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Review article

The effect of the urban exposome on COVID-19 health outcomes: A systematic review and meta-analysis

Laura Houweling[a,b,*], Anke-Hilse Maitland-Van der Zee[b,c,d], Judith C.S. Holtjer[a], Somayeh Bazdar[b,c,d], Roel C.H. Vermeulen[a,e], George S. Downward[a,e,1], Lizan D. Bloemsma[b,c,d,1]

[a] Department of Environmental Epidemiology, Institute for Risk Assessment Sciences (IRAS), Utrecht University, Utrecht, the Netherlands
[b] Dept. of Pulmonary Medicine, Amsterdam UMC, Amsterdam, the Netherlands
[c] Amsterdam Institute for Infection and Immunity, Amsterdam, the Netherlands
[d] Amsterdam Public Health, Amsterdam, the Netherlands
[e] Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht, the Netherlands

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ABSTRACT

Background: The global severity of SARS-CoV-2 illness has been associated with various urban characteristics, including exposure to ambient air pollutants. This systematic review and meta-analysis aims to synthesize findings from ecological and non-ecological studies to investigate the impact of multiple urban-related features on a variety of COVID-19 health outcomes.

Methods: On December 5, 2022, PubMed was searched to identify all types of observational studies that examined one or more urban exposome characteristics in relation to various COVID-19 health outcomes such as infection severity, the need for hospitalization, ICU admission, COVID pneumonia, and mortality.

Results: A total of 38 non-ecological and 241 ecological studies were included in this review. Non-ecological studies highlighted the significant effects of population density, urbanization, and exposure to ambient air pollutants, particularly $PM_{2.5}$. The meta-analyses revealed that a 1 $\mu g/m^3$ increase in $PM_{2.5}$ was associated with a higher likelihood of COVID-19 hospitalization (pooled OR 1.08 (95% CI:1.02–1.14)) and death (pooled OR 1.06 (95% CI:1.03–1.09)). Ecological studies, in addition to confirming the findings of non-ecological studies, also indicated that higher exposure to nitrogen dioxide (NO_2), ozone (O_3), sulphur dioxide (SO_2), and carbon monoxide (CO), as well as lower ambient temperature, humidity, ultraviolet (UV) radiation, and less green and blue space exposure, were associated with increased COVID-19 morbidity and mortality.

Conclusion: This systematic review has identified several key vulnerability features related to urban areas in the context of the recent COVID-19 pandemic. The findings underscore the importance of improving policies related to urban exposures and implementing measures to protect individuals from these harmful environmental stressors.

1. Background

The novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) emerged in December 2019, and the resulting COVID-19 pandemic has currently caused more than 6.8 million deaths worldwide (WHO, 2023). However, certain regions have experienced a disproportionate impact relative to their population, particularly the United States and Europe, where a significant number of these deaths have occurred (WHO Coronavirus, 2022). Even though the underlying causes of this pattern are not thoroughly understood, the current evidence base, in combination with lessons learned from previous epidemics, indicate that urban environmental factors, such as ambient air pollutants (AAP) and meteorological conditions, may contribute to this phenomenon (Aggarwal et al., 2021). As the global urban population continues to grow (United Nations et al., 2018), more individuals are exposed to these specific environmental factors, which remains a global

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* Corresponding author. Department of Environmental Epidemiology, Institute for Risk Assessment Sciences (IRAS), Utrecht University, Utrecht, the Netherlands.
E-mail address: l.houweling@uu.nl (L. Houweling).

[1] Co-last authors.

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public health concern.

The urban exposome refers to the set of urban outdoor environmental factors to which people residing in urban areas are exposed, including air pollutants, meteorological conditions, noise, and characteristics of the built environment (Robinson et al., 2018). The high density of the population, activities in urban areas, and the fact that residents are often exposed to air pollution levels that exceed standards set by the World Health Organization (WHO), predispose them to various adverse health outcomes (Sharifi et al., 2020). Moreover, the global impact of COVID-19 has been associated with aspects of the urban exposome (Barouki et al., 2021). Specifically, there have been observations linking AAP concentrations to the severity of SARS-CoV-2 infection, although most of the evidence comes from ecological studies (Ali et al., 2021). The association seems to be strongest for exposure to particulate matter (PM), especially fine particulate matter ($PM_{2.5}$), but ambient levels of ozone (O_3), nitrogen dioxide (NO_2), carbon monoxide (CO) and sulphur dioxide (SO_2) also seem to play a role (Marquès et al., 2022a). Additionally, meteorological factors such as ambient temperature and relative humidity may contribute to the severity and mortality of COVID-19, partially through their influence on AAP concentrations and their versatile influence on virus transmission (De Angelis et al., 2021). Finally, the pandemic induced a range of behavioural and social changes, leading to diverse environmental and health implications which also interacted with the severity of COVID-19 (Barouki et al., 2021).

Numerous studies, both ecological and non-ecological, have been conducted to determine associations between specific environmental exposures and outcomes of SARS-CoV-2 infection. In contrast to non-ecological studies, where individual-level exposure, confounder, and disease information are analysed, ecological studies examine exposure and disease information at a group level (Rothman et al., 2012). Given that COVID-19 outcomes are primarily influenced by individual characteristics, obtaining high-quality, individual-level data is critical to accurately assess the influence of environmental risk factors on COVID-19 outcomes. However, ecological studies are susceptible to ecological fallacies due to their reliance on aggregated data rather than individual data (Wu et al., 2020; Heederik et al., 2020). To investigate the effect of potential ecological bias that may arise from the design of these studies, it is crucial to synthesize and compare the findings of ecological and non-ecological studies. Additionally, it is essential to differentiate between ecological and non-ecological study designs in the context of COVID-19 research to ensure that research findings are correctly interpreted. Integrating insights from both approaches facilitates a more complete understanding of the impact of the pandemic and supports evidence-based decision-making. Furthermore, as urban exposome features are highly interrelated (Robinson et al., 2015), a holistic approach that examines the impact of all urban-related features on various COVID-19 health outcomes is needed. Therefore, the aim of this systematic review is to integrate evidence from ecological and non-ecological studies to evaluate the impact of multiple urban exposome features on a wide range of COVID-19 health outcomes. By considering the urban exposome as a whole, our review provides a comprehensive assessment of the relationship between urban environments and COVID-19 health outcomes.

2. Methods

On December 5th, 2022, PubMed was searched for studies that examine associations of the urban exposome with various COVID-19 health outcomes. The full search term is detailed in Table S1. PRISMA *(Table S2)* and MOOSE *(Table S3)* reporting requirements were met, and a protocol of this review has been registered in the PROSPERO database (ID: CRD42021293298).

2.1. Eligibility criteria

The scope of this systematic review was defined using the 'Population, Exposure, Comparison, Outcome, and Study design' (PECOS) framework. The selection of urban exposures included in this review was based on an initial literature review and discussions with experts in the field. The included urban exposures encompassed the following features: AAP, meteorological factors, noise, traffic, walkability, urbanization, population density, the built environment (including green and blue space) and land-use. We focused on English language studies that investigated at least one of these urban exposures in the general human population (age ≥18 years) and examined one or more COVID-19 health outcomes as the primary outcome. The COVID-19 health outcomes explored in this review included disease severity, hospitalization, emergency department (ED) visit, intensive care unit (ICU) admission, intensive respiratory support (IRS), occurrence of COVID pneumonia, and mortality related to SARS-CoV-2 infection. This systematic review included several types of studies, including pre-prints and letters to the editor. However, experimental and animal studies were excluded, as were studies with COVID-19 transmission or incidence as the primary outcome. Additionally, studies focusing on excess mortality as a proxy for COVID-19 deaths and those conducted in nursing homes were also excluded. Furthermore, articles that investigated specific groups of individuals, such as diabetic patients or pregnant women, were also not included. The snowball method was employed to screen the reference lists of relevant reviews.

2.2. Selection and data extraction

The primary reviewer (LH) conducted an initial screening based on the title and abstract, and subsequently extracted data from the included studies following a second full-text screening. If the full text was unavailable, the authors of the respective papers were contacted. To ensure quality control, a random 10% of the papers underwent both initial and second screenings by two independent reviewers (SB, JCSH), as well as extraction of the data from all included non-ecological papers and a random 10% of included ecological papers. Conflicts between the two independent reviewers arose for thirteen articles based on the pre-established inclusion criteria. These conflicts were resolved through discussion and a third screening, resulting in the inclusion of three of these papers in the current systematic review. From the original articles, relevant information including the study's title, author, year of publication, study design, study area, sample size, study period, studied urban exposure, source of exposure data, outcome definition, source of outcome data, and a summary of results were extracted. Furthermore, individual covariates and statistical analyses employed in non-ecological studies were also documented. Given the increased risk of ecological bias associated with studies with larger units of observation, the results of the ecological papers were classified based on the geographical scale at which the statistical analyses were conducted. These scales included global, country, region (such as county or province level), city, and smaller than city. Moreover, exposure to air pollutants was categorized according to the duration of exposure examined, distinguishing between long-term exposure (>one year), medium-term exposure (<one year, >one month), and short-term exposure (<one month).

2.3. Risk of bias evaluation

The primary reviewer (LH) evaluated the methodological quality of the included non-ecological studies using the National Heart, Lung, and Blood Institute (NIH) Study Quality Assessment Tool for Observational Cohort and Cross-sectional Studies, which consists of fourteen items (Quality, 2014). Each question in the tool was answered as either yes (+1), no, cannot determine (CD), not applicable (NA), or not reported (NR). The total score for each individual study was calculated and expressed as a percentage, ranging from 0% to 100%. These scores were then categorized into four groups: poor (0–25%), fair (25–50%), good (50–75%), and excellent (75–100%) (Maass et al., 2015). Since there is currently no standardized quality assessment tool for ecological study designs to evaluate potential ecological bias (Romero Starke et al., 2021), we instead examined common forms of ecological bias and fallacies.

2.4. Meta-analyses

The decision was made to not perform a meta-analysis of the results of ecological studies due to the increased risk of ecological bias, which would render the pooled estimate relatively unreliable. Following our protocol, a random-effects meta-analysis was conducted when a minimum of five non-ecological studies examining urban features exhibited sufficient similarity in terms of outcomes and exposures. From the eligible studies, adjusted effect estimates (odds ratio (OR)/relative risk (RR)/hazard ratio (HR)), confidence intervals (CI), and increment units of the air pollutants were extracted and standard errors (SE) were calculated. Standardized effect estimates were computed to indicate the impact on specific COVID-19 outcomes per 1 μg/m^3 increase in air pollution exposure. The formula used for calculation was: exp(ln(OR)ˆ1/increment). In cases where the unit of concentration of NO$_2$ was reported as parts per billion (ppb), a conversion factor of 1.91 μg/m^3 was applied (EPA, 2021). The standardized effect estimates per 1 μg/m^3 were utilized to determine the pooled effect estimates using a random-effects model. Forest plots were used to visually represent the associations observed in each study and the pooled effect. To assess heterogeneity among the eligible studies, the I^2 index was employed, whereby an I^2 value of 75% or higher indicated significant heterogeneity (Cochrane, 2022). Finally, in order to evaluate potential publication bias, a funnel plot analysis and Egger's test were to be conducted if at least ten non-ecological studies were eligible for meta-analysis. However, for this particular case, the criteria for performing these analyses were not met (Sterne et al., 2011). All statistical analyses were performed using IBM SPSS Statistics release 28.0.1.1.

