italy as a whole 239,410 Covid 19 cases by 5/24/20 and 743,419 cases by 11/30/20 | March to October 2020 | A 1-μg/m³ PM$_{2.5}$ increase is associated with an increased Covid 19 incidence of 1.56 per 10,000 people ($p < 0.001$) |
| PM$_{2.5}$ | (Barnett-Itzhaki and Levi 2021) | 10 nations with highest reported Covid 19 cases by 11/15/2020: the USA, India, Brazil, Russia, Spain, the UK, Italy, Peru, Iran, Chile | 2/1/2020 to 6/30/20 | Higher PM$_{2.5}$ is associated with more cases $p < 0.01$ and more mortality $p < 0.05$ |
| PM$_{2.5}$ | (Cascetta et al. 2021) | Italy 107 provinces | Up until 7/27/20—246,286 Covid 19 cases and 35,112 Covid 19 deaths | If all Italy below 25 μg/m³ PM$_{2.5}$, it was estimated that 7339 fewer cases up to July 2020. Covid 19 cases also significantly lower in seacoast areas |
| PM$_{2.5}$ | (Bianconi et al. 2020) | Italy 110 provinces | 3/1/20 to 3/31/20 | Higher PM$_{2.5}$/PM$_{10}$ is associated significantly more Covid 19 cases $p = 0.003$ and mortality $p = 0.004$% |
| PM$_{2.5}$ | (Fattorini and Regoli 2020) | Italy—total cases not reported | 2/24/20 to 4/27/20 | Long-term (2016–2020) PM$_{2.5}$ exposure is associated with significantly increased Covid 19 cases |
| PM$_{2.5}$ | (Dragone et al. 2021) | Italy 12 provinces Lombardy | 2/24/20 to 3/31/20 for Covid 19 cases—for air pollution data 2/1/20 to 3/31/20 | Higher PM$_{2.5}$ is associated with increased Covid 19 cases but no $p$ values listed. This study also reported higher PM$_{10}$, NO$_2$, NH$_3$, CO, and SO$_2$ positively associated Covid 19 cases and O$_3$ negatively associated Covid 19 cases, but no $p$ values provided |
| PM$_{2.5}$ | (Adhikari and Yin 2020) | Queens, New York City | 42,033 Covid 19 cases and 3221 Covid 19 deaths | Higher PM$_{2.5}$ is associated with a significantly lower risk of Covid 19 cases ($p < 0.001$) and mortality ($p < 0.044$) |
| PM$_{2.5}$ | (Bashir et al. 2020) | California, USA | 39,000 Covid 19 cases and 1800 deaths to 3/24/20 | Increasing PM$_{2.5}$ is associated fewer cases $p < 0.01$ and fewer deaths $p < 0.01$ |
| PM$_{2.5}$ | (Vasquez-Apestegui et al. 2020) | Lima, Peru | All of Peru until 6/12/20-220,749 total Covid 19 cases and 2382 Covid 19 mortality | Previous PM$_{2.5}$ levels (2010–2016) are associated with significantly higher cases and significantly |
| Pollutant | Study reference | Location | Sample size and demographics | Time period of study | Covid 19 outcomes with increased pollutant |
|-----------|----------------|----------|----------------------------|---------------------|------------------------------------------|
| PM$_{2.5}$ | (Liu et al. 2021) | 9 nations: China, Korea, Japan, Canada, the USA, Russia, England, Germany, France | Over 2.6 million Covid 19 cases from 9 nations to 5/20/20 | 1/21/20 to 5/20/20 | higher case fatality rates ($p > 0.05$ both cases) |
| PM$_{2.5}$ | (Kolluru et al. 2021) | 5 Indian mega cities: New Delhi, Kolkata, Mumbai, Bangalore, Chennai | In May and June 2020—total Covid 19: 153,629 cases in 5 megacities and 6449 total Covid 19 deaths | February (pre—lockdown), May (lockdown), and June (unlock) 2020 | Increased PM$_{2.5}$ is associated with significantly increased Covid 19 cases—May $p < 0.01$ June $p = 0.04$ and mortality (May $p = 0.02$ and June $p = 0.37$) |
| PM$_{2.5}$ | (Jain et al. 2021) | 6 South Asian nations: Afghanistan, Bangladesh, India, Nepal, Pakistan, Sri Lanka | 11.2 million Covid 19 cases and 163,945 Covid 19 deaths | Up to 12/16/20 | Increased PM$_{2.5}$ is associated with significantly increased Covid 19 cases and mortality. Temperature increases are associated with both increased and decreased Covid 19 patients depending upon the nation |
| PM$_{2.5}$ | (Yao et al. 2020) | China | 82,214 cases up to 4/12/20 | Up till 4/12/20 | PM$_{2.5}$ 10 $\mu g/m^3$ increase is associated with CFR (case fatality rate) increase 0.24% $p = 0.0042$ |
| PM$_{2.5}$ | (Hou et al. 2021) | 14 major cities in China | 4294 cases up till 4/28/20 | Up to 4/28/20 | Long-term PM$_{2.5}$ over 2015–2020 is associated significantly higher Covid 19 CFR |
| PM$_{2.5}$ | (Travaglio et al. 2021) | England | 300,000 cases up to December 2020 | Till December 20 | Increased PM$_{2.5}$ 1 $\mu g/m^3$ is associated with 12% increased Covid 19 mortality |
| PM$_{2.5}$ | (Bilal et al. 2020) | Germany | About 180,000 cases by middle of June 2020 | 2/24/20 to 7/2/20 | Increased PM$_{2.5}$ is associated with significantly less Covid 19 cases ($p < 0.01$) |
| PM$_{2.5}$ | (Pei et al. 2021) | China | 325 cities | Daily case rate during lockdown 2.26 per 100,000 | Up till 5/27/20 | Increased PM$_{2.5}$ is associated with significantly increased Covid 19 cases $p < 0.05$ |
| PM$_{2.5}$ | (Landoni et al. 2021) | 33 European nations | 1.48 million Covid 19 cases | 2/11/20 to 4/17/20 | Increased PM$_{2.5}$ both cases $p = 0.0001$ and mortality $p < 0.0001$ increased |
| PM$_{2.5}$ | (Chakrabarty et al. 2021) | 50 US states | About 609,000 US Covid 19 cases by April 20/20 | 3/2/20 to 4/30/20 | Each 1 $\mu g/m^3$ raised $R_{0}$ by 0.25 ($p = 0.006$). Data adjusted for 43 factors including age, ethnic groups, health care, and many socioeconomic factors |
| PM$_{10}$ | (Solimini et al. 2021) | 63 nations, 730 regions, 5 continents | 237,749 Covid 19 cases | Study begun after 10+ Covid 19 Cases obtained in region until 5/20/20 | Each 10 $\mu g/m^3$ increase PM$_{10}$ is associated with 11.5% increased (95% CI 7.8–14.9%) Covid 19 cases over 14-day lag |
| PM$_{10}$ | (Zhu et al. 2020) | 120 cities all over China | | | |

