PM_{2.5}, NO₂, 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}, PM₁₀, NO₂, O₃, SO₂, 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-μg/m³ 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} · PM₁₀ · Nitrogen dioxide (NO₂) · Ozone (O₃) · 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}, NO₂, and O₃ 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}, PM₁₀, 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 PM₁₀, 2 that measured AQI (Air Quality Index), 13 papers for NO₂, 8

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papers which measured O₃, 5 papers which measured SO₂, 5 papers which measured CO, and 1 paper each for NH₃, methane, lead, total volatile organics, and non-methane volatile organics. Table 1 is sorted first by various pollutants (PM_{2.5}, 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 R_0 (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 PM_{2.5}, 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 PM_{2.5} and other air pollutants increase Covid 19 morbidity and mortality

Key points

- Most studies have reported that higher outdoor levels of PM_{2.5}, 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 PM_{2.5} and NO₂ are associated with significantly higher R_0 —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 PM_{2.5}, 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 PM_{2.5}, 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 PM_{2.5} 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 PM_{2.5} (de Angelis et al. 2021, López-Feldman et al. 2021, Meo et al. 2021a, b, Sahoo 2021, Solimini 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 PM_{2.5} 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 PM_{2.5} was associated with an 8.1% (95% CI 5.4 to 10.5%) increase in Covid 19 cases in a 14-day window (Solimini et al. 2021). Barnett reported that both ambient PM_{2.5} 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 PM_{2.5} 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 PM_{2.5} 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 PM_{2.5} 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 PM_{2.5} 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	3087 US 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			

Table 1 (continued)

Pollutant	Study reference	Location	Sample size and demographics	Time period of study	Covid 19 outcomes with increased pollutant
		62 out of 110 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	A 1- $\mu\text{g}/\text{m}^3$ 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}	(Sharma et al. 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	10 nations with total of number of 34,526,346 Covid 19 cases and 813,442 Covid 19 deaths by 11/16/20 (note date different study period)	2/1/2020 through 6/30/20	Higher PM _{2.5} is associated with more cases $p < 0.01$ and more mortality $p < 0.05$ Also higher ambient temperature is associated with significantly lower Covid 19 cases and mortality ($p < 0.05$ both cases)
PM _{2.5}	(Barnett-Itzhaki and Levi 2021)	36 OECD nations	36 OECD nations—population and Covid 19 cases not listed	1/20/20 to 6/7/20	2017 levels of PM _{2.5} are associated with significantly more Covid 19 cases and mortality 40 days after the 1st confirmed case in each nation ($p < 0.05$)
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	Up to 7/27/20	If all Italy below 25 $\mu\text{g}/\text{m}^3$ 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	105,792 deaths and 12,428 cases	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	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	42,823 Covid 19 cases	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	3/1/20 to 4/30/20	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	3/4/20- 4/24/20	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	Until 6/12/20	Previous PM _{2.5} levels (2010–2016) are associated with significantly higher cases and significantly

Table 1 (continued)

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) Increased PM _{2.5} is associated with higher Covid 19 cases especially in Russia, England, Germany, America, and Canada
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 $\mu\text{g}/\text{m}^3$ 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 $\mu\text{g}/\text{m}^3$ 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 $\mu\text{g}/\text{m}^3$ 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 $\mu\text{g}/\text{m}^3$ increase PM10 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			

Table 1 (continued)

Pollutant	Study reference	Location	Sample size and demographics	Time period of study	Covid 19 outcomes with increased pollutant
			Over 58,000 cases in 120 cities comprising about 70% China's population	1/23/20 to 2/29/20	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	(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 2.67% increased cases (95% CI 0.33 to 5.01%)
PM ₁₀	(Zheng et al. 2021)	China 324 cities	81,132 Covid 19 cases 50,783 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	Italy—total number of cases not reported	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} ,	(Pei et al. 2021)	325 Chinese cities	Daily case rate during lockdown 2.26 per 100,000	Up to 5/27/20	Higher AQI is associated with significantly higher Covid 19 cases

Table 1 (continued)