3. Results

3.1. Identification of studies

The literature search identified a total of 6852 records. After removing duplicates (n = 138), and performing title and abstract screening, 606 articles remained eligible for full-text review, after which 38 non-ecological and 241 ecological studies were included (Fig. 1). Due to the substantial number of the included ecological studies, we only present the key findings of these studies in the main text. More comprehensive descriptions and specific examples can be found in the text provided in *S4*.

3.2. Methodological quality of the included non-ecological studies

Table S5 provides the results of the methodological quality and risk of bias assessment of the included non-ecological studies using the NIH tool. In summary, the overall methodological quality was categorized as either fair (n = 5), good (n = 30), or excellent (n = 3). The summary percentage scores ranged from 35.7% to 78.6%, indicating the extent to which the studies adhered to methodological standards and minimized potential biases.

3.3. Urban exposures influencing COVID-19 health outcomes in non-ecological studies

A total of 38 non-ecological studies were identified examining the relationships between urban exposome characteristics and various COVID-19 health outcomes (Tables 1,2 and 3). The number of participants in the studies ranged from 147 (Di Ciaula et al., 2022) to 1,778, 670 (Rostila et al., 2021), indicating a wide range of sample sizes. To visualize the direction of associations observed for the studied exposures, Fig. 2 provides a graphical representation. Further details and additional characteristics of these studies can be found in Table S6.

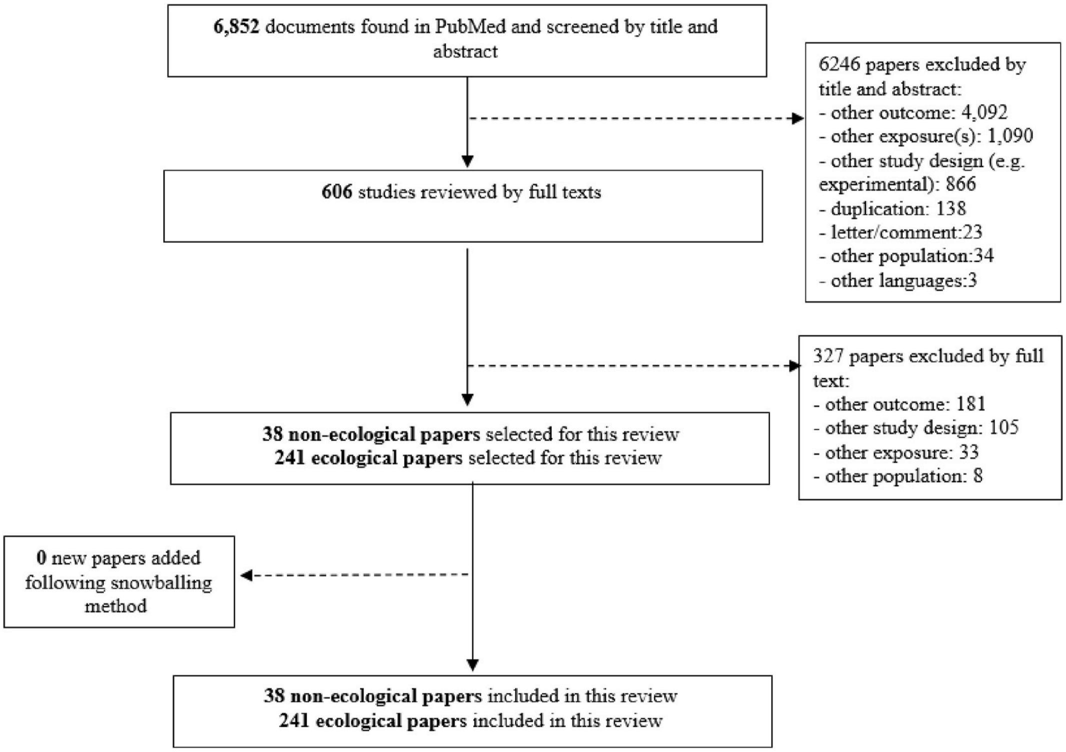

Fig. 1. PRISMA flow diagram of the search strategy.

Table 1

Characteristics of the included non-ecological studies on the associations of ambient air pollution with COVID-19 health outcomes.

Author, reference	Study design	Sample size, study area	Time period of study	Urban exposure	COVID-19 outcome(s)	Findings	Risk of Bias
Ciaula et al., (Di Ciaula et al., 2022)	Longitudinal study	147 patients admitted at the hospital due to acute SARS-CoV2 infection with pneumonia, ten cities in Apulia (Southern Italy)	March 2020–April 2021	Individual exposure to PM_{10} and NO_2 in the 2 weeks before hospital admittance.	Hospital discharge at home vs in-hospital death	Average NO_2 air concentrations in the two weeks before hospital admission (OR: 1.029, 95% CI: 1.0008–1.059) were a significant predictor of mortality. No significant effect was observed for PM_{10}.	Low
Mendy et al., (1), (Mendy et al., 2021a)	Retrospective observational study	14,783 participants, Ohio, University of Cincinnati	13 March 2020–30 September 2020	$PM_{2.5}$ exposure (aggregate annual $PM_{2.5}$ exposure estimates at the zip code of the patients' residential address over the 10-year period from 2009 to 2018)	COVID-19 hospitalization	After adjusting for covariates, a 1 $\mu g/m^3$ increment in the 10-year annual average $PM_{2.5}$ was associated with an 18% increase in admission to hospital (OR: 1.18, 95% CI: 1.11–1.26).	Low
Mendy et al., (2), (Mendy et al., 2021b)	Retrospective observational study	1128 patients, University of Cincinnati hospitals, USA	March 13, 2020–July 5, 2020	Estimated $PM_{2.5}$ exposure over a 10-year period (2008–2017) at their residential zip codes	Hospitalization defined as admission for a duration of $\geq$24 h	Long-term exposure to $PM_{2.5}$ was significantly associated with higher odds of hospitalization in COVID-19 patients with pre-existing asthma or COPD. However, this association is not observed for all participants (OR: 0.99, 95% CI: 0.79–1.23).	Low
Chen et al., (1), (Chen et al., 2021)	Multiethnic retrospective cohort study	75,010 COVID-19 patients, Southern California	March 1, 2020–August 31, 2020	NRAP = NOx 1 month and 1 year before infection.	COVID-19-related hospitalizations, intensive respiratory support (IRS), and ICU admissions	Exposure to NRAP was associated with higher OR of COVID-19-related ICU admission (OR: 1.07, 95% CI: 1.01–1.13), IRS (OR: 1.11, 95% CI: 1.04–1.19), and increased mortality risk (HR: 1.10, 95% CI: 1.03–1.18). No significant associations were found between freeway NRAP and COVID-19 outcomes. The associations remained significant after adjusting for regional air pollutant exposures.	Low
Bowe et al., (Bowe et al., 2021)	Cohort study	169,102 Veterans, USA	March 2, 2020–January 31, 2021,	Estimates of annual average ground level $PM_{2.5}$ in 2018 were available at approximately 1 km^2 resolution.	COVID-19 hospitalization, mechanical ventilation	A 1.9 $\mu g/m^3$ increase in $PM_{2.5}$ was associated with a 10% (95% CI: 8%–12%) increased risk of COVID-19 related hospitalization. Notably, this risk was observed even at $PM_{2.5}$ levels that were below the regulatory standards.	Low
Elliott et al., (Elliott et al., 2021)	Biobank cohort study	459 COVID-19 deaths and 2626 non-COVID-19 deaths, United Kingdom	January 2020–21 September 2020	Modelled levels of nitrogen oxides (NOx) and PM_{10}, $PM_{2.5}$ and $PM_{2.5}$ absorbance at residential address in 2010	Risk of COVID-19 mortality	After adjusting for other covariates, no effect of $PM_{2.5}$ was observed (OR: 0.94, 95% CI: 0.75–1.18).	Low
López-Feldman et al., (López-Feldman et al., 2021)	Cross-sectional study	196,273 and 71,620 patients, Mexico City Metropolitan Area (MCMA) and Mexico City	Until October 7th, 2020	Long-term $PM_{2.5}$ exposure (2000–2018) and short-term $PM_{2.5}$ exposure (two-week average mean before onset of symptoms. temperature, population density	Confirmed COVID-19 deaths	$PM_{2.5}$ was positively associated with COVID-19 mortality, driven mainly by long-term exposure but with potential effects from short-term exposure as well. Each 1 $\mu g/m^3$ increase in $PM_{2.5}$ is estimated to raise the mortality risk by 7.4%.	Low
Marquès et al., (Marquès et al., 2022b)	Retrospective observational study	2112 patients admitted to Catalan hospitals, Spain	April–June 2020	NO_2 and PM_{10} (hourly and long-term)	The severity and mortality of COVID-19	PM_{10} had significant effects on the severity and mortality of COVID-19, with an OR of 1.67 and 2.38, respectively. A 1 $\mu g/m^3$ increase in long-term PM_{10} exposure corresponded to a 3.06% increase in severe cases and a 2.68% increase in deaths. NO_2 importance was low.	Low
Pegoraro et al., (Pegoraro et al., 2021)	Retrospective observational study	6483 Covid-19 patients, Italy	March 18th, 2020–June 30th, 2020	PM_{10} daily concentration data for the period January 2020–June 2020	Presence/absence of registration of Covid-19 with pneumonia	Patients with PM_{10} exposure falling in the second tertile had a 30% higher likelihood of developing pneumonia compared to patients in the first tertile. Furthermore, for those in the third tertile, the risk was nearly doubled compared to the first tertile.	Low

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Table 1 (*continued*)