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**Table 1** (continued)
| Pollutant | Study reference | Location | Sample size and demographics | Time period of study | Covid 19 outcomes with increased pollutant |
|-----------|-----------------|----------|-----------------------------|---------------------|-----------------------------------------|
| PM$_{10}$ | (Sahoo 2021)    | 288 districts in India covering 65% India’s total Covid 19 cases | 21,700 cases India to 4/23/20 with about 65% in study region | 1/23/20 to 4/23/20 | PM$_{10}$—each 10 μg/m$^3$ increase is associated with a 1.76% increased mortality (95% CI 0.89 to 2.23%) lag 0–14 days |
| PM$_{10}$ | (Zheng et al. 2021) | China 324 cities | 81,132 Covid 19 cases in Wuhan | 12/31/19 to 3/6/20 | PM$_{10}$ 10 μg/m$^3$ 14.2% increased cases (95% CI 7.9 to 20.5%) |
| PM$_{10}$ | (Bianconi et al. 2020) | Italy 110 provinces | 105,672 Covid 19 cases and 12,428 Covid 19 deaths | 3/1/20 to 3/31/20 | Higher PM$_{2.5}$/PM$_{10}$ is associated with significantly more Covid 19 cases p = 0.003 and mortality p = 0.004% |
| PM$_{10}$ | (Fiasca et al. 2020) | Italy 67 provinces | Italy as a whole 239,410 Covid 19 cases by 5/24/20 and 743,419 cases by 11/30/20 | March to October 2020 | PM$_{10}$ each 1 μg/m$^3$ cases increased 1.26 per 10,000 population (p < 0.001) |
| PM$_{10}$ | (Bashir et al. 2020) | California | 39,000 Covid 19 cases and 1800 deaths to 3/24/20 | 3/2/20 to 4/24/20 | PM$_{10}$ significantly fewer cases and deaths p < 0.05 both |
| PM$_{10}$ | (Pei et al. 2021) | 325 Chinese cities | Daily case rate during lockdown 2.26 per 100,000 | Up to 5/27/20 | Higher PM$_{10}$ is associated with higher Covid 19 cases |
| PM$_{10}$ | (Hou et al. 2021) | China 14 major cities | 4294 Covid 19 cases | Up till 4/28/20 | Higher PM$_{10}$ over 5 year period (2015–2020) is associated with significantly higher Covid 19 case fatality rate |
| PM$_{10}$ | (Liu et al. 2021) | 9 nations | Over 2.6 million Covid 19 cases from 9 nations to 5/20/20 | 1/21/20 to 5/20/20 | PM$_{10}$ is associated with significantly higher PM$_{10}$ incidence, especially in Russia, England, and Germany |
| PM$_{10}$ | (Kolluru et al. 2021) | 5 Indian mega cities | In May and June 2020, total Covid 19 153,629 cases in 5 megacities and 6449 total Covid 19 deaths | March 2020 (pre–lockdown), May 2020 (lockdown), June 2020 (unlock) | PM$_{10}$ is associated with higher rates Covid 19 cases (May 2020 p = 0.03, June 2020 p = 0.32), but not significantly associated Covid 19 mortality (May 2020 p = 0.30, June 2020 p = 0.25) |
| PM$_{10}$ | (Bilal et al. 2020) | Germany | 180,000 Covid 19 cases in Germany up to June 2020 | 2/24/20 to 7/2/20 | PM$_{10}$ not significantly related to Covid 19 cases (p > 0.20) |
| PM$_{10}$ | (Fattorini and Regoli 2020) | Italy—total number of cases not reported | 180,000 Covid 19 cases in Germany up to June 2020 | 2/24/20 to 4/27/20 | PM$_{10}$ long-term (2016–2020) exposure is associated with significant higher Covid 19 cases |
| PM$_{10}$ | (Landoni et al. 2021) | 33 European nations | 1.48 million cases Covid 19 by 5/17/20 | 2/11/20 to 5/17/20 | PM 10 increases cases p = 0.0035 but not mortality p = 0.44 |

AQI = Air Quality Index consisting of PM$_{2.5}$. 

