Association of Short-term Air Pollution Exposure With SARS-CoV-2 Infection Among Young Adults in Sweden

Zhebin Yu, PhD; Tom Bellander, PhD; Anna Bergström, PhD; Joakim Dillner, MD, PhD; Kristina Eneroth, PhD; Magnus Engardt, PhD; Antonios Georgelis, PhD; Inger Kull, PhD; Petter Ljungman, MD, PhD; Göran Pershagen, MD, PhD; Massimo Stafoggia, PhD; Erik Melén, MD, PhD; Olena Gruzieva, MD, PhD; and the BAMSE COVID-19 Study Group

Abstract

IMPORTANTIE Mounting ecological evidence shows an association between short-term air pollution exposure and COVID-19, yet no study has examined this association on an individual level.

OBJECTIVE To estimate the association between short-term exposure to ambient air pollution and SARS-CoV-2 infection among Swedish young adults.

DESIGN, SETTING, AND PARTICIPANTS This time-stratified case-crossover study linked the prospective BAMSE (Children, Allergy Milieu, Stockholm, Epidemiology [in Swedish]) birth cohort to the Swedish national infectious disease registry to identify cases with positive results for SARS-CoV-2 polymerase chain reaction (PCR) testing from May 5, 2020, to March 31, 2021. Case day was defined as the date of the PCR test, whereas the dates with the same day of the week within the same calendar month and year were selected as control days. Data analysis was conducted from September 1 to December 31, 2021.

EXPOSURES Daily air pollutant levels (particulate matter with diameter ≤2.5 μm [PM\textsubscript{2.5}], particulate matter with diameter ≤10 μm [PM\textsubscript{10}], black carbon [BC], and nitrogen oxides [NO\textsubscript{x}]) at residential addresses were estimated using dispersion models with high spatiotemporal resolution.

MAIN OUTCOMES AND MEASURES Confirmed SARS-CoV-2 infection among participants within the BAMSE cohort. Distributed-lag models combined with conditional logistic regression models were used to estimate the association.

RESULTS A total of 425 cases were identified, of whom 229 (53.9%) were women, and the median age was 25.6 (IQR, 24.9-26.3) years. The median exposure level for PM\textsubscript{2.5} was 4.4 [IQR, 2.6-6.8] μg/m\textsuperscript{3} on case days; for PM\textsubscript{10}, 7.7 [IQR, 4.6-11.3] μg/m\textsuperscript{3} on case days; for BC, 0.3 [IQR, 0.2-0.5] μg/m\textsuperscript{3} on case days; and for NO\textsubscript{x}, 8.2 [5.6-14.1] μg/m\textsuperscript{3} on case days. Median exposure levels on control days were 3.8 [IQR, 2.4-5.9] μg/m\textsuperscript{3} for PM\textsubscript{2.5}, 6.6 [IQR, 4.5-10.4] μg/m\textsuperscript{3} for PM\textsubscript{10}, 0.2 [IQR, 0.2-0.4] μg/m\textsuperscript{3} for BC, and 7.7 [IQR, 5.3-12.8] μg/m\textsuperscript{3} for NO\textsubscript{x}. Each IQR increase in short-term exposure to PM\textsubscript{2.5} on lag 2 was associated with a relative increase in positive results of SARS-CoV-2 PCR testing of 6.8% (95% CI, 2.1%-11.8%); exposure to PM\textsubscript{10} on lag 2, 6.9% (95% CI, 2.0%-12.1%); and exposure to BC on lag 1, 5.8% (95% CI, 0.3%-11.6%). These findings were not associated with NO\textsubscript{x}, nor were they modified by sex, smoking, or having asthma, overweight, or self-reported COVID-19 respiratory symptoms.

CONCLUSIONS AND RELEVANCE The findings of this case-crossover study of Swedish young adults suggest that short-term exposure to particulate matter and BC was associated with increased...
Abstract (continued)

risk of positive PRC test results for SARS-CoV-2, supporting the broad public health benefits of reducing ambient air pollution levels.