Author, reference	Study design	Sample size, study area	Time period of study	Urban exposure	COVID-19 outcome(s)	Findings	Risk of Bias
Nobile et al., (Nobile et al., 2022)	Longitudinal study	All subjects aged ≥30 years resident (n = 1,594,308), Rome, Italy	1 January 2020–15 April 2021	Annual average concentrations of $PM_{2.5}$ and NO_2 were estimated for 2019	COVID-19 mortality	$PM_{2.5}$ and NO_2 showed strong associations with COVID-19 mortality, with a HR of 1.08 (95% CI: 1.03–1.13) and 1.09 (95% CI: 1.02–1.16) per one IQR increment.	Low
Sheridan et al., (Sheridan et al., 2022)	Biobank cohort study	UK Biobank participants who resided in England (n = 424,721), United Kingdom	March–December 2020	Annual average air pollution, $PM_{2.5}$, PM_{10}, and NO_2 at residential address in 2010	COVID-19 hospitalizations and deaths	In minimally adjusted models, $PM_{2.5}$ and NO_2 were positively associated with COVID-19 hospitalizations and deaths. However, these associations did not remain significant in fully adjusted models. No associations were found for PM_{10}.	Low
Chen et al., (2), (Chen et al., 2022a)	Retrospective study	All people with confirmed SARS-CoV-2 infection, aged 20 years and older and not residing in a long-term care facility during 2020 (n = 151,105), Ontario, Canada,	Year 2020 (followed up for outcomes until May 2021)	Long-term exposure to $PM_{2.5}$, NO_2 and ground-level O_3 based on their residence from 2015 to 2019	Risk of COVID-19-related hospital admission, intensive care unit (ICU) admission and death	For each IQR increase in $PM_{2.5}$ exposure (1.70 μg/m^3), the OR were 1.06 (95% CI: 1.01–1.12) for hospital admission, 1.09 (95% CI: 0.98–1.21) for ICU admission, and 1.00 (95% CI: 0.90–1.11) for death. No significant associations were found for NO_2. In addition, for each IQR increase in O_3 (5.14 ppb), the OR were 1.15 (95% CI: 1.06–1.23) for hospital admission, 1.30 (95% CI: 1.12–1.50) for ICU admission, and 1.18 (95% CI: 1.02–1.36) for death.	Low
Chen et al., (3), (Chen et al., 2022b)	Cohort study	Approximately 75,000 patients, Kaiser Permanente Southern California	March 1 - August 31, 2020	One-year and 1-month averaged ambient air pollutant $PM_{2.5}$, NO_2, and O_3 exposures before COVID-19 diagnosis	COVID-19–related hospitalizations, IRS, and ICU admissions within 30 days and mortality within 60 days after COVID-19 diagnosis	For a 1-SD increase in 1-year $PM_{2.5}$ (1.5 μg/m^3), the ORs were 1.24 (95% CI: 1.16–1.32) for hospitalization, 1.33 (95% CI: 1.20–1.47) for IRS, and 1.32 (95% CI: 1.16–1.51) for ICU admission. For a 1-month increase in NO_2 (SD: 3.3 ppb), the corresponding ORs were 1.12 (95% CI: 1.06–1.17) for hospitalization, 1.18 (95% CI: 1.10–1.27) for IRS, and 1.21 (95% CI: 1.11–1.33) for ICU admission. The HR for mortality were 1.14 (95% CI: 1.02–1.27) for 1-year $PM_{2.5}$ and 1.07 (95% CI: 0.98–1.16) for 1-month NO_2.	Low
Bozack et al., (Bozack et al., 2022)	Retrospective study	6542 SARS-CoV-2 PCR–positive patients, seven New York City hospitals	March 8, 2020–August 30, 2020	Annual average $PM_{2.5}$, NO_2, and BC concentrations at patients' residential address.	COVID-19 mortality, ICU admission and intubation	Long-term exposure to $PM_{2.5}$ was associated with a higher risk of mortality (RR: 1.11, 95% CI: 1.02–1.21 per 1-μg/m3 increase) and ICU admission (RR: 1.13, 95% CI: 1.00–1.28 per 1-μg/m3 increase). However, there were no associations found between NO_2 or BC exposure and COVID-19 mortality, ICU admission, or intubation.	Very low
Lavigne et al., (Lavigne et al., 2022)	Case-crossover study	78,255 COVID-19 ED visits, Alberta and Ontario, Canada	1 March 2020–31 March 2021	Daily air pollution data $PM_{2.5}$, NO_2 and O_3 were assigned to individual case of COVID-19 in 10 km × 10 km grid resolution.	COVID-19 ED visits	Cumulative ambient exposure to $PM_{2.5}$ (OR: 1.010, 95% CI: 1.004–1.015, per 6.2 μg/m^3) and NO_2 (OR: 1.021, 95% CI: 1.015–1.028, per 7.7 ppb) was associated with ED visits for COVID-19. O_3 showed a positive association, but only among hospitalized cases.	Low
Beloconi & Vounatsou., (Beloconi et al., 2023)	Retrospective study	28,540 patients, Switzerland	February 2020–May 2021	$PM_{2.5}$ and NO_2 concentrations for each year between 2014 and 2019	Hospitalization, admission to ICU, and death	Long-term exposure to $PM_{2.5}$ and NO_2 is associated with a higher risk of mortality during the first major wave of the pandemic with an OR of 1.16 (95% CI: 1.04–1.28) and 1.15 (95% CI: 1.03–1.27) respectively. Additionally, exposure to NO_2 increases the	

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Table 1 (*continued*)

Author, reference	Study design	Sample size, study area	Time period of study	Urban exposure	COVID-19 outcome(s)	Findings	Risk of Bias
						odds of requiring ICU admission (OR: 1.17, 95% CI: 1.05–1.30).	
Li et al., (Li et al., 2022a)	Retrospective study & time series	476 patients, Nanjing Public Health Medical Center	July 20, 2021–August 17, 2021	Daily average concentrations of PM_{10}, $PM_{2.5}$. Daily average temperature (°C) and daily average wind speed (m/s)	COVID-19 severity (we combined the severe and critical categories, referred to as “severe”)	A 1-unit increase in PM_{10} was associated with an 81.70% increase in the risk of severe COVID-19 (95% CI: 35.45–143.76). Similarly, a 1-unit increase in $PM_{2.5}$ was associated with a 299.08% (95% CI: 92.94–725.46) increase in the risk of severe COVID-19. These associations remained significant when considering lags of 0–7 days, 0–14 days, and 0–28 days in the multipollutant models.	Low
Kim et al., (Kim et al., 2022)	Case-Crossover study	7462 deaths from COVID-19, Cook County, Illinois	Up to 28 February 2021	Short-term exposures to $PM_{2.5}$ and O_3 on the day of death and up to 21 d before death at location of death with COVID-19.	COVID-19 deaths	A 5.2 $\mu g/m^3$ increase in $PM_{2.5}$ exposure was associated with a 69.6% (95% CI: 34.6–113.8) increase in the risk of COVID-19 mortality. Similarly, an 8.2 $\mu g/m^3$ increase in O_3 exposure was associated with a 29.0% (95% CI: 9.9–51.5) increase in the risk of COVID-19 mortality.	Low
Hoskovec et al., (Hoskovec et al., 2022)	Retrospective study	55,273 COVID-19 cases (of which 62.2% (n = 34,401) had partially missing health outcomes), Denver, Colorado	March 6, 2020–February 28, 2021	Annual average exposure to $PM_{2.5}$, O_3 (ppb), and temperature (degrees Fahrenheit) in the year prior to the COVID-19 pandemic	Hospitalized, admitted to an ICU, placed on a mechanical ventilator, or died due to COVID-19.	A one IQR increase in $PM_{2.5}$ exposure was associated with a 9% increased risk of severe COVID-19 (OR:1.09, 95% CI: 1.02–1.18). Long-term exposure to $PM_{2.5}$, along with elevated levels of ozone and temperature, was associated with a higher risk of hospitalization and ICU admission compared to being asymptomatic.	Very low
Rzymski et al., (Rzymski et al., 2022)	Retrospective study	4432 hospitalized patients, Poland	March 2020–July 2021	Benzo(a)pyrene (B(a)P) and PM_{10}, $PM_{2.5}$ during a week before their hospitalization	COVID-19 clinical outcomes & death	Exposures to $PM_{2.5}$ and B(a)P above the established guidelines were linked to higher odds of early respiratory symptoms of COVID-19, hyperinflammatory state, the need for oxygen therapy, and mortality. Additionally, except for the mean 24-h PM_{10} level, exceeding the limits for other air pollution parameters was associated with an increased likelihood of oxygen saturation below 90%.	Low
English et al., (English et al., 2022)	Retrospective study	3.1 million SARS-CoV-2 infections and 49,691 COVID-19 deaths, California, USA	February 2020–February 2021	$PM_{2.5}$ (individual address data on COVID-19 deaths and assigned 2000–2018 1 km–1km gridded $PM_{2.5}$)	COVID-19 deaths	Individuals residing in the highest quintile of long-term $PM_{2.5}$ exposure had a 51% higher risk of COVID-19 mortality compared to those in the lowest quintile of long-term $PM_{2.5}$ exposure. The estimated risk of death associated with each 1 $\mu g/m^3$ increase in $PM_{2.5}$ long-term exposure was 1.041 (95% CI 1.029–1.052).	Low
Soltan et al., (Soltan et al., 2021)	Multicenter cohort study	Hospitalized patients with COVID-19 (n = 3671), four hospitals across the West Midlands, University Hospitals of Birmingham	1 February 2020–1 September 2020	Index of Multiple Deprivation (IMD) subdomains: indoor LE, outdoor LE	ICU admission details and hospitalized episode outcomes (multilobar pneumonia)	Air pollution deprivation was associated with multilobar pneumonia upon presentation and ICU admission. LE was associated with multilobar pneumonia upon presentation (OR: 1.76, 95% CI: 1.51–2.06) and ICU admission (OR: 1.49, 95% CI: 1.16–1.90).	Moderate

HR=Hazard Ratio. OR=Odds Ratio. AHR = Average Hazard Ratio. CI=Confidence Interval. ICU=Intensive Care Unit. RR=Relative Risk. IQR=Interquartile Range. $PM_{2.5}$ = fine Particulate Matter. PM_{10} = Particulate Matter. NOx = Nitrogen Oxides. NO_2=Nitrogen Dioxide. NRAP= Near-roadway Air Pollution Exposure. O_3 = ozone. BC=Black Carbon. LE = Living Environment. ppb = parts per billion. ED = emergency department. IRS=Intensive Respiratory Support.

Table 2
Characteristics of the included non-ecological studies on the associations of urbanization and population density with COVID-19 health outcomes.