Higher AQI is associated with significantly higher Covid 19 cases.
| Pollutant | Study reference | Location | Sample size and demographics | Time period of study | Covid 19 outcomes with increased pollutant |
|-----------|-----------------|----------|-----------------------------|----------------------|-------------------------------------------|
| PM₁₀, SO₂, NO₂, and O₃ | AQI (Air Quality Index) | (Hou et al. 2021) | 14 Chinese cities | 4294 Covid 19 cases | Up till 4/28/20 | Higher AQI over 2015–2020 is associated with significantly higher Covid 19 case fatality rate |
| NO₂ | (Zhu et al. 2020) | China | 120 cities | Over 58,000 cases in 120 cities comprising about 70% China’s population | 1/23/20 to 2/29/20 | A 10-µg/m³ increase in NO₂ is associated with 6.94% increase in Covid 19 cases (95% CI 2.38 to 11.51) 0 to 14-day lag |
| NO₂ | (Zheng et al. 2021) | China 324 Cities | 81,132 cases overall 50,783 in Wuhan (62.6%) | 12/31/19 to 3/6/20 | Each 10 µg/m³ increase in NO₂ is associated with 37.8% increased Covid 19 cases (95% CI 23.8–52.0%) |
| NO₂ | (Sahoo 2021) | 288 districts in India covering 65% India’s total Covid 19 cases | 21,700 cases India to 4/23/20 with about 65% cases in study region | 1/30/20 to 4/23/20 | A-10 µg/m³ increase in NO₂ is associated with 4.56% increased Covid 19 cases (95% CI 2.22 to 6.90) 0–14-day lag |
| NO₂ | (de Angelis et al. 2021) | Lombardy, Italy 1439 out of 1507 municipalities | 62,377 Covid 19 cases | 3/1/20 to 4/30/20 | A 10-µg/m³ NO₂ increase is associated with a 7% decrease in Covid 19 cases (IRR 0.93, 95% CI 0.88–0.99, p = 0.03) |
| NO₂ | (Ogen 2020) | Italy, Spain, France, Germany | 4443 fatal Covid 19 cases to 3/19/2020—of which 3487 in Northern Italy or Central Spain | 3/19/20 | 83% deaths in areas with NO₂ above 100 µg/m² NO₂ |
| NO₂ | (Bashir et al. 2020) | California | 39,000 Covid 19 cases and 1800 deaths to 3/24/20 | 3/2/20 to 4/24/20 | NO₂ is associated with significantly reduced cases and deaths (p < 0.05 for both cases) |
| NO₂ | (Liu et al. 2021) | 9 nations | Over 2.6 million Covid 19 cases from 9 nations to 5/20/20 | 1/21/20 to 5/20/20 | Increased NO₂ is associated with significantly higher Covid 19 cases |
| NO₂ | (Bilal et al. 2020) | Germany | 180,000 cases Germany up to mid-June 2020 | 2/24/20 to 7/2/20 | Increased NO₂ is Associated with significantly more Covid 19 cases (p < 0.01) |
| NO₂ | (Fiasca et al. 2020) | 67 out of 110 Italian provinces | Italy overall 239,410 cases by 5/24/20 and 743,141 cases by 11/3/2020 | March–October 2020 | Each 1 µm/m³ NO₂ is associated with increased Covid 19 cases by 1.24 per 10,000 in population (p < 0.0001) |
| NO₂ | (Fattorini and Regoli 2020) | Italy—total cases not reported | | 2/24/20 to 4/27/20 | Long-term NO₂ exposure (2016–20) is associated with significantly higher Covid 19 cases |
| NO₂ | (Landoni et al. 2021) | 33 European nations | | 2/11/20 to 5/17/20 | Increased NO₂ is associated with significantly greater cases (p < 0.0001) and mortality (p < 0.0001) |
| NO₂ | (Barnett-Izchaki and Levi 2021) | 36 OECD nations—population and Covid 19 cases not listed | | 1/20/20 to 6/7/20 | Higher NO₂ is associated with significantly greater Covid 19 mortality (but not cases) by day 60 after first Covid 19 cases in various nations |
| Pollutant | Study reference | Location | Sample size and demographics | Time period of study | Covid 19 outcomes with increased pollutant |
|----------|----------------|----------|-----------------------------|---------------------|-----------------------------------------|
| NO₂      | (Yao et al. 2021) | 63 Chinese cities, including Wuhan, other Hubei provinces, cities, and non-Hubei cities | Number of Covid 19 cases on 2/8/20 in study area not reported | 1/1/20 to 2/8/20 | Each increase of 10 μg/m³ NO₂ is associated with R₀ increase of 0.12 (95% CI 0.02–0.23) outside Hubei Province and 0.52 (95% CI – 0.30 to 1.25) inside Hubei Province. |
| O₃       | (Zhu et al. 2020) | 120 cities in China | Over 58,000 Cases in 120 cities comprising about 70% China’s population | 1/23/20 to 2/29/20 | A 10-μg/m³ O₃ increase is associated with 4.76% more cases (95% CI 1.99 to 7.52) 0 to 14-day lag |
| O₃       | (Meo et al. 2021a) | London, England | Median 168 cases and 4 deaths per day over a 253 day period | 2/24/20 to 11/2/20 | 10 ppb O₃ is associated with 0.8% increase in Covid 19 cases (p < 0.001) and 4.4% increase in Covid 19 deaths (p < 0.001) |
| O₃       | (Adhikari and Yin 2020) | Queens, New York—population 2,253,858 | 42,023 Covid 19 cases and 3221 deaths | 3/1/20 to 4/20/20 | O₃ related to more cases (p < 0.001) but significantly lower Covid 19 mortality (p = 0.0038) |
| O₃       | (Liu et al. 2021) | 9 nations | Over 2.6 million Covid cases from 9 nations to 5/20/20 | 1/21/20 to 5/20/20 | Higher O₃ is associated with higher Covid 19 incidence, especially Canada and the USA |
| O₃       | (Bilal et al. 2020) | Germany | 180 Covid 19 cases Germany to mid-June 20 | 2/24/20 to 7/2/20 | Higher O₃ is associated with more cases (p < 0.05) |
| O₃       | (Kolluru et al. 2021) | 5 megacities in India | In May and June 2020, total Covid 19: 153,629 cases in 5 megacities and 6449 total Covid 19 deaths | March 2020 (pre-lockdown), May 2020 (lockdown), and June 2020 (unlock.) | Higher O₃ is associated with significantly lower number Covid 19 cases (May and June 2020, both p < 0.01) and mortality (May and June 2020, both p < 0.01) |
| O₃       | Fattorini and Regoli 2020 | Italy | Italy—total Covid 19 cases not reported | 2/24/ to 4/27/20 | O₃ long-term exposure (2016–2020) is associated with significantly more Covid 19 cases |
| O₃       | (Tripepi et al. 2020) | Italy | 53,518 cases Italy up to 3/21/20 | Up to 3/21/20 | Covid 19 cases and mortality greater in areas near Lodi, Lombardy, and in areas with higher O₃ (modification p = 0.001) |
| SO₂      | (Zhu et al. 2020) | 120 cities in China | Over 58,000 cases in 120 cities comprising about 70% China’s population | 1/23/20 to 2/29/20 | A SO₂ 10-μg/m³ increase is associated with 7.79% decreases in cases (95% CI – 14.57 to – 1.01%) 0 to 14-day lag |
| SO₂      | (Sahoo 2021) | 288 districts in India covering 65% India’s total Covid 19 cases | 21,700 cases India to 4/23/20 with about 65% in study region | 1/30/20 to 4/23/20 | A SO₂ 10-μg/m³ increase related to significantly less Covid 19 cases – 7.23% (95% – 10.99 to – 3.47%) 0–14 day lag |
| SO₂      | (Bashir et al. 2020) | California | 39,000 Covid 19 cases and 1800 deaths to 3/24/20 | 3/4/20 to 3/24/20 | Increased SO₂ is associated with significantly more cases and deaths (p < 0.001 both cases) |