Pollutant	Study reference	Location	Sample size and demographics	Time period of study	Covid 19 outcomes with increased pollutant
PM ₁₀ , SO ₂ , NO ₂ , and O ₃ 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
NO ₂	(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/m ³ increase is associated with 6.94% increase in Covid 19 cases (95% CI 2.38 to 11.51) 0 to 14-day lag
NO ₂	(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/m ³ NO ₂ is associated with 37.8% increased Covid 19 cases (95% CI 23.8–52.0%)
NO ₂	(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/m ³ increase in NO ₂ is associated with 4.56% increase in Covid 19 cases (95% CI 2.22 to 6.90) 0–14-day lag
NO ₂	(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/m ³ NO ₂ increase is associated with a 7% decrease in Covid 19 cases (IRR 0.93, 95% VI 0.88–0.99, <i>p</i> = 0.03)
NO ₂	(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 NO ₂ above 100 μg/m ² NO ₂
NO ₂	(Bashir et al. 2020)	California	39,000 Covid 19 cases and 1800 deaths to 3/24/20	3/2/20 to 4/24/20	NO ₂ is associated with significantly reduced cases and deaths (<i>p</i> < 0.05 for both cases)
NO ₂	(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 NO ₂ is associated with significantly higher Covid 19 cases
NO ₂	(Bilal et al. 2020)	Germany	180,000 cases Germany up to mid-June 2020	2/24/20 to 7/2/20	Increased NO ₂ is Associated with significantly more Covid 19 cases (<i>p</i> < 0.01)
NO ₂	(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/m ³ NO ₂ is associated with increased Covid 19 cases by 1.24 per 10,000 in population (<i>p</i> < 0.0001)
NO ₂	(Fattorini and Regoli 2020)	Italy	Italy—total cases not reported	2/24/20 to 4/27/20	Long-term NO ₂ exposure (2016–20) is associated with significantly higher Covid 19 cases
NO ₂	(Landoni et al. 2021)	33 European nations	1.48 million Covid 19 Cases	2/11/20 to 5/17/20	Increased NO ₂ is associated with significantly greater cases (<i>p</i> < 0.0001) and mortality (<i>p</i> < 0.0001)
NO ₂	(Barnett-Itzhaki and Levi 2021)	36 OECD nations	36 OECD nations—population and Covid 19 cases not listed	1/20/20 to 6/7/20	Higher NO ₂ is associated with significantly greater Covid 19 mortality (but not cases) by day 60 after first Covid 19 cases in various nations

Table 1 (continued)

Pollutant	Study reference	Location	Sample size and demographics	Time period of study	Covid 19 outcomes with increased pollutant
NO ₂	(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/m ³ NO ₂ is associated with R_0 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
O ₃	(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/m ³ O ₃ increase is associated with 4.76% more cases (95% CI 1.99 to 7.52) 0 to 14-day lag
O ₃	(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 O ₃ is associated with 0.8% increase in Covid 19 cases ($p < 0.001$) and 4.4% increase in Covid 19 deaths ($p < 0.001$)
O ₃	(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	O ₃ related to more cases ($p < 0.001$) but significantly lower Covid 19 mortality ($p = 0.0038$)
O ₃	(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 O ₃ is associated with higher Covid 19 incidence, especially Canada and the USA
O ₃	(Bilal et al. 2020)	Germany	180 Covid 19 cases Germany to mid-June 20	2/24/20 to 7/2/20	Higher O ₃ is associated with more cases ($p < 0.05$)
O ₃	(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 O ₃ is associated with significantly lower number Covid 19 cases (May and June 2020, both $p < 0.01$) and mortality (May and June 2020, both $p < 0.01$)
O ₃	Fattorini and Regoli 2020	Italy	Italy—total Covid 19 cases not reported	2/24/ to 4/27/20	O ₃ long-term exposure (2016–2020) is associated with significantly more Covid 19 cases
O ₃	(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 O ₃ (modification $p = 0.001$)
SO ₂	(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 SO ₂ 10-µg/m ³ increase is associated with 7.79% decreases in cases (95% CI –14.57 to –1.01%) 0 to 14-day lag
SO ₂	(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 SO ₂ 10-µg/m ³ increase related to significantly less Covid 19 cases –7.23% (95% –10.99 to –3.47%) 0–14-day lag
SO ₂	(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 SO ₂ is associated with significantly more cases and deaths ($p < 0.001$ both cases)
SO ₂		9 nations			

Table 1 (continued)

Pollutant	Study reference	Location	Sample size and demographics	Time period of study	Covid 19 outcomes with increased pollutant
	(Liu et al. 2021)		Over 2.6 million Covid cases from 9 nations to 5/20/20	1/21/20 to 5/20/20	Higher SO ₂ is associated with significantly more Covid 19 cases
SO ₂	(Landoni et al. 2021)	33 European nations	1.48 million Covid 19 cases	2/11/20 to 5/17/20	Higher SO ₂ 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 µg/m ³ 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
NH ₃ (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 NH ₃ 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)

Fig. 1 Relationships between 1 $\mu\text{g}/\text{m}^3$ increase ambient $\text{PM}_{2.5}$ and percentage change in Covid 19 cases

between ambient $\text{PM}_{2.5}$ 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 $\text{PM}_{2.5}$ 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 $\mu\text{g}/\text{m}^3$ increase in $\text{PM}_{2.5}$, 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 $\mu\text{m}/\text{m}^3$ were associated with 83% of the Covid 19 deaths (Ogen 2020). A study in Lima, Peru, reported that higher $\text{PM}_{2.5}$ 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 $\mu\text{g}/\text{m}^3$ increase in $\text{PM}_{2.5}$ 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 $\text{PM}_{2.5}$, 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 $\text{PM}_{2.5}$ and PM_{10} on Covid 19 incidence are more sensitive in Russia, England, Germany, and France, while O_3 and $\text{PM}_{2.5}$ 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 $\text{PM}_{2.5}$, 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.