Author, reference	Study design	Sample size, study area	Time period of study	Urban exposure	COVID-19 outcome (s)	Findings	Risk of Bias
Boudou et al., (Boudou et al., 2021)	Retrospective study	47,265 laboratory-confirmed cases, Republic of Ireland	29th February - 30th November 2020	Scale ranging from 'city' (1) to 'highly rural/remote areas' (6), deprivation index	Hospitalizations, ICU admissions, and deaths	Residing in rural areas was found to be associated with a higher likelihood of hospitalization (OR: 1.200, 95% CI: 1.143–1.261). Urban living was associated with an increased probability of ICU admission (OR: 1.533, 95% CI: 1.606–1.682). Urban residents were approximately 1.5 times more likely to require critical care compared to their rural counterparts.	Low
Verma et al., (Verma et al., 2021)	Retrospective study	824 patients, India, Rajasthan	July 10 - October 26, 2020	Living in an urban area	Days of hospital stay and deaths	Rural patients exhibited a notably lower risk of mortality (HR: 1.29, 95% CI: 1.17–2.15) compared to their urban counterparts.	Low
Brainard et al., (Brainard et al., 2022)	Secondary analysis of patient records	1977 unique individual patient records, Confined area of eastern England,	May 31, 2020–September 22, 2020.	Residence area data on air quality, rurality, access to employment centers, population density, relative transport accessibility.	Date of death when applicable	Regions characterized by lower levels of rurality exhibited a higher number of COVID-19 fatalities. Relative transport accessibility and air quality indicators did not emerge as significant predictors. Population density had no independent impact on either the number of cases or deaths.	Low
Hamdan et al., (Hamdan et al., 2021)	Cross-sectional study	300 recovered patients with COVID-19 infection, Hebron city, Palestine	August 2020–December 2020	Urban vs camp/village living	COVID-19 hospitalizations	People living in urban areas had a significantly higher risk of COVID-19 hospitalization compared to those living in camps/villages, with an OR of 3.6 (95% CI: 1.82–6.95).	Moderate
Mengist et al., (Mengist et al., 2022)	Retrospective study	552 laboratory-confirmed COVID-19 cases hospitalized at DMU and TGH treatment centers, Northwest Ethiopia	March 2020–March 2021	Urban - rural	COVID-19 death/discharge	Rural residence was significantly associated with mortality (AHR: 0.18; 95% CI: 0.05–0.64). COVID-19 patients from urban residences have a higher risk of death.	Moderate
Sohrabi et al., (Sohrabi et al., 2022)	Cross-sectional	234,418 COVID-19 patients, Province of Tehran, Iran	March 2020–March 2021	Living in an urban vs sub-urban area	Intensive care unit (ICU) admission, and the COVID-19 deaths	Living in urban areas was associated with a higher likelihood of ICU admission (OR: 1.27, 95% CI: 1.240–1.305). Patients residing in sub-urban areas exhibited a greater vulnerability to fatal outcomes of COVID-19 infection (OR: 1.13, 95% CI: 1.105–1.175).	Low
Hamilton et al., (Hamilton et al., 2022)	Retrospective study	155 patients admitted to a single-centre tertiary academic hospital, Augusta, Georgia	March 13, 2020–June 25, 2020	Urban – rural (county populations of ≥50,000 are classified as urban)	COVID-19 outcomes	Urban individuals had higher floor admission rates, while rural individuals had higher rates of escalated medical care within 24 h. No significant differences were found in discharge disposition, readmissions, hospital length of stay, ICU length of stay, or mortality rates between rural and urban individuals.	Moderate
Denslow et al., (Denslow	Retrospective study	3991 people hospitalized with SARS-CoV-2	March 1 - September 30, 2020	Urban – rural	COVID-19 hospitalization and mortality	Rural patients had 1.3 times the odds of dying or being discharged to hospice	Low

(continued on next page)

Table 2 (*continued*)

Author, reference	Study design	Sample size, study area	Time period of study	Urban exposure	COVID-19 outcome (s)	Findings	Risk of Bias
et al., 2022)		infections among 17 hospitals, North Carolina				compared to urban patients, according to the crude model (95% CI: 1.1–1.6). The estimate only slightly decreased in adjusted models, with an OR of 1.2 (95% CI: 1.0–1.5).	
Sansone et al., (Sansone et al., 2022)	Retrospective study	585,655 hospitalized individuals, Brazil	February 22, 2020, - April 04, 2021	Place of residence (urban, rural, and peri-urban)	COVID-19 hospitalization, ICU, death	Living in rural areas (OR: 1.22, 95% CI: 1.18–1.26) or peri-urban places (OR: 1.25, 95% CI: 1.11–1.40) was associated with higher COVID-19 mortality.	Low
Shukla et al., (Shukla et al., 2022)	Cross-sectional study	51,425 individuals, Gwalior district of central India	30 March 2020–17 May 2021	Place of residence (urban, rural)	COVID-19 deaths	In urban areas, the CFR was 1.43% during the first wave and 0.80% during the second wave, compared to 0.63% and 0.66% for rural areas.	Moderate
Yemata et al., (Yemata et al., 2022)	Prospective Cohort Study	202 adult COVID-19 patients in the South Gondar zone treatment centers, Northwest Ethiopia	December 2020–April 2021	Residence: urban - rural	COVID-19 severity	No significant difference in severity rate was observed between individuals residing in urban and rural areas. Similarly, there was no significant difference in COVID-19 severity outcomes between patients living in urban and rural areas (CHR: 1.34, 95% CI: 0.86–2.10; AHR: 1.92, 95% CI: 0.86–3.46).	Low
Rostila et al., (Rostila et al., 2021)	Total-Population–Based Cohort Study,	Adults living in Stockholm, Sweden (n = 1,778,670)	January 31, 2020–May 4, 2020	Neighborhood population density grouped into 5 quintiles	COVID-19 mortality	Among migrant groups in Sweden, there was a positive association between higher neighborhood population density (quintiles 3–5) and COVID-19 mortality, even after adjusting for age and gender (Q3: RR: 1.28, 95% CI: 1.02–1.61; Q5: RR: 1.59, 95% CI: 1.24–2.04).	Low
Surendra et al., (Surendra et al., 2022)	Retrospective study	Individual-level data were collected from all cases (n = 842,646), 44 subdistricts in DKI Jakarta	2 March 2020–31 August 2021	Population density	COVID-19 deaths (deceased vs recovered)	Higher subdistrict population density was significantly associated with an increased risk of death. Residents of subdistricts with the highest population density had a higher risk of death compared to those in the lowest density category (OR: 1.34, 95% CI: 1.14–1.58).	Low
Islamoska et al., (Islamoska et al., 2022)	Retrospective study	2232 individuals, Denmark	February–June 2020	Population density based on quartiles into: <83 persons/km^2, 83–310 persons/km^2, ≥310 persons/km^2.	Hospitalization with COVID-19	Lower population density (<83 km^2) and population density between 83 and 310 km^2 were associated with reduced odds of COVID-19 hospitalization (OR: 0.36, 95% CI: 0.32–0.40 and OR: 0.37, 95% CI: 0.33–0.41, respectively).	Low

HR=Hazard Ratio. OR=Odds Ratio. AHR = Average Hazard Ratio. CI=Confidence Interval. ICU=Intensive Care Unit. RR=Relative Risk. IQR=Interquartile Range. ED = emergency department. IRS=Intensive Respiratory Support.

3.3.1. *Ambient air pollution*

A total of 22 non-ecological studies were conducted to investigate the impact of AAP. These studies were conducted in several countries representing the continents of Europe, North America and Asia. Among these studies, eleven focused on long-term exposure, seven examined short-term exposure, and four investigated both short and long-term exposure (Table 1) (Di Ciaula et al., 2022; Mendy et al., 2021a, 2021b; Chen et al., 2021, 2022a, 2022b; Bowe et al., 2021; Elliott et al., 2021; López-Feldman et al., 2021; Marquès et al., 2022b; Pegoraro et al., 2021; Nobile et al., 2022; Sheridan et al., 2022; Bozack et al., 2022;

Table 3
Characteristics of the included non-ecological studies on the associations of meteorological factors with COVID-19 health outcomes.

Author, reference	Study design	Sample size, study area	Time period of study	Urban exposure	COVID-19 outcome(s)	Findings	Risk of Bias
Hachim'et al., (Hachim et al., 2021)	Retrospective cohort study	434 COVID-19 patients, Al Kuwait Hospital, Dubai, UAE	January–June 2020	Temperature, wind speed, cloud cover, precipitation rate, relative humidity, sunshine duration, wind direction dominant	COVID-19 deaths and organ failure	Elevated temperature, increased solar radiation, and lower humidity levels were found to be associated with more severe cases of COVID-19, including critical illness, ICU admission, and higher mortality rates.	Low
Solmaz et al., (Solmaz et al., 2021)	Retrospective observational study	1950 patients hospitalized for COVID-19, Diyarbakır Gazi Yaşargil Hospital, Turkey	March 16 – July 15, 2020	Seasonal temperature	Need for intensive care	Seasonal temperature change did not have a significant impact on the requirement for ICU admission.	Low

ICU=Intensive Care Unit.

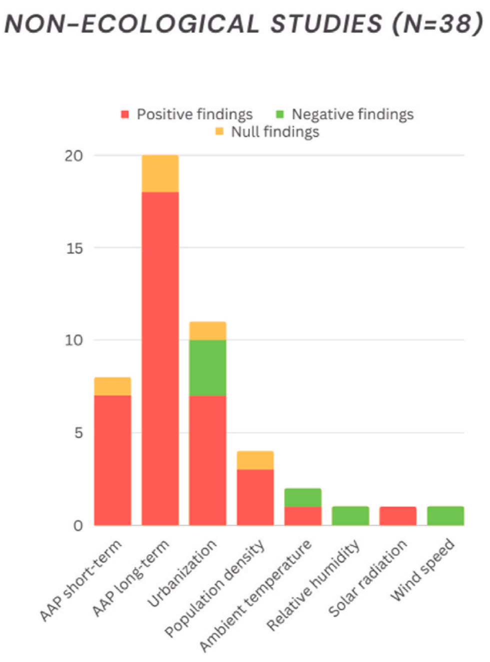


Fig. 2. Bar chart showing the direction of the relationships between the urban exposures studied and various COVID-19 health outcomes in non-ecological studies. If a study showed multiple effects, all directions found are shown. Null findings (orange) indicate that no effect was observed. AAP = ambient air pollution.

Lavigne et al., 2022; Beloconi et al., 2023; Li et al., 2022a; Kim et al., 2022; Hoskovec et al., 2022; Rzymski et al., 2022; English et al., 2022; Soltan et al., 2021). Out of these studies, seventeen specifically investigated the effect of exposure to $PM_{2.5}$ (Mendy et al., 2021a, 2021b; Bowe et al., 2021; Elliott et al., 2021; López-Feldman et al., 2021; Nobile et al., 2022; Sheridan et al., 2022; Chen et al., 2022a, 2022b; Bozack et al., 2022; Lavigne et al., 2022; Beloconi et al., 2023; Li et al., 2022a; Kim et al., 2022; Hoskovec et al., 2022; Rzymski et al., 2022; English et al., 2022), of which fifteen found significant positive associations between either short or long-term exposure and various COVID-19 health outcomes (Mendy et al., 2021a, 2021b; Bowe et al., 2021; López-Feldman et al., 2021; Nobile et al., 2022; Chen et al., 2022a, 2022b; Bozack et al., 2022; Lavigne et al., 2022; Beloconi et al., 2023; Li et al., 2022a; Kim et al., 2022; Hoskovec et al., 2022; Rzymski et al., 2022; English et al., 2022). One of the studies reporting positive findings, however, only found a significant association with $PM_{2.5}$ in participants with any respiratory disease (OR:1.65, 95% CI:1.16–2.35), patients with asthma (OR:1.82, 95% CI:1.13–2.93), and patients with chronic obstructive pulmonary disease (COPD) (OR:1.65, 95% CI:1.05–2.60) (Mendy et al., 2021b). Another study only found significant associations during the first wave of the pandemic, specifically before October 2020 (Beloconi et al., 2023). Studies tended to examine $PM_{2.5}$ in single pollutant models, probably due to data availability constraints. Nevertheless, some studies did utilize multi-pollutant modelling approaches. For example, one study of 74,915 patients from Southern California utilized both single and multipollutant models (Chen et al., 2022b). For a 1-year exposure, the positive associations between $PM_{2.5}$ and all examined COVID-19 health outcomes (hospitalization, IRS, ICU admission, and death) remained after adjusting for NO_2 exposure (NO_2 exposures were significantly positive in single pollutant models but became non-significant in the two-pollutant model). At the 1-month exposure level, after adjusting for NO_2, the positive associations for 1-month $PM_{2.5}$ exposure were significant for COVID-19 deaths, but not for the other outcomes (NO_2 remained significantly positive in both single and multi-pollutant models) (Chen et al., 2022b). Furthermore, three-pollutant models were examined, incorporating $PM_{2.5}$, NO_2, and O_3 exposure. In these models, statistically significant associations were observed between 1-month $PM_{2.5}$ exposure and IRS, as well as ICU admission and death (Chen et al., 2022b). Seven studies assessed the effect of PM_{10} exposure, with four of them focusing on short-term exposure (Di Ciaula et al., 2022; Pegoraro et al., 2021; Li et al., 2022a; Rzymski et al., 2022), and three investigating long-term exposure (Elliott et al., 2021; Marquès et al., 2022b; Sheridan et al., 2022). Four studies among these found significant positive associations of PM_{10} exposure with COVID-19 outcomes (Marquès et al., 2022b; Pegoraro et al., 2021; Li et al., 2022a; Rzymski et al., 2022). However, the three remaining studies did not find a significant association (Di Ciaula et al., 2022; Elliott et al., 2021; Sheridan et al., 2022). Elliott et al. used data from the UK Biobank and examined the effects of nitrogen oxides (NO_x), $PM_{2.5}$, and PM_{10} on COVID-19 outcomes (Elliott et al., 2021). This study found a slight increase in the probability of COVID-19 death associated with a 1-SD (1.90 $\mu g/m^3$) increase in PM_{10} concentrations at the residential address, but this association was not statistically significant in fully adjusted models (OR: 1.08, 95% CI: 0.92–1.26) (Elliott et al., 2021).