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| Pollutant          | Study reference        | Location                      | Sample size and demographics                                   | Time period of study | Covid 19 outcomes with increased pollutant                                                                 |
|-------------------|------------------------|-------------------------------|----------------------------------------------------------------|--------------------|----------------------------------------------------------------------------------------------------------|
| SO₂               | (Landoni et al. 2021)  | 33 European nations           | 1.48 million Covid 19 cases                                     | 2/11/20 to 5/17/20  | Higher SO₂ is not associated with Covid 19 cases or mortality ($p = 0.44$ and 0.99)                      |
| CO                | (Zhu et al. 2020)      | China                         | Over 58,000 cases in 120 cities comprising about 70% China's population | 1/23/20 to 2/29/20  | Higher CO 10 $\mu$g/m³ is associated with 15.11% increase in cases (95% CI 0.44 to 29.77%)               |
| CO                | (Meo et al. 2021a)     | London, England—not clear whether it means central London or metro area | Median 168 cases and 4 deaths per day over a 253 day period     | 2/24/20 to 11/2/20  | CO—1 ppm increase is associated with 21.3% increase in Covid 19 cases ($p = 0.057$) and 21.8% Covid 19 deaths ($p = 0.047$) |
| CO                | (Bashir et al. 2020)   | California                    | 39,000 Covid 19 cases and 1800 deaths to 3/24/20                | 3/2/20 to 4/24/20   | Higher CO is associated with significantly more cases and deaths ($p < 0.05$ both cases)                |
| CO                | (Kolluru et al. 2021)  | 5 Indian megacities           | In May and June 2020—total Covid 19: 153,629 cases in 5 megacities and 6449 total Covid 19 deaths | March 2020 pre-lockdown, May 2020 (lockdown), June 2020 (unlock) | Higher CO not is associated with significantly more cases (May 2020 $p = 0.47$ and June 2020 $p = 0.97$) and mortality (May 2020 $p = 0.28$, June 2020 $p = 0.70$) |
| CO                | (Liu et al. 2021)      | 9 nations                     | Over 2.6 million Covid 19 cases from 9 nations to 5/20/20      | 1/21/20 to 5/20/20  | Higher CO is associated with more Covid 19 cases in China and Japan                                      |
| NH₃ (ammonia)     | (Landoni et al. 2021)  | 33 European nations           | 1.48 million Covid 19 cases till 5/17/20                       | 2/11/20 to 5/17/20  | Higher NH₃ is associated with significantly more cases ($p < 0.0001$) and mortality ($p < 0.0001$)     |
| Methane           | (Landoni et al. 2021)  | 33 European nations           | 1.48 million Covid 19 cases till 5/17/20                       | 2/11/20 to 5/17/20  | Higher methane is associated with significantly more cases ($p < 0.0001$) and mortality ($p < 0.0001$) |
| Non-methane volatile organics | (Landoni et al. 2021)  | 33 European nations           | 1.48 million Covid 19 cases till 5/17/20                       | 2/11/20 to 5/17/20  | Higher volatile organics is associated with significantly more cases ($p < 0.0001$) and mortality ($p = 0.0002$) |
| Total volatile organics | (Bashir et al. 2020)  | California, USA               | 39,000 Covid 19 cases and 1800 deaths to 3/24/20              | 3/2/20 to 4/24/20   | No significant relationship between total volatile organics and Covid 19 cases and mortality ($p > 0.10$ both cases) |
| Airborne lead levels | (Bashir et al. 2020)  | California, USA               | 39,000 Covid 19 cases and 1800 deaths to 3/24/20              | 3/2/20 to 4/24/20   | No significant relationship between airborne lead and Covid 19 cases and mortality ($p > 0.10$ both cases) |
between ambient PM$_{2.5}$ and significantly increased rates of Covid 19 cases, hospitalizations, and deaths (Bianconi et al. 2020; Cascetta et al. 2021; Fiasca et al. 2020). A study in all 107 Italian provinces reported that Covid 19 incidence and mortality were significantly higher in areas closest to Lodi, Lombardy and these effects were amplified by higher ozone levels (Tripepi et al. 2020). A study in Queens, New York, reported that increased ambient ozone were associated with increased Covid 19 cases ($p < 0.001$) but fewer Covid 19 deaths ($p = 0.38$), while increased PM$_{2.5}$ were actually associated with lower risk of Covid 19 cases ($p < 0.001$) and mortality ($p = 0.044$) (Adhikari and Yin 2020).

A study of 49 Chinese cities reported that for every 10 μg/m$^3$ increase in PM$_{2.5}$, the case fatality rate (CFR) of Covid 19 increased by 0.24% (95% CI of 0.01–0.48%) (Yao et al. 2020). A nitrogen dioxide mapping study in Italy, Spain, France, and Germany reported that nitrogen dioxide levels above 100 μm/m$^3$ were associated with 83% of the Covid 19 deaths (Ogen 2020). A study in Lima, Peru, reported that higher PM$_{2.5}$ levels were associated with significantly higher Covid 19 incidence and case mortality rates (Vasquez-Apestegui et al. 2020). A study of 111 regions in all Canadian provinces reported that each 1 μg/m$^3$ increase in PM$_{2.5}$ was associated with a 7% increased incidence of Covid 19 (OR 1.07, 95% CI 0.97–1.18) (Stieb et al. 2020).

A large study in 9 nations (China, Japan, Korea, Canada, the USA, Russia, England, Germany, and France) reported that higher levels of PM$_{2.5}$, PM$_{10}$, SO$_2$, NO$_2$, and O$_3$ generally were associated with significantly higher rates of Covid 19 infection (Liu et al. 2021). This study also concluded that the effects of PM$_{2.5}$ and PM$_{10}$ on Covid 19 incidence are more sensitive in Russia, England, Germany, and France, while O$_3$ and PM$_{2.5}$ effects are more sensitive to Covid 19 incidence in the USA and Canada (Liu et al. 2021).

A study of about 1.48 million Covid 19 cases in 33 European Nations from 2/11/20 to 5/17/20 reported that increasing outdoor concentrations of PM$_{2.5}$, NO$_2$, NH$_3$, methane, and non-methane volatile organic compounds were all independently associated with significantly increased risk of both Covid 19 incidence and deaths (Landoni et al. 2021). Increasing PM$_{10}$ was associated with significantly greater Covid 19 cases but not significantly Covid 19 mortality.
Increasing SO$_2$ was not associated with significantly greater Covid 19 cases and mortality (Landoni et al. 2021).

A large study of more than 58,000 Covid 19 cases in 120 Chinese cities reported that 10 μg/m$^3$ increases (lag 0–14) in the following pollutants were associated with the following increases in Covid 19 cases: PM$_{2.5}$ 2.24% (95% CI 1.02 to 3.46), PM$_{10}$ 1.76% (95% CI 0.89 to 2.63), NO$_2$ 6.94% (2.38 to 11.51), O$_3$ 4.76% increase (95% CI 1.99 to 7.52), and CO 15.11% increase (0.44 to 29.77%) (Zhu et al. 2020). A 10-μg/m$^3$ increase in SO$_2$ was associated with a 7.79% decrease in Covid 19 cases (95% CI –14.57 to –1.01) (Zhu et al. 2020). A German study involving 123,248 Covid 19 cases reported that higher levels of NO$_2$ and O$_3$ were all associated with significantly higher rates of Covid 19 cases and deaths, while higher levels of PM$_{2.5}$ were associated with significantly lower levels of Covid 19 cases and deaths (Bilal et al. 2020). A geographically weighted regression model in China reported that both higher outdoor levels of PM$_{2.5}$ and higher AQI (Air Quality Index) (consisting of PM$_{2.5}$, PM$_{10}$, SO$_2$, NO$_2$, CO, and ozone) were associated with significantly higher Covid 19 incidences (Pei et al. 2021).