Fig. 2 Relationships between 1 $\mu\text{g}/\text{m}^3$ increase ambient PM_{10} and changes in Covid 19 cases

Fig. 3 Relationships between 1 $\mu\text{g}/\text{m}^3$ increase ambient NO_2 and Covid 19 cases

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 $10 \mu\text{g}/\text{m}^3$ increases (lag 0–14) in the following pollutants were associated with the following increases in Covid 19 cases: $\text{PM}_{2.5}$ 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 $10\text{-}\mu\text{g}/\text{m}^3$ 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 $\text{PM}_{2.5}$ 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 $\text{PM}_{2.5}$ and higher AQI (Air Quality Index) (consisting of $\text{PM}_{2.5}$, 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 $\text{PM}_{2.5}$ 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 $10 \mu\text{g}/\text{m}^3$ increase during (Lag 0–14 days) of the following outdoor air pollutants were associated with significantly increased risk of Covid 19 infections $\text{PM}_{2.5}$ 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 $\text{PM}_{2.5}$, 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 $10 \mu\text{g}/\text{m}^3$ 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%), $\text{PM}_{2.5}$ 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 $\text{PM}_{2.5}$ 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 $1 \mu\text{g}/\text{m}^3$ increase in $\text{PM}_{2.5}$ 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 O_3 0.8 and 4.4% increases in cases and mortality (Meo et al. 2021b).

An English study of over 300,000 Covid 19 cases reported that each $1 \mu\text{g}/\text{m}^3$ increase in outdoor $\text{PM}_{2.5}$ 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 , $\text{PM}_{2.5}$, PM_{10}) during the period 2016–2020 were associated with significantly higher levels of Covid 19 cases (Fattorini and Regoli 2020).

Ambient $\text{PM}_{2.5}$ and NO_2 increases R_0 rate of Covid 19 R_0 is described as the basic reproduction ratio for Covid 19. The R_0 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_0 rates and their relationships between ambient $\text{PM}_{2.5}$ from the period March 2 to April 30, 2020 (Chakrabarty et al. 2021). Each increment in ambient $1 \mu\text{g}/\text{m}^3$ $\text{PM}_{2.5}$ was associated with a significant 0.25 increase in R_0 (95% CI 0.048–0.447) (Chakrabarty et al. 2021). During this time, R_0 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_0 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_0 basic reproduction rate (Yao et al. 2021). Each $10 \mu\text{g}/\text{m}^3$ increase in NO_2 was associated with a R_0 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 $\text{PM}_{2.5}$ 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 $\text{PM}_{2.5}$, 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 $\text{PM}_{2.5}$ levels were associated with significantly higher rates of lower respiratory illness (Horne 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 PM_{2.5} and other pollutants (Srivastava 2021).

An analysis of 10,000+ sampling sites in 380 World Cities reported that during the 2020 lockdown periods PM_{2.5} 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 PM_{2.5} of 11% (Rodríguez-Urrego and Rodríguez-Urrego 2020). A study of more than 1500 air monitoring sites in 377 Chinese cities reported a mean 16 and 20% reduction of PM_{2.5} 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 PM_{2.5} during the March 1 to July 24, 2020, as compared to 2019 (Hashim et al. 2021). Another study noted significant drops in outdoor PM_{2.5} 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 PM_{2.5} 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 PM_{2.5} 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, PM_{2.5}, 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 PM_{2.5} 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 PM_{2.5} 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 PM_{2.5} 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 PM_{2.5} 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 PM_{2.5} 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 2.284, 95% CI 1.765–2.954, 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 (Middelton 2020). Every year, about half a billion tons of desert dust become airborne and can travel for thousands of miles (Middelton 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.

- Viability of SARS Cov 2 has been estimated to be perhaps about 1.2 h in air and from several hours to several days on living and inanimate surfaces.

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 PM₁₀ fractions of air (Tung et al. 2021). Viable SARS Cov 2 has been detected on PM₁₀ 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 Cov2 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 inflation.

- PM_{2.5}, NO₂, and other air pollutants may increase Covid 19 susceptibility by altering the ACE2 or angiotension 2 receptor which is a binding site for SAR Cov2.

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 NO₂ 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 Cov2 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 NO₂ 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 NO₂ 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 NO₂ “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

(Samavati and Uhal 2020). For a good 2020 discussion on ACE2 receptors, please see Samavati and Uhal (2020)

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_{2.5} enhanced survival of the influenza virus by downregulating pulmonary macrophage Kdm6a and altering histone modification in IL-6 and IFN β promoter regions (Ma et al. 2017). Another murine study reported that intratracheal PM_{2.5} exposure reduces influenza immunity by inhibiting activation of NLRP3 inflammasome and expression of interferon- β (Tao et al. 2020).

Discussion

Many environmental exposures have been strongly linked to higher Covid 19 morbidity and mortality including PM_{2.5}, PM₁₀, NO₂, O₃, 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_{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_{2.5} increases Covid 19 factors varies considerable 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_{2.5} in 27 out of 29 studies, PM₁₀ in 12 out of 14 studies, NO₂ in 11 out of 13 cases, O₃ in 7 out of 8 cases, SO₂ 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, socio-economic 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; Nussbaumer-Streit et al. 2020; Pradhan et al. 2020; Rodríguez 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 9 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_{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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