Nine non-ecological studies examined associations of NO_2 exposure with COVID-19 outcomes. Out of these, five reported significant positive associations (Di Ciaula et al., 2022; Nobile et al., 2022; Chen et al., 2022b; Lavigne et al., 2022; Beloconi et al., 2023), with one specifically indicating that this association was only present during the first wave of the pandemic (Beloconi et al., 2023). Ciaula et al., reported that the average NO_2 air concentrations in the two weeks before hospital admission due to SARS-CoV-2 infection were a significant predictor for mortality due to altered immune function with an OR of 1.05 (95% CI:

1.00–1.09) (Di Ciaula et al., 2022). Four other studies investigating the effect of NO_2, did not find significant effects in their multivariable analyses (Marquès et al., 2022b; Sheridan et al., 2022; Chen et al., 2022a; Bozack et al., 2022). In terms of O_3 exposure, five studies were conducted, and four of them found significant positive associations with COVID-19 outcomes (Chen et al., 2022a; Lavigne et al., 2022; Kim et al., 2022; Hoskovec et al., 2022). Notably, one study reported a significant positive association of ozone along with increased long-term exposure to $PM_{2.5}$ and temperature on hospitalization and ICU admission compared to being asymptomatic. (Hoskovec et al., 2022). Additionally, one study observed an inverse association between O_3 and COVID-19 hospitalization and IRS, likely due to its negative correlation with NO_2 exposure (Chen et al., 2022b). Chen et al. also conducted another study in Southern California and found significant positive associations between short- and long-term non-freeway near-roadway air pollution exposures (NRAP) and COVID-related IRS, ICU admission, and death, which remained after adjusting for regional $PM_{2.5}$ and NO_2 concentrations (Chen et al., 2021).

Black carbon (BC) exposure was examined in a single study, which did not find a significant association with ICU admission, intubation, or COVID-19 mortality (Bozack et al., 2022). Another study assessed the effect of benzo(a)pyrene (B(a)P), an environmental pollutant resulting from incomplete combustion of organic materials, and found significant positive associations with an increased odds of oxygen saturation below 90%, the need for oxygen therapy and death (Rzymski et al., 2022).

3.3.2. *Urbanization and population density*

The characteristics of the studies examining urbanization and population density are provided in Table 2. Eleven non-ecological studies examined the effect of urbanization, of which seven reported that urban living was associated with a higher risk of COVID-19 hospitalization and mortality (Boudou et al., 2021; Verma et al., 2021; Brainard et al., 2022; Hamdan et al., 2021; Mengist et al., 2022; Sohrabi et al., 2022; Hamilton et al., 2022). Conversely, three studies found that rural living is associated with COVID-19 mortality (Denslow et al., 2022; Sansone et al., 2022; Shukla et al., 2022). One study, conducted in Northwest Ethiopia, did not find a significant difference in COVID-19 outcomes between urban and rural areas (Yemata et al., 2022). Furthermore, four studies examined the effect of population density (Rostila et al., 2021; Brainard et al., 2022; Surendra et al., 2022; Islamoska et al., 2022). One study found no significant effect of population density on COVID-19 deaths (Brainard et al., 2022), while three other studies reported an increased risk of death and hospitalization for residents living in regions with higher population density (Rostila et al., 2021; Surendra et al., 2022; Islamoska et al., 2022).

3.3.3. *Meteorological factors*

Four non-ecological studies investigated associations of meteorological factors with SARS-CoV-2 infection outcomes, yielding varied findings (Li et al., 2022a; Hoskovec et al., 2022; Hachim et al., 2021; Solmaz et al., 2021). In addition, four studies that examined the impact of exposure to AAP adjusted their results to account for meteorological factors such as ambient temperature and humidity, which improved the fit of their models (Lavigne et al., 2022; Beloconi et al., 2023; Kim et al., 2022; English et al., 2022). Table 3 presents the characteristics of the two studies that solely focused on investigating the main effects of meteorological factors. To avoid duplication, the two other studies that also examined AAP exposure are included in Table 1 (Li et al., 2022a; Hoskovec et al., 2022). One cohort study in Dubai including 434 COVID-19 patients found that patients admitted on days with higher ambient temperature, increased solar radiation, and lower relative humidity had a higher risk of severe and critical COVID-19 outcomes, leading to ICU admission or death (Hachim et al., 2021). Another study adjusted their air pollutant models for daily average wind speed and found negative associations of wind speed with more severe COVID-19 outcomes (Li et al., 2022a). Additionally, another study reported an interaction effect: higher ambient temperature combined with elevated levels of $PM_{2.5}$ and O_3 was associated with increased risk of hospitalization and ICU admission, compared to asymptomatic cases (Hoskovec et al., 2022). However, the final study conducted in Turkey found no evidence of a significant association between seasonal temperature changes and the need for ICU admission among COVID-19 patients (Solmaz et al., 2021).

3.3.4. *Meta-analyses*

Beyond summarizing the findings of the non-ecological studies descriptively, three random-effect meta-analyses were performed to assess the effects of $PM_{2.5}$ and NO_2 on COVID-19 outcomes. The corresponding forest plots are shown in Fig. 3. The first meta-analysis, pooling data from eight non-ecological studies, found that individuals exposed to a 1 $\mu g/m^3$ increase in $PM_{2.5}$ are at higher risk for COVID-19 death (pooled OR:1.06(95%CI:1.03–1.09)) with moderate heterogeneity observed ($I^2 = 66.8\%$) (Elliott et al., 2021; López-Feldman et al., 2021; Nobile et al., 2022; Sheridan et al., 2022; Chen et al., 2022a, 2022b; Bozack et al., 2022; English et al., 2022). Similarly, the second meta-analysis, pooling findings from six studies, showed that a 1 $\mu g/m^3$ increase in $PM_{2.5}$ was associated with COVID-19 hospitalization (pooled OR:1.08(95%CI:1.02–1.14)), but with substantial heterogeneity among the studies ($I^2 = 92\%$) (Mendy et al., 2021a, 2021b; Bowe et al., 2021; Sheridan et al., 2022; Chen et al., 2022a, 2022b). The third meta-analysis, pooling results from six non-ecological studies did not find an association between NO_2 and the risk of death from SARS-CoV-2 infection (pooled OR:1.01(95%CI:0.99–1.01)) (Marquès et al., 2022b; Nobile et al., 2022; Sheridan et al., 2022; Chen et al., 2022a, 2022b; Bozack et al., 2022). There was no evidence of heterogeneity with respect to this finding ($I^2 = 0\%$).

3.4. *Urban exposures influencing COVID-19 health outcomes in ecological studies*

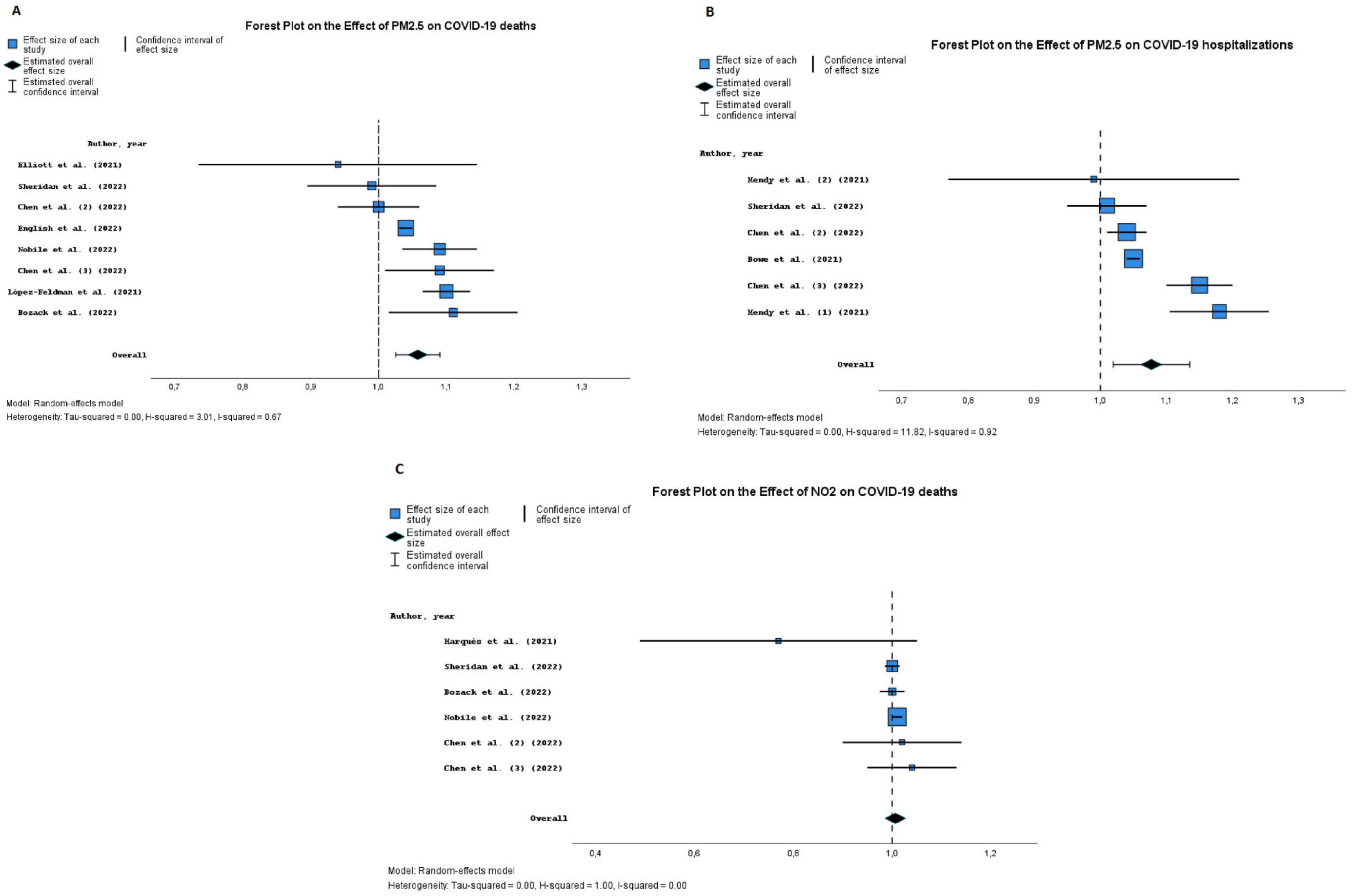
We identified 241 ecological studies examining associations between urban exposome characteristics and various COVID-19 health outcomes. The characteristics and findings of these studies can be found in Table S7, while Fig. 4 provides a visual representation of the direction of the observed associations.