Hou reported that long-term (1, 3, or 5) years, worse (higher) AQI in 14 Chinese cities was associated significantly higher Covid 19 case fatality rate (Hou et al. 2021). A study in 12 Lombardy, Italy, provinces reported that ambient PM$_{2.5}$ exposure was associated with significantly greater rates of Covid 19 infection with lag rates as high as 10 days (Dragone et al. 2021). An Indian study reported that 10 μg/m$^3$ increase during (Lag 0-14 days) of the following outdoor air pollutants were associated with significantly increased risk of Covid 19 infections PM$_{2.5}$ 2.21% increase (95% CI 1.13 to 3.29%), PM$_{10}$ 2.67% increase (95% CI 0.33 to 5.01%), and NO$_2$ 4.56% increase (95% CI 2.22 to 6.90%) (Sahoo 2021). A study in 5 Indian megacities (Bangalore, Chennai, Delhi, Kolkata, and Mumbai) reported that higher outdoor levels of PM$_{2.5}$, PM$_{10}$, CO, and O$_3$ were associated with significantly higher levels of both Covid 19 cases and deaths (Kolluru et al. 2021).

A study in 324 Chinese cities reported that each increase of 10 μg/m$^3$ of the following pollutants was associated with a significant increase in Covid 19 rates: NO$_2$ 37.8% increase (95% CI 23.8–53.0%), PM$_{2.5}$ 32.3% increase (95% CI 22.5–42.4%), and PM$_{10}$ 14.2% increase (7.9–20.5%) (Zheng et al. 2021). A study of more than 11 million Covid 19 cases in 6 South Asian nations (Afghanistan, Bangladesh, India, Nepal, Pakistan, and Sri Lanka) reported that higher outdoor PM$_{2.5}$ was associated with significantly higher rates of both Covid 19 infection and death (Jain et al. 2021).

A study in London, England, reported that the following increases in outdoor air pollutants were associated with the following increases in Covid 19 cases and Covid 19 deaths respectively: for each 1 μg/m$^3$ increase in PM$_{2.5}$ 1.1 and 2.3% increases in cases and mortality, for each 1 ppm increase in CO 21.3 and 21.8% increases in cases and mortality, and for each 10 ppb 03 0.8 and 4.4% increases in cases and mortality (Meo et al. 2021a).

An English study of over 300,000 Covid 19 cases reported that each 1 μg/m$^3$ increase in outdoor PM$_{2.5}$ was associated with a 12% increase in Covid 19 cases (Travaglio et al. 2021). An Italian study reported that relatively high levels of long-term exposure to outdoor pollutants (NO$_2$, O$_3$, PM$_{2.5}$, PM$_{10}$) during the period 2016–2020 were associated with significantly higher levels of Covid 19 cases (Fattorini and Regoli 2020).

### Ambient PM$_{2.5}$ and NO$_2$ increases $R_o$ rate of Covid 19

$R_o$ is described as the basic reproduction ratio for Covid 19. The $R_o$ rates for Covid 19 are generally between 1.0 and 3.0, with higher values representing higher Covid 19 reproduction rates. A study in all 50 US states compared Covid 19 $R_o$ rates and their relationships between ambient PM$_{2.5}$ from the period March 2 to April 30, 2020 (Chakrabarty et al. 2021). Each increment in ambient 1 μg/m$^3$ PM$_{2.5}$ was associated with a significant 0.25 increase in $R_o$ (95% CI 0.084–0.447) (Chakrabarty et al. 2021). During this time, $R_o$ was the highest in New Jersey at 3.41 and New York at 3.30 and lowest in Alaska at 1.60 and Wyoming at 1.76 (Chakrabarty et al. 2021). During this time period, $R_o$ values generally dropped from early March to late April 2020 with the institution of social distancing and school/workplace closures (Chakrabarty et al. 2021).

A study of 63 Chinese cities also reported that higher outdoor NO$_2$ levels were associated with significantly higher $R_o$ basic reproduction rate (Yao et al. 2021). Each 10 μg/m$^3$ increase in NO$_2$ was associated with a $R_o$ increase of 0.12 outside Hubei Province and 0.52 inside Hubei Province (Yao et al. 2021).

### Air pollution increases risk of respiratory infection in general

Other studies have reported that higher air pollution levels can significantly increase risk of respiratory infections in general.

A study of 6814 multi-ethnic adults aged 44 to 84 years in 6 US cities reported that an increase of estimated PM$_{2.5}$ and NO$_x$ from 25 to 75% percentile increased the risk of respiratory infections by 1.04 (OR 1.04, 95% CI 1.00 to 1.09) and 1.15 (OR 1.15, 95% CI 1.10 to 1.20), respectively (Kirwa et al. 2021). A Chinese study reported that increased outdoor levels of PM$_{2.5}$, PM$_{10}$, CO, and SO$_2$ were associated with significantly higher levels of influenza-like illness in both children and adults (Su et al. 2019). A Utah study involving 112,467 subjects with lower respiratory infection (77% of which were 2 years or less) reported that higher PM$_{2.5}$ levels were associated with significantly higher rates of lower respiratory illness (Home et al. 2018).

A 2002–2003 Chinese study reported that higher levels of API (air pollution index consisting of airborne outdoor levels of particulate matter, sulfur and nitrogen dioxides, carbon
monoxide, and ground level ozone) were associated with significantly higher mortality rates due to SARS (severe acute respiratory syndrome) (Cui et al. 2003). A 2019 Korean study linked higher ambient levels of PM10 with significantly higher rates of adenovirus (HAdV), metapneumovirus (HMPV), human coronavirus (HCoV), human bocavirus (HBov), human parainfluenza virus (HPIV), and influenza virus (IV) (Cheon et al. 2019).

Covid 19 restrictions and lowered outdoor air pollutants

Key points

- Most, but not all, studies have reported that airborne levels of many pollutants have fallen significantly during the Covid 19 lockdowns.

On the positive side, a number of studies have noted that Covid 19 lockdowns and reduced industrial/traffic activity have been associated with drops in ambient levels of PM2.5 and other pollutants (Srivastava 2021).