3.4.1. *External exposome-wide association study (ExWAS)*

One ExWAS was conducted in the United States, investigating the potential associations between 337 external exposome factors and COVID-19 mortality (Hu et al., 2021). Among these factors, four urban exposures were identified as particularly influential in their impact on COVID-19 deaths. These included exposure to NO_2, exposure to benzidine, a measure of vacant land indicating the percentage of addresses not occupied in the previous quarter but currently in use, and a measure of the food environment representing the county-level percentage of students eligible for free or reduced-price lunch in 2015 (Hu et al., 2021). These findings were used to highlight the importance of these specific urban-related factors in influencing the risk of COVID-19 mortality.

3.4.2. *Ambient air pollution*

Exposure to AAP was investigated by 107 ecological studies (Aggarwal et al., 2021), (Pozzer et al., 2020; Barnett-Itzhaki et al., 2021; Coccia, 2021; Lembo et al., 2021; Ngepah, 2021; Meo et al., 2021a, 2021b; Naqvi et al., 2021a; Bouba et al., 2021; Fernández et al., 2021; Pana et al., 2021; Kianfar et al., 2022; Stojkoski et al., 2022; Tchicaya et al., 2021; Samillan et al., 2021; Linares et al., 2021a; Beig et al., 2020; Pacheco et al., 2020; Haque et al., 2022; Garcia et al., 2022; Prinz et al., 2022; Semczuk-Kaczmarek et al., 2022; Ghanim, 2022; Aloisi et al., 2022; Liang et al., 2020; Bray et al., 2020; Cazzolla Gatti et al., 2020; Khan, 2022; Zhou et al., 2021; Ilardi et al., 2021a; Sanchez-Piedra et al., 2021; Páez-Osuna et al., 2022; Berg et al., 2021; Liu et al., 2020a;



$PM_{2.5}$=fine Particulate Matter. NO_2=Nitrogen Dioxide.

Fig. 3. Forest plots for the studies showing the effect of A: $PM_{2.5}$ on COVID-19 deaths, B: $PM_{2.5}$ on COVID-19 hospitalizations, C: NO_2 on COVID-19 deaths. All effect estimates, including the pooled effects, are presented per 1 μg/m^3 increment in air pollution exposure.

Pansini et al., 2020; Bianconi et al., 2020; Dettori et al., 2021; Hutter et al., 2020; Dales et al., 2021; Isphording et al., 2021; Ho et al., 2021; Persico et al., 2021; Deguen et al., 2021), (Sciannameo et al., 2022; Mathieu et al., 2022; Li et al., 2022b; Sahu et al., 2022; Anand et al., 2021; Ibarra-Espinosa et al., 2022; Meo et al., 2022; Shao et al., 2022; Norouzi et al., 2022; Mangla et al., 2021; Ismail et al., 2022; Khursheed et al., 2021; Fareed et al., 2020; Kolluru et al., 2022; Zoran et al., 2022c; Barcellos et al., 2021; Singh, 2021; Khorsandi et al., 2021; Meo et al., 2021d; Gupta et al., 2021; Hou et al., 2021; Meo et al., 2020a; Zheng et al., 2021; Chaudhary et al., 2022; Ribeiro et al., 2022; Santos et al., 2022; Karimi et al., 2022; Serio et al., 2022; Beig et al., 2022; Ma et al., 2020; Adhikari et al., 2020; Halos et al., 2022; Yue et al., 2021; Naudé et al., 2022; Loomba et al., 2021; Aykaç et al., 2022; Borna et al., 2022; Adin et al., 2022; Boluwade et al., 2022; Bossak et al., 2022; Chakraborty et al., 2022; Czwojdzińska et al., 2021; Filippini et al., 2021; Koch et al., 2022; Kutralam-Muniasamy et al., 2021; Lee et al., 2022; Leirião et al., 2022; Levi et al., 2021; Linares et al., 2021b; Marian et al., 2022; Marquès et al., 2021; Marwah et al., 2022; Meo et al., 2021e; Miller et al., 2022; Moshammer et al., 2021; Naqvi et al., 2021b; Ogen, 2020; Renard et al., 2022; Rodriguez-Villamizar et al., 2021; Rohrer et al., 2020; Sannigrahi et al., 2022; Sethi et al., 2022; Valdés Salgado et al., 2021; Villeneuve et al., 2022). Among these studies, 87 reported a positive relationship between one or more air pollutants and various COVID-19 health outcomes, although the strength of association varied across the studies. The only global study indicated that long-term exposure to $PM_{2.5}$ contributed to approximately 15%(95%CI:7–33%) of the total COVID-19 mortality worldwide (Pozzer et al., 2020). However, thirteen analyses operating at the country-level reported a combination of positive and null findings. Six of these studies, examining between seventeen and 196 countries, reported a positive correlation with $PM_{2.5}$ and COVID-19 mortality (Barnett-Itzhaki et al., 2021; Coccia, 2021; Lembo et al., 2021; Ngepah, 2021; Meo et al., 2021a; Fernández et al., 2021). On the other hand, five other studies encompassing twelve countries to all countries worldwide, did not find an effect of $PM_{2.5}$ exposure (Naqvi et al., 2021a; Bouba et al., 2021; Pana et al., 2021; Kianfar et al., 2022; Stojkoski et al., 2022). Besides $PM_{2.5}$, positive correlations and/or associations were observed at the country level for medium- and long-term exposure to NO_2, NO_x, SO_2, PM_{10}, CO, O_3, NH_3, non-methane volatile organic compounds (NMVOCs) and greenhouse gas elements (Barnett-Itzhaki et al., 2021; Lembo et al., 2021; Meo et al., 2021a; Naqvi et al., 2021a; Haque et al., 2022). However, for long-term O_3 and CO, negative associations with COVID-19 mortality were found (Haque et al., 2022). The findings of 73 regional-scale studies were more consistent, with 61 studies reporting positive associations between various COVID-19 health outcomes and one or more pollutants, with $PM_{2.5}$, PM_{10} and NO_2 being the most commonly studied pollutants ($n = 58$) (Hu et al., 2021; Naqvi et al., 2021a), (Tchicaya et al., 2021; Samillan et al., 2021; Linares et al., 2021a; Beig et al., 2020; Pacheco et al., 2020), (Garcia et al., 2022; Prinz et al., 2022; Semczuk-Kaczmarek et al., 2022; Ghanim, 2022; Meo et al., 2021b; Aloisi et al., 2022; Liang et al., 2020; Bray et al., 2020; Cazzolla Gatti et al., 2020; Khan, 2022; Zhou et al., 2021; Ilardi et al., 2021a; Sanchez-Piedra et al., 2021;

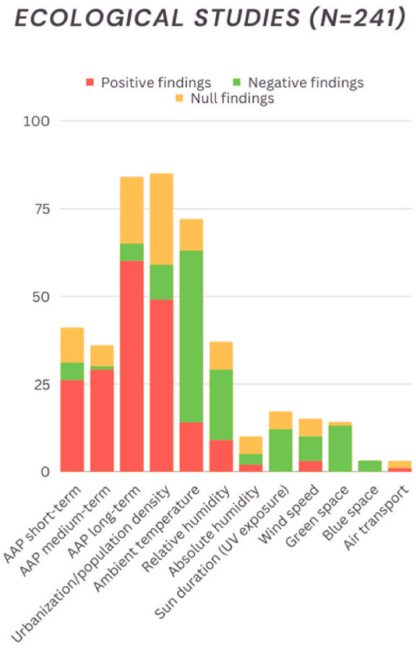


Fig. 4. Bar chart showing the direction of the relationships between the urban exposures studied (n ≥ 3) and various COVID-19 health outcomes in ecological studies. If a study showed multiple effects, all directions found are shown. Null findings (orange) indicate that no effect was observed. AAP = ambient air pollution. UV=Ultraviolet.

Páez-Osuna et al., 2022; Berg et al., 2021; Liu et al., 2020a; Pansini et al., 2020; Bianconi et al., 2020; Dettori et al., 2021; Hutter et al., 2020; Dales et al., 2021; Isphording et al., 2021; Ho et al., 2021; Persico et al., 2021; Deguen et al., 2021; Correa-Agudelo et al., 2021; Coker et al., 2020; Perone, 2021; Sarmadi et al., 2021; Travaglio et al., 2021; Meo et al., 2021c; Cascetta et al., 2021; Naqvi et al., 2022; Zoran et al., 2022a; Amoroso et al., 2022; Mathys et al., 2023; Zoran et al., 2022b; Culqui et al., 2022; Bañuelos Gimeno et al., 2022; Culqui et al., 2022; Adin et al., 2022; Boluwade et al., 2022; Bossak et al., 2022; Chakraborty et al., 2022; Koch et al., 2022; Lee et al., 2022; Leirião et al., 2022; Linares et al., 2021b; Marian et al., 2022; Marwah et al., 2022; Naqvi et al., 2021b; Renard et al., 2022; Sannigrahi et al., 2022; Villeneuve et al., 2022). Additionally, out of the 33 city-level studies, 28 found positive associations for short, medium, and long-term exposure to one or more pollutants (Aggarwal et al., 2021; Barnett-Itzhaki et al., 2021; Linares et al., 2021a; Ibarra-Espinosa et al., 2022; Meo et al., 2020a, 2021d, 2022; Shao et al., 2022; Norouzi et al., 2022; Mangla et al., 2021; Ismail et al., 2022; Khursheed et al., 2021; Fareed et al., 2020; Kolluru et al., 2022; Zoran et al., 2022c; Barcellos et al., 2021; Singh, 2021; Khorsandi et al., 2021; Gupta et al., 2021; Hou et al., 2021; Zheng et al., 2021; Chaudhary et al., 2022; Ribeiro et al., 2022; Santos et al., 2022; Karimi et al., 2022; Serio et al., 2022; Beig et al., 2022; Hadei et al., 2021; Levi et al., 2021). However, some of these studies also reported negative associations with O_3 (Kolluru et al., 2022; Zoran et al., 2022c; Karimi et al., 2022), SO_2 (Shao et al., 2022), $PM_{2.5}$ and PM_{10} (Khursheed et al., 2021; Ma et al., 2020), NO_2 and CO (Khursheed et al., 2021; Karimi et al., 2022) and NH_3 (Khursheed et al., 2021). Three studies conducted at the neighborhood level presented conflicting findings, with limited evidence of a short term effect of AAP (Adhikari et al., 2020), but more positive associations were observed for long term exposure (Aykaç et al., 2022; Borna et al., 2022).