An analysis of 10,000+ sampling sites in 380 World Cities reported that during the 2020 lockdown periods PM2.5 and NO2 fell by an average of 16.1 and 45.8%, while ozone levels rose by an average of 5.4% (He et al. 2021). A study of 50 more polluted capital cities reported a mean drop in PM2.5 of 11% (Rodriguez-Urrego and Rodriguez-Urrego 2020). A study of more than 1500 air monitoring sites in 377 Chinese cities reported a mean 16 and 20% reduction of PM2.5 and PM10 when comparing January 20 to April 8, 2020, with the same period in 2019 (Fan et al. 2020). A study in Baghdad, Iran, reported mean pollution drops of 6% for NO2, and 8% for PM2.5 during the March 1 to July 24, 2020, as compared to 2019 (Hashim et al. 2021). Another study noted significant drops in outdoor PM2.5 during the Covid 19 crisis in 9 world cities including New York City, Los Angeles, Zaragoza, Rome, Dubai, Delhi, Mumbai, Beijing, and Shanghai (Chauhan and Singh 2020). Studies in 4 large Pakistani cities (Lahore, Islamabad, Karachi, and Peshawar) reported that during the Covid 19 period, average PM2.5 levels fell 13 to 33% in satellite observations and 23 to 58% in ground based observations (Ali et al. 2021). A Chinese study reported that comparing outdoor pollutant levels from January 21 to March 23 during the both 2020 and 2019, reported that average PM2.5 levels fell by an average of 35%, 29%, and 19% respectively in Wuhan, Hubei (Wuhan excluded), and China (Hubei excluded) and NO2 levels fell by an average of 53%, 50%, and 30% respectively in Wuhan, Hubei, and China respectively (Chu et al. 2021). During the lockdown period between March 1 to May 31, 2020, mean outdoor levels of PM10, PM2.5, NO, NO2, and CO levels fell by an average of 58%, 47%, 76%, 68 and 58% respectively in Delhi, India, as compared to the 2019 values (Srivastava et al. 2021). A study in 7 Korean cities reported that mean PM2.5 levels fell by an average of 7.5 to 24.9% during the 2020 lockdown as compared to 2019 (Kwak et al. 2021). An Italian study reported reductions in outdoor PM2.5 as high as 53% and reductions in NO2 as high as 67% (Donzelli et al. 2021).

At least two studies have reported significant declines in average ambient volatile organic compounds (VOCs) during the lockdown period—including a 37–57% reduction of total VOCs in China (Li et al. 2020) and a 48–68% reduction in benzene in Italy (Collivignarelli et al. 2020).

Wildfires are associated with increased Covid 19 rates

Key points

- Two California studies have reported significant increases in both ambient PM2.5 and Covid 19 cases and/or deaths during heavy wildfire burning periods.

Wildfires and extensive wood burning both produce large quantities of carbon monoxide, fine particulates, and other toxic chemicals (such as carcinogenic polycyclic aromatic hydrocarbons or PAHs) which have been documented to be associated with significantly higher rates of respiratory and cardiovascular problems (Larson and Koenig 1994; Naeher et al. 2007; Reid et al. 2016; Youssouf et al. 2014). A study of 10 California counties affected by the severe 2020 wildfires reported that during the heavy burning period between August 15, 2020, and September 22, 2020, mean PM2.5 levels increased by 221% (92.91 vs 28.97 μg/m3, *p* < 0.001), mean carbon monoxide levels increased by 151% (4.77 vs 1.90 ppm, *p* < 0.001), and during this same wildfire period, Covid 19 cases jumped by 57% (*p* < 0.001), and the number of Covid 19-related deaths rose by 148% (*p* < 0.001) (Meo et al. 2021a). A study conducted by same authors reported significantly higher rates of Covid 19 cases and significantly higher PM2.5 outdoor levels in San Francisco during this same 2020 wildfire period (Meo et al. 2020).

Other studies and reviews have reported that exposure to wildfire smoke in firefighters are associated with significantly greater risk of respiratory infections such as pneumonia and acute bronchitis (Navarro et al. 2021).

Smoking increases Covid 19 risk

Key points

- Most studies have reported that Covid 19 morbidity and mortality rates are significantly higher in smokers.

A number of studies have reported that tobacco smoking is related to increased Covid 19 risk. Salah’s meta-analysis
reported smoking about doubled Covid 19 mortality risk (OR 2.07, 95% CI 1.59–2.69, 10 studies of 11,189 patients) (Salah et al. 2020). A July 2020 meta-analysis of 47 studies of 32,849 hospitalized Covid 19 patients reported that current smokers had much greater risks of severe Covid 19 disease versus former smokers/non-smokers, including greater risk of severe Covid 19 (OR 1.31, 1.12–1.54) and Covid 19 mortality (OR 1.26, 95% CI 1.20–1.32) (Reddy et al. 2021). A meta-analysis of 22 published studies on 5689 Covid 19 patients reported that severe disease risk was significantly greater in smokers (OR 1.34, 95% CI 1.07–1.67) (Karanasos et al. 2020). A 2021 meta-analysis of 19 studies reported that smoking was associated with an almost doubled risk of worse Covid 19 progression (OR 1.96, 95% CI 1.36–2.82) (Jiménez-Ruiz et al. 2021). A 2021 analysis of 109 articles involving 517,020 Covid 19 patients reported that a smoking history was associated with a significantly increased risk of ICU admission (OR 1.73, 95% CI 1.36–2.19) and significantly increased risk of death (OR 1.58, 95% CI 1.38–1.81) (Zhang et al. 2021). A 2021 review reported that there have not been any studies so far on the associations between secondhand tobacco smoke and Covid 19 (Brandt and Mersha 2021).

Smoking increases risk of other respiratory infections Smoking can also increase the risk of other respiratory infections such as influenza and tuberculosis. A 2019 meta-analysis of 9 studies with 40,685 participants reported that current smokers are more than 5 times more likely to develop laboratory-confirmed influenza than never smokers (OR 5.69, 95% CI 2.79–11.60, 3 studies). Meta-analyses of the relationships between smoking and tuberculosis (TB) have reported that active smoking is associated with a 2.284-fold increased risk of developing pulmonary TB (OR 2284, 95% CI 1765–2954, 14 studies) and a 2.236-fold increased risk of dying from TB (OR 2.236, 95% CI 1.340–3.732, 6 studies) (Slama et al. 2007). Secondhand tobacco exposure as compared to no first- or secondhand exposure was associated with a 3.353-fold increased risk of TB (OR 3.353, 95% CI 2.028–5.543, 3 studies) (Slama et al. 2007).

Other possible environmental risk factors for Covid 19 transmission—incense, pesticides, metals, desert dust/sand, toxic waste sites, volcanic emissions

Key points

- Other possible risk factors for Covid 19 incidence and/or mortality include incense, pesticides, metals, sand, toxic waste sites, and volcanic emissions.

Some researchers have postulated that exposure to incense sticks (Amoatey et al. 2020), pesticides (Rajak et al. 2021), and heavy metals (Skalny et al. 2020) may increase risk of Covid 19 morbidity and mortality. It has been hypothesized that pesticides exposure may increase risk of Covid 19 by damaging the respiratory, immune, cardiovascular, hepatic, and nervous systems (Rajak et al. 2021). Many toxic heavy metals can damage the immune system, and human and animal studies have reported that toxic heavy metal exposure can increase risk of respiratory infections like respiratory syncytial virus (RSV) and influenza (Skalny et al. 2020). Some researchers have suggested that indoor incense exposure may increase Covid 19 risks (Amoatey et al. 2020). A US study of 3143 counties up to May 31, 2020, reported that diesel particulate concentrations and proximity to Risk Management Plan (RMP) and toxic waste sites were associated with significantly higher Covid 19 mortality rates (Hendryx and Luo 2020).

Some have postulated that dust storms may also be associated with greater Covid 19 risk (Middleton 2020). Every year, about half a billion tons of desert dust become airborne and can travel for thousands of miles (Middleton 2020). Dust storms may also spread influenza (both Covid 19/SARS Cov2 and influenza are RNA respiratory viruses). A Taiwan study reported that mean outdoor airborne influenza concentrations were 21 to 31 times higher during 24 days of dust storms as compared to 10 control days (mean concentrations of influenza per cubic meter of outdoor air at Wan-Li station 268 vs. 13, p = 0.02, at Shin-Jhaung station 276 vs. 9, p = 0.01) (Chen et al. 2010).

Other researchers have noted that viable Covid 19 is found in human sewage, which may potentially be a major source of Covid 19 infection (Rooney et al. 2021; Senatore et al. 2021). An Italian study reported significantly lower Covid 19 mortality rates in heavily forested areas (more than 1 hectare forest per person) (Roviello and Roviello 2020). The authors hypothesized that the lower Covid 19 death rates in the forested Italian regions could be due to the PM$_{2.5}$ filtering ability of forests and/or the production of anti-viral volatile organics (which are both volatilized in the atmosphere and present in foodstuffs like Bay leaves) by common Italian trees/shrubs such as Laurus nobilis or bay laurel (Roviello and Roviello 2020).

Italian researchers reported relatively high Covid 19 infection rates on Sicily east of volcanic Mt. Etna (which have been active for much of 2020 and early 2021) and hypothesized that toxic gases and trace metals may play some role in promoting Covid 19 (Raciti and Calabrò 2020).

Is SARS Cov 2/Covid 19 spread by airborne dust?

Key points

- SARS Cov 2 and other respiratory viruses like virus may possibly be spread by airborne dust as well as by droplet nuclei.
PM$_{2.5}$ may possibly serve as a direct vector for transmission of Covid 19/SARS Cov2 and other viruses. SARS Cov 2 has been found to bind to particulate matter surrounded by water (Borisova and Komisarenko 2020). In addition, PM$_{2.5}$ and SARS Cov 2 can enter the nose to brain olfactory nerve delivery system and cause neurological symptoms (Borisova and Komisarenko 2020). Several studies have reported viable SARS Cov2 can be detected in PM$_{2.5}$ or PM$_{10}$ fractions of air (Tung et al. 2021). Viable SARS Cov 2 has been detected on PM$_{10}$ fractions on 2020 outdoor air in Italy (Chirizzi et al. 2021; Setti et al. 2020) and on PM$_{2.5}$ and smaller airborne fractions from 2 Chinese hospitals (Liu et al. 2020). A Malaysian study reported that RNA from SARS Cov 2 was collected from the PM$_{2.5}$ from the air of hospital wards housing SARS Cov 2 patients (Nor et al. 2021). On the other hand, a study in Leipzig, Germany, found no evidence of SARS Cov 2 RNA in either 8 weekly outdoor air particulate samples collected during the pandemic or in purified extracts from 9 species of pollen (Dunker et al. 2021).

To spread Covid 19, the virus would have to survive its travel on droplets or air particulates. Information on SARS Cov2 virus survival time in air droplets or particulates is sparse. Von Dormelan reported that SARS Cov 2 has a median half-life of about 1.1–1.2 h on airborne aerosols (van Doremalen et al. 2020). SARS Cov 2/Covid 19 survival on inanimate surfaces vary considerable from study to study—they had been reported as long as 3 to 9 days on plastic surfaces, 2 days on stainless steel, 1 day on cardboard, and 4 h on copper (Marquès and Domingo 2020). SARS Cov2 viability is generally longer under conditions of lower temperature and humidity (Marquès and Domingo 2020). Viability/survival of SARS Cov2/Covid 19 has been estimated at 9 h for hands as compared to influenza (another RNA respiratory virus) of 1.8 h (Hirose et al. 2020). Some studies have suggested that particulate pollution may increase airborne survival of many types of viruses times by binding to bacteria and providing protection from UV light and by reducing dehydration (Navarro et al. 2021; Reche et al. 2018).

### Other possible mechanisms in which air pollutants may increase risk of Covid 19 infection/death, lung damage, oxidation/inflammation, and overexpression of angiotensin-converting enzyme 2

**Key points**

- Air pollution may possibly increase Covid 19 morbidity and mortality by promoting oxidation and inflammation.
- PM$_{2.5}$, NO$_2$, and other air pollutants may increase Covid 19 susceptibility by altering the ACE2 or angiotension 2 receptor which is a binding site for SAR Cov 2.

Besides direct transmission on particulates, air pollutants may also help spread Covid 19 infection by other mechanisms including promoting lung damage, or binding to and overexpression of angiotensin-converting enzyme 2 (Comunian et al. 2020). Various human, animal, and cell studies have reported that exposure to particulate pollution can increase lung inflammation and oxidation (Comunian et al. 2020).

Exposure to PM$_{2.5}$ and NO$_2$ may increase incidence and severity of Covid 19 by altering expression of angiotensin-converting enzyme 2 (ACE2) in respiratory cells (Alifano et al. 2020; Paital and Agrawal 2020; Samavati and Uhal 2020). ACE2 is a membrane enzyme found in the lungs, nasal epithelium, arteries, kidney, heart, and intestines and regulates blood pressure by modifying angiotensin 2 into angiotensin 1–7, which is a vasodilator and anti-inflammatory agent (Comunian et al. 2020). ACE2 receptors are a receptor for coronavirus binding including SARS Cov 2/Covid 19 (Alifano et al. 2020; Paital and Agrawal 2020). SARS Cov 2 binding to these ACE2 receptors can alter expression causing increased inflammation and cardiac damage (Comunian et al. 2020; Samavati and Uhal 2020). Exposure to airborne PM$_{2.5}$ has been shown to increase ACE2 receptors in mice (Lin et al. 2018). ACE2 receptors tend to both more common in older humans, and the greater number of ACE2 receptors in elders may partially explain the significantly higher Covid 19 morbidity and mortality seen in older patients (Comunian et al. 2020; Wong et al. 2020). The significantly higher rates of Covid 19 cases and death seen in African Americans in the USA may be due to a number of factors including ACE2 genetic polymorphisms, higher average exposures to PM$_{2.5}$ and other pollutants, more crowded housing, and socioeconomic factors (Brandt et al. 2020; Phillips et al. 2020).