3.4.3. *Urbanization and population density*

The effect of urbanization and population density was investigated in 60 studies, either as a main effect, but mainly accounted for in, for example, AAP models (Ngepah, 2021; Bouba et al., 2021), (Pana et al., 2021; Kianfar et al., 2022; Stojkoski et al., 2022), (Samillan et al., 2021; Bray et al., 2020; Ilardi et al., 2021a; Pansini et al., 2020; Dettori et al., 2021; Deguen et al., 2021; Perone, 2021; Amoroso et al., 2022; Li et al., 2022b; Sahu et al., 2022), (Yue et al., 2021; Naudé et al., 2022; Loomba et al., 2021), (Borna et al., 2022; McLaughlin et al., 2021), (Tzampoglou et al., 2020; Cifuentes-Faura, 2021; Gerli et al., 2020; Hashim et al., 2020; Yang et al., 2021; Asem et al., 2021; Leffler et al., 2020; Siddiqui et al., 2021; Torres-Ibarra et al., 2022; Papadopoulos et al., 2022; Tragaki et al., 2022; Faramarzi et al., 2022; Kumru et al., 2022; Sobczak et al., 2022; Chang et al., 2022a; Khan et al., 2022; Okoli et al., 2022; Klement et al., 2022; Feng, 2022; James et al., 2022; Basellini et al., 2022; Antonio-Villa et al., 2022; Bhadra et al., 2021; Pekmezaris et al., 2021; Fielding-Miller et al., 2020; Lee et al., 2021; Contreras-Manzano et al., 2020; Mizumoto et al., 2020; Rideout et al., 2021; Viezzer et al., 2021; Ramírez-Aldana et al., 2021; Imai et al., 2021; Mejdoubi et al., 2021; Kodera et al., 2020; Simoes et al., 2021; Amate-Fortes et al., 2022; Riley et al., 2022; (Carozzi et al., 2022) (Marquès et al., 2021)). One global-scale study, found that population density correlated weakly with COVID-19 death rates (Tzampoglou et al., 2020). Among the 25 studies conducted at the national level, five reported positive associations, two showed negative associations, and seventeen found no significant effect (Ngepah, 2021; Bouba et al., 2021; Pana et al., 2021; Kianfar et al., 2022; Stojkoski et al., 2022; Naudé et al., 2022; Cifuentes-Faura, 2021; Gerli et al., 2020; Hashim et al., 2020; Yang et al., 2021; Asem et al., 2021; Leffler et al., 2020; Siddiqui et al., 2021; Torres-Ibarra et al., 2022; Papadopoulos et al., 2022; Tragaki et al., 2022; Faramarzi et al., 2022; Kumru et al., 2022; Sobczak et al., 2022; Chang et al., 2022a; Khan et al., 2022; Okoli et al., 2022; Klement et al., 2022; James et al., 2022; Feng et al., 2022). On a regional scale, 55 studies were conducted, and 40 of them reported positive associations, although the degree and direction of the associations varied across different locations (Bray et al., 2020; Ilardi et al., 2021a; Pansini et al., 2020; Sahu et al., 2022; Yue et al., 2021; McLaughlin et al., 2021), (Basellini et al., 2022; Antonio-Villa et al., 2022; Bhadra et al., 2021; Pekmezaris et al., 2021; Fielding-Miller et al., 2020; Lee et al., 2021; Contreras-Manzano et al., 2020; Mizumoto et al., 2020; Rideout et al., 2021; Viezzer et al., 2021; Ramírez-Aldana et al., 2021; Imai et al., 2021; Mejdoubi et al., 2021; Kodera et al., 2020; Simoes et al., 2021; Amate-Fortes et al., 2022; Riley et al., 2022; Fonseca-Rodríguez et al., 2021; Ziyadidegan et al., 2022; Suligowski et al., 2023; Chang et al., 2022b; Frisina Doetter et al., 2022; Itzhak et al., 2022; Li et al., 2022c; Lamichhane et al., 2022; Roviello et al., 2022; Aouissi et al., 2022; Blair et al., 2022; Nasiri et al., 2022; Semati et al., 2022; Nightingale et al., 2021; Haider et al., 2022; Schnake-Mahl et al., 2022; Ilardi et al., 2021b). When examining urbanicity on a regional scale, eight studies found that rural areas had significantly higher mortality rates compared to urban areas (Rifat et al., 2021; Hamidi et al., 2020; Kaufman et al., 2020; Huang et al., 2021; Anzalone et al., 2022; Pascoal et al., 2022; Grome et al., 2022; Iyanda et al., 2022). At the neighborhood level, three studies examined the impact of population density. Two of these studies reported positive associations/correlations (Borna et al., 2022; Feng, 2022), while one study found no significant effect (Jannot et al., 2021).

3.4.4. *Meteorological factors*

Various meteorological factors and their associations with COVID-19 outcomes were investigated in a total of 87 ecological studies (Bouba et al., 2021; Fernández et al., 2021; Pana et al., 2021; Kianfar et al., 2022; Stojkoski et al., 2022; Tchicaya et al., 2021; Samillan et al., 2021; Linares et al., 2021a; Beig et al., 2020; Pacheco et al., 2020; Perone, 2021), (Zoran et al., 2022a, 2022b; Amoroso et al., 2022; Mathys et al., 2023; Culqui et al., 2022; Bañuelos Gimeno et al., 2022; Culqui et al., 2022), (Sciannameo et al., 2022; Shao et al., 2022), (Mangla et al., 2021; Ismail et al., 2022; Khursheed et al., 2021; Fareed et al., 2020; Kolluru et al., 2022; Zoran et al., 2022c; Barcellos et al., 2021; Singh, 2021; Khorsandi et al., 2021), (Ma et al., 2020; Adhikari et al., 2020; Halos et al., 2022; Yue et al., 2021; Naudé et al., 2022; Loomba et al., 2021;

Tzampoglou et al., 2020), (Yang et al., 2021; Asem et al., 2021; Leffler et al., 2020; Siddiqui et al., 2021; Chang et al., 2022a), (Imai et al., 2021; Mejdoubi et al., 2021; Kodera et al., 2020; Simoes et al., 2021; Amate-Fortes et al., 2022; Riley et al., 2022; Malki et al., 2020), (Feng et al., 2022; Iloanusi et al., 2021; Alemu, 2020; Sobral et al., 2020; Meo et al., 2020b; Meo et al., 2020c; Basray et al., 2021; Vahedian et al., 2022; Olinto et al., 2022; Faruk et al., 2022a; Saddik et al., 2022; Mohammadpour et al., 2022; Sabarathinam et al., 2022; Karim et al., 2022; Hamd et al., 2022; Rahman et al., 2021; Thazhathedath Hariharan et al., 2021; Zilberlicht et al., 2021; Hassan et al., 2020; Rehman et al., 2020; Ogaugwu et al., 2020; Li et al., 2020; Cacho et al., 2020; Cherrie et al., 2021; Quilodrán et al., 2021; Thangariyal et al., 2020; Bochenek et al., 2022; Isaia et al., 2021; Mejdoubi et al., 2020; Zhu et al., 2021; Cai et al., 2020; Huang et al., 2020; Dagi et al., 2022; Trajanoska et al., 2022; Song et al., 2022; Liang et al., 2022; Nicolaou et al., 2022; Tapia-Muñoz et al., 2022; Zhang et al., 2022). Among these studies, ambient temperature was examined in 76 studies, with 44 of them reporting a correlation between increasing temperatures and less severe COVID-19 outcomes. Similarly, the effect of relative humidity on COVID-19 outcomes was evaluated in 31 studies, which provided evidence of an inverse relationship (Zoran et al., 2022a, 2022b, 2022c; Amoroso et al., 2022; Mathys et al., 2023; Culqui et al., 2022; Bañuelos Gimeno et al., 2022; Culqui et al., 2022; Mangla et al., 2021; Ismail et al., 2022; Khursheed et al., 2021; Fareed et al., 2020; Kolluru et al., 2022; Barcellos et al., 2021; Ma et al., 2020; Halos et al., 2022; Asem et al., 2021; Simoes et al., 2021; Riley et al., 2022; Malki et al., 2020; Meo et al., 2020b, 2020c; Basray et al., 2021; Vahedian et al., 2022; Olinto et al., 2022; Faruk et al., 2022a; Saddik et al., 2022; Mohammadpour et al., 2022; Sabarathinam et al., 2022; Karim et al., 2022; Hamd et al., 2022). However, positive and null effects were also reported in some studies. Absolute humidity was studied by ten studies, with two reporting positive associations (Culqui et al., 2022; Kodera et al., 2020), three reporting inverse relationships (Mathys et al., 2023; Culqui et al., 2022; Vahedian et al., 2022), and five not finding any significant effect (Shao et al., 2022; Adhikari et al., 2020; Zhu et al., 2021; Cai et al., 2020; Huang et al., 2020). Twelve studies found that higher sunshine duration was associated with less severe COVID-19 outcomes (Zoran et al., 2022a, 2022b, 2022c; Barcellos et al., 2021; Siddiqui et al., 2021; Simoes et al., 2021; Cacho et al., 2020; Cherrie et al., 2021; Quilodrán et al., 2021; Thangariyal et al., 2020; Bochenek et al., 2022; Isaia et al., 2021), while five studies did not find a significant effect (Halos et al., 2022; Naudé et al., 2022; Loomba et al., 2021; Mejdoubi et al., 2020; Huang et al., 2020). Wind speed was investigated in sixteen studies, with three reporting positive associations (Zoran et al., 2022a; Mathys et al., 2023; Faruk et al., 2022a), eight reporting negative associations (Sanchez-Piedra et al., 2021; Zoran et al., 2022b, 2022c; Sciannameo et al., 2022; Faruk et al., 2022a; Saddik et al., 2022; Mohammadpour et al., 2022; Sabarathinam et al., 2022), and five showing weak associations or no effect (Kolluru et al., 2022; Halos et al., 2022; Bochenek et al., 2022; Huang et al., 2020; Dagi et al., 2022). The effect of precipitation was examined in seven studies, with one study reporting a positive association (Sanchez-Piedra et al., 2021), two studies finding negative associations (Mathys et al., 2023; Faruk et al., 2022a), and four studies reporting no significant effect (Kianfar et al., 2022; Loomba et al., 2021; Huang et al., 2020; Dagi et al., 2022). Finally, the findings from six studies examining air pressure, sky clearness, altitude, and dew point were mixed (Mathys et al., 2023; Zoran et al., 2022b, 2022c; Faruk et al., 2022a; Hamd et al., 2022; Nicolaou et al., 2022).

3.4.5. Built environment characteristics

The influence of green space on COVID-19 outcomes was explored in twelve ecological studies conducted at a regional scale (Samillan et al., 2021; Dettori et al., 2021; Falco et al., 2023; Li et al., 2022b; Lee et al., 2021; Viezzer et al., 2021; Suligowski et al., 2023; Roviello et al., 2021, 2022; Russette et al., 2021; Sikarwar et al., 2022; Yang et al., 2022), one study at a national scale (Meo et al., 2021a) and one study at a city scale (Peng et al., 2022). Except for one regional scale study that reported no relationship (Dettori et al., 2021), all other studies reported that green space was protective against COVID-19 severity. Additionally, three studies examined the effect of blue space such as sea exposure on a regional scale, all of them finding protective effects (Cascetta et al., 2021; Suligowski et al., 2023; Roviello et al., 2022). The effect of air transport was investigated in three studies, with one study indicating that counties with or near airports had a higher risk of COVID-19-related death (Correa-Agudelo et al., 2021), while the other two studies did not find a significant effect (Kianfar et al., 2022; Stojkoski et al., 2022). Another study revealed that areas with high residential, commercial, and administrative density had a higher number of COVID-19 patients, whereas areas with a high density of industries had fewer patients (Nasiri et al., 2022). The results of another study show that neighborhoods with more pedestrian-friendly streets, a mix of homes and workplaces, and limited car access tend to have fewer COVID-19 hospitalizations and deaths (Wali et al., 2021). Lastly, noise was examined in one study showing that higher noise levels were associated with COVID-19 hospitalization and ICU admission (Díaz et al., 2021).

4. Discussion

4.1. Summary of results

This systematic review aimed to assess the impact of various urban factors on different health outcomes related to COVID-19, distinguishing between non-ecological and ecological studies. The findings of 38 non-ecological studies revealed that individuals residing in more urbanized areas, regions with higher population density, or those exposed to higher levels of air pollutants, specifically $PM_{2.5}$, are more prone to experiencing more severe COVID-19 outcomes. However, the examination of meteorological factors as a main effect was less extensive ($n = 4$), leading to the inability to establish a clear relationship at the individual level. Furthermore, the analysis of 241 ecological studies indicated that COVID-19 patients living in more urbanized areas, areas with higher population density, elevated levels of air pollutants (especially $PM_{2.5}$, PM_{10}, and NO_2), reduced UV exposure, and limited access to green and blue spaces face an increased risk of developing severe and critical COVID-19. A comparison between the findings of non-ecological and ecological studies demonstrated a general consistency in the overall direction of the relationships for the impact of urbanization/population density and $PM_{2.5}$ exposure. However, due to the considerably smaller number of non-ecological studies available, it is challenging to make a comprehensive comparison for all urban exposures.

4.2. Exploration of findings

The risk of suffering from more severe COVID-19 outcomes is, in part, related to the risk of SARS-CoV-2 transmission. Modeling this transmission relies on several factors, with urban exposures also playing an important role. In densely populated urban areas, close-distance contact is more likely, thereby increasing the risk of viral transmission. In addition, urban environments are characterized by a higher rate of potential sources of infection, such as crowded public transportation and busy streets, both of which can promote rapid spread of the virus (Saadat et al., 2020). These increased interpersonal interactions and urban-specific routes of transmission underscore the importance of also accounting for the effect of urbanization. Besides, airborne transmission of the virus is also possible, and studies indicate that concentrations of ambient air pollutants (AAP), particularly $PM_{2.5}$ and PM_{10}, can affect the stability and infectivity of the virus, potentially increasing the chances of viral transmission (Groulx et al., 2018; Al Huraimel et al., 2020). Meteorological factors also play a role because of their impact on SARS-CoV-2 transmission, as well as their correlation with air pollution concentrations (Faruk et al., 2022b; Guo et al., 2021). However, the impact of urban exposures is complicated due to the implementation of mitigation measures such as social distancing, which have led to subsequent decreases in air pollution, which also varied across countries (Barouki et al., 2021; Venter et al., 2021). Moreover, different SARS-CoV-2 strains were dominant during the pandemic, which also showed marked variation in transmissibility, morbidity and mortality, altering the impact of the studied urban exposures (Tracking, 2023). Furthermore, the administration of COVID-19 vaccinations in the late 2020s has also been considered influential by reducing the risk of severe disease (Li et al., 2021). However, relatively few studies within this systematic review accounted for these factors. The limited number of studies that did consider these features suggested that the effects of urban exposures on COVID-19 outcomes varied between periods of absence and presence of COVID-19 vaccination (Arbel et al., 2022; Song et al., 2022; D'Amico et al., 2022), as well as between the different waves of the pandemic (Beloconi et al., 2023; Shukla et al., 2022; Bañuelos Gimeno et al., 2022; Mathieu et al., 2022; Kolluru et al., 2022; Taylor et al., 2022; Suligowski et al., 2023; Schnake-Mahl et al., 2022). Studies found a stronger effect of urban exposures during the first wave of the pandemic, when public health services were not fully in effect. However, the studies that took COVID-19 vaccination into account found varying effects, indicating that no clear difference could be observed between the periods before and after the rollout of vaccination.

Beyond considering the previously mentioned concerns regarding the investigation of urban exposures on various COVID-19 health outcomes, this review identified several notable effects. One notable finding is the positive association between air pollution, particularly $PM_{2.5}$, and COVID-19 outcomes, as supported by the results of meta-analyses. A potential mechanism underlying this is that exposure to AAP may weaken and disrupt the immune response leading to respiratory problems and lung dysfunction, as well as increased respiratory symptoms, infections and mortality (Jiang et al., 2016). Air pollution has also been shown to impair the host's immune response to invading pathogens in the respiratory tract and by inhibiting the expression of key inflammatory mediators (Marquès et al., 2022a; Adaji et al., 2019). The effects found for ambient temperature and humidity were contradictory, indicating possible non-linear associations, with several studies reporting U-shaped relationships. This observation aligns with previous findings on the effect of these meteorological factors on SARS-CoV-2 transmission (Zhai et al., 2023; Nottmeyer et al., 2022), and is also considered in the effect on influenza virus mortality (Deyle et al., 2016). However, most of the ecological studies included in this review showed an inverse relationship between ambient temperature and humidity and COVID-19 outcomes. This may be attributed to the observation that breathing in colder air allows for increased growth of the SARS-CoV-2 virus in the upper respiratory tract, which is strongly correlated with adverse health outcomes in COVID-19 patients (Liu et al., 2020b; Kang et al., 2021). A smaller number of ecological studies also suggested a protective effect of sunshine duration and exposure to green and blue space. Accordingly, UVA and UVB radiation may be beneficial in reducing the severity of COVID-19 infection through mediators such as vitamin D and nitric oxide (NO) production in the skin (Gorman et al., 2020; Whittemore, 2020). Moreover, exposure to nature can influence various immunological parameters, including increased activity of natural killer (NK) cells, which may modify the risk of developing severe COVID-19 (Andersen et al., 2021). However, it should be noted that there is a negative correlation between green/blue space and other urban exposures such as air pollution, which could potentially explain the observed effects. The vast majority of the included studies do not adequately account for other urban exposures, making it challenging to determine the independent effect of green and blue spaces. One city-level study that considered these factors, found that the effect of residential green space was more prevalent in regions with lower population density and economic levels, with air pollutants, mainly NO_2, mediating part of the relationship (Peng et al., 2022).

4.3. Risk of bias of included studies

The quality of the 38 included non-ecological studies ranged from fair (n = 5), good (n = 30) to excellent (n = 3), indicating an overall moderate to low risk of bias in these studies. However, it is important to note that the conclusions drawn from the 241 ecological studies presented in this systematic review, are limited by the high risk of ecological bias. This bias could arise from potential exposure misclassification due to within-area variation, and individuals moving within an area, as well as outcome misclassification resulting from the use of publicly available aggregated COVID-19 data at the area-level. Moreover, these studies inadequately adjusted their results for individual-level covariates further contributing to the risk of ecological fallacy (Wu et al., 2020). As a result, it is not possible to draw definitive cause-effect conclusions at the individual level based on this type of research. To address the risk of ecological bias in future studies, there is a need for standardized quality assessment tools explicitly designed for this purpose. Efforts should be made to explicitly acknowledge and account for this risk when interpreting the results of ecological studies (Romero Starke et al., 2021). One of the main challenges in understanding the effect of urban exposome factors with regard to both non-ecological and ecological study designs, is the lack of taking into consideration the viral dose exposure. The current analyses have predominantly used the urban exposome as a main effect in their risk model where in practice it is modelling an interaction between SARS-CoV-2 exposure and COVID-19 severity. This interaction is further described and visualised in Fig. S8. Given that the SARS-CoV-2 dose has been variable in time and space, estimates of both ecological and non-ecological studies could be severely biased (Heederik et al., 2020).

4.4. Strengths, limitations and recommendations

This systematic review has taken a unique approach by distinguishing between ecological and non-ecological studies when analyzing the effects of multiple urban environmental features on various COVID-19 health outcomes. To our best knowledge, this is the first review to make such a distinction and investigate the collective impact of the urban exposome on COVID-19 health outcomes. To provide a comprehensive understanding, we included a wide range of urban characteristics, aiming to capture the vulnerability of individuals residing in urban areas. This review also included a wide range of COVID-19 health outcomes, including hospitalization, ICU admission, risk of pneumonia, and mortality. Moreover, we conducted three meta-analyses to pool the results from non-ecological studies focusing on the effect of $PM_{2.5}$ and NO_2 exposure on COVID-19 hospitalization and death. To ensure reliability and reproducibility of the results, three independent reviewers performed screenings and data extraction, enhancing the robustness of our findings. However, there are some limitations to our conducted meta-analyses. The small number of eligible studies prevented us from conducting sensitivity analyses and assessing publication bias. Additionally, considerable heterogeneity was observed among studies in the meta-analysis on the effect of $PM_{2.5}$ and COVID-19 hospitalizations. Another limitation of this review is that some urban exposures, such as meteorological factors and green/blue spaces, were not adequately studied in non-ecological research, making it challenging to compare their findings to ecological studies and draw conclusions at the individual level. Consequently, more non-ecological studies examining associations between multiple correlated urban exposures and diverse COVID-19 health outcomes are needed. Finally, we recommend further investigation into the impact of urban environmental risk factors on the recovery after the acute SARS-CoV-2 infection. Individuals who experienced a more severe infection appear to be at a higher risk of developing long-term symptoms, known as long COVID (Crook et al., 2021). Given the increasing concerns about long COVID as a significant health problem (Venkatesan, 2021), more research using non-ecological study designs that address the aforementioned concerns is essential.

5. Conclusion

The findings of current systematic review and meta-analysis suggest that a variety of urban exposome characteristics significantly influenced the severity of the COVID-19 pandemic by impacting various COVID-19 health outcomes. Urbanization and increased ambient air pollution emerged as major contributors, with exposure to $PM_{2.5}$ having the most prominent effect. Our findings emphasize the need for further research to explore associations between multiple, correlated urban exposures and diverse COVID-19 health outcomes taking into consideration individual health characteristics and incorporate virus dose more accurately into their risk models. Understanding the factors that may increase the risk of death from COVID-19 is crucial so that policy makers and urban planners can design and implement effective policies to protect the increasingly large population residing in urban environments.

Declaration of competing interest

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Data availability

No data was used for the research described in the article.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envres.2023.117351.

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