Italian researchers have proposed a “double-hit” hypothesis in which combined exposure to PM$_{2.5}$ and NO$_2$ can increase susceptibility to Covid 19 (Frontera et al. 2020). In the first step, chronic exposure to PM$_{2.5}$ causes lung damage, inflammation, increased susceptibility to viral infection, and alveolar ACE-2 overexpression (Frontera et al. 2020). This may increase viral load by depleting ACE-2 receptors and impairing host defenses. Exposure to NO$_2$ can then cause additional lung damage including inflammation and edema, and increased susceptibility to infections including Covid 19 (Frontera et al. 2020). After the lungs have experienced a PM$_{2.5}$ and NO$_2$ “double hit,” they are much more susceptible to SARS Cov 2 binding the ACE-2 sites and causing serious infection (Frontera et al. 2020).

Much more study on the relationships on the ACE2 receptors, SARS Cov 2/Covid-19, and air pollutants are needed.
Mechanisms in which air pollution increases influenza infection rates

Particulate pollution may also increase the risk of many other infections. A mouse study reported that long-term exposure to PM\textsubscript{2.5} enhanced survival of the influenza virus by downregulating pulmonary macrophage Kdm6a and altering histone modification in IL-6 and IFN\(\beta\) promoter regions (Ma et al. 2017). Another murine study reported that intratracheal PM\textsubscript{2.5} exposure reduces influenza immunity by inhibiting activation of NLRP3 inflammasome and expression of interferon-\(\beta\) (Tao et al. 2020).

Discussion

Many environmental exposures have been strongly linked to higher Covid 19 morbidity and mortality including PM\textsubscript{2.5}, PM\textsubscript{10}, NO\textsubscript{2}, O\textsubscript{3}, wildfires, and smoking. Other exposures which may possibly be related to higher Covid 19 morbidity and mortality include sulfur oxides, carbon monoxide, volatile organic chemicals, incense, pesticides, heavy metals, dust/sandstorms, toxic waste sites, and volcanic emissions.

Outdoor exposure to PM\textsubscript{2.5} and other particulate fractions have been consistently associated with higher levels of Covid 19 incidence, severity, and mortality, although the degree in which a given amount of PM\textsubscript{2.5} increases Covid 19 factors varies considerably from study to study (Table 1). Table 1 notes that significantly higher rates of Covid 19 morbidity and/or mortality were associated with higher outdoor levels of the following pollutants: PM\textsubscript{2.5} in 27 out of 29 studies, PM\textsubscript{10} in 12 out of 14 studies, NO\textsubscript{2} in 11 out of 13 cases, O\textsubscript{3} in 7 out of 8 cases, SO\textsubscript{2} in 2 out of 5 cases, and CO in 4 out of 5 cases.

One limitation of this review is that most of these studies published to date have involved air pollution and Covid 19 morbidity and mortality only during the early pandemic period up until sometime between January and October 2021 (please see Table 1). Additional studies examining the effects of air pollutants on Covid 19 cases/deaths during the late pandemic period in late 2020 or 2021 might yield interesting information.

Most of the studies to date have compared Covid 19 rates while measuring only one outdoor air pollutant and have not considered multiple outdoor air pollutants at the same time. Of course, interactions and correlations between pollutants could have played a major role in influencing Covid 19 morbidity and mortality rates. In the future, large epidemiological studies with good statistical power of Covid 19 and multiple air pollutants might be able to yield useful data on the interactions between pollutants. In addition to epidemiological studies, more studies are needed to study the effects on air pollution and infection at the molecular and cellular levels.

A complication with comparing outdoor pollution levels with Covid 19 morbidity and mortality is that many other factors can also play a role in determining Covid 19 morbidity and mortality: including weather, social distancing measures, Covid 19 vaccines, population density, age structure, socioeconomic factors, the quality and affordability of health care systems, mask wearing, handwashing, nasal disinfection, surface cleaning, HEPA air filters, quarantine, and nutrition (Aggarwal et al. 2020; Ayenigbara et al. 2020; Calzetta et al. 2021; Chiesa et al. 2021; Chu et al. 2020; Curtis 2021; Ferrer and Sanchez-Gonzalez 2021; Fouladi Dehaghi et al. 2020; Hradsky and Komarek 2021; Matrajt and Leung 2020; Mechanick et al. 2021; Nussbamer-Streit et al. 2020; Pradhan et al. 2020; Rodriguez et al. 2021; Romano Spica et al. 2020; Thu et al. 2020). A meta-analysis of 29 unadjusted and 9 adjusted studies has reported that social distancing measures can play a major role in reducing Covid 19 spread (Chu et al. 2020). On the other hand, lack of social distancing, mask wearing, and other protective behaviors can increase risk of Covid 19 spread. For example, the Sturgis, South Dakota, USA Motorcycle Rally which was held from August 7 to 16, 2020, had about 500,000 attendees from all over the USA, had relatively little social distancing and mask usage, and was estimated to cause an additional 115,208 to 266,790 cases of Covid 19 throughout the USA (Dave and Sabia 2020). Social distancing may play a major role in modifying the effects of air pollution on Covid 19 morbidity and mortality. However, a limitation of this review is the fact that many of the studies cited in Table 1 did not describe social distancing methods in detail. Therefore, social distancing methods was not reported in Table 1, although they might have been very interesting. Further study is needed to determine how various factors like air pollution, social distancing, mask usage, handwashing, surface cleaning, HEPA, quarantine, medical care, Covid 19 vaccinations, social-economic factors, and nutrition interact with each other.

Another limitation of this review is that it reviewed papers published only up to March 21, 2021. Certainly, more useful papers and insights on air pollution effects on Covid 19 will be produced after 3/21/21. Hopefully, this review will encourage other clinicians, researchers, and public health experts to further examine the complex relationships between air pollution and infection with Covid 19 and other pathogens.

These studies linking higher Covid 19 morbidity and mortality offer additional arguments for reducing air pollution levels in both the developed and developing worlds. In 2015, it was estimated that outdoor PM\textsubscript{2.5} pollution alone caused 4.2 million annual deaths (95% CI 3.7 to 4.8 million) and 103.1 million (95% CI 90.8 to 115.1 million) disability-adjusted life-years (Cohen et al. 2017). Cutting back on air...
pollution by using cleaner transportation, heating, and industrial methods and by reducing biomass (wood/leaves/straw/forest/wildfire) burning can reduce risk of many health problems including Covid 19 and other respiratory infections. Use of face masks can also reduce risk from both PM$_{2.5}$ and Covid 19 exposure (Xu et al. 2020).

**Conclusions**

Airborne pollutants play an important role in Covid 19 infection and severity. Limiting environmental exposures offer great potential for reducing both morbidity and mortality from Covid 19 and other respiratory infections like influenza. Much more research on the interplay between Covid 19/other infections, air pollutants, and other factors such as handwashing/vaccination/nutrition are needed.

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