---


Introduction

As of February 2022, the COVID-19 pandemic has resulted in more than 410 million confirmed cases and has caused more than 5.8 million deaths globally.\(^1\) Concerns have been raised about whether ambient air pollution could increase the risk of infection with SARS-CoV-2 as well as the severity of disease after infection because air pollution has long been recognized as a potential contributor to respiratory infectious diseases such as influenza,\(^2\) severe acute respiratory syndrome,\(^3\) and dengue.\(^4\)

Two key pathways for the plausible mechanism between air pollution and COVID-19–related outcomes have been summarized\(^5\): (1) modifying host susceptibility to infection and/or disease severity and (2) elevating the risk of comorbidities. The former pathway can be mediated through upregulation of proteins critical to viral entry\(^6,7\) and by immune system suppression due to oxidative stress,\(^8\) epithelial damage,\(^9\) and pulmonary inflammation.\(^10\) Complementary to the experimental evidence, emerging ecological studies linking short-term (daily variation) exposure to air pollution and aggregated population-level data suggest a relevant role of air pollution in SARS-CoV-2 infection\(^11,12\); however, previous short-term studies lack individual-level exposure data, termed ecological fallacy.\(^13,14\) Statistically, the correlation tends to be overestimated when the association is assessed at the group level rather than at the individual level.\(^15\) A recent study\(^16\) indicated that ecological analyses are prone to showing spurious associations between air pollution and COVID-19. Furthermore, little is known regarding the association between short-term exposure to air pollution and COVID-19 among young adults.\(^12\) No single study or subgroup analysis has been reported among this age group yet, although young adults have been considered the major spreader of the virus since autumn 2020.\(^17\)

The purpose of this study was to examine the association between short-term exposure to air pollution estimated at the individual residence level and the risk of SARS-CoV-2 infection among Swedish young adults. In addition, we assessed whether this association differs by sex, having overweight, having asthma, smoking status, season, and self-reported COVID-19–related respiratory symptoms.

Method

Study Population and Outcome

This case-crossover study was based on the BAMSE (Children, Allergy Milieu, Stockholm, Epidemiology [in Swedish]) population-based birth cohort including 4089 newborns in 1994 to 1996. Details on study design, recruitment procedures, and data collection have been provided elsewhere.\(^18\) Follow-ups were conducted at the ages of 1, 2, 4, 8, 12, 16, and 24 years. From 2016 to 2019, the 24-year follow-up\(^19\) was conducted with a total of 2270 participants both attending the clinical examination and questionnaire survey. Starting August 1, 2020, these participants were further invited to a new COVID-19 follow-up,\(^18,20\) which includes a web questionnaire from August to November 2020 (phase 1), a clinical examination and a new web questionnaire from October 2020 to June 2021 (phase 2), and an ongoing web questionnaire (phase 3). In the present study, cases with confirmed positive results for SARS-CoV-2 polymerase chain reaction (PCR) testing (for the presence of the virus’s genetic material or its fragments to detect active infection) to March 31, 2021, within the BAMSE cohort were identified through data linkage of unique personal identifier codes to the...
Air Pollution Exposure Assessment

Daily ambient air pollutant levels (particulate matter with diameter ≤10 μm [PM_{10}]; particulate matter with diameter ≤2.5 μm [PM_{2.5}]; black carbon [BC]; and nitrogen oxides [NOx]) at the individual residential address were calculated using a Gaussian air quality dispersion model and a wind model, both part of the Airviro air quality management system, described elsewhere. Briefly, an emission inventory including local emissions from road traffic (exhaust and nonexhaust), residential wood combustion, energy production, industrial processes, and other sources (eg, off-road machinery and agriculture) in Stockholm and Uppsala counties was used as input to the dispersion modeling. In this region, road traffic is the dominant source of air pollutants. Road traffic exhaust emissions were described with emission factors for different vehicle and road types according to the European emission model HBEFA (Handbook Emission Factors for Road Transport), version 4.1. Emissions of wear particles were calculated using the NORTTRIP model, which accounts for the number of vehicles with studded winter tires, sanding and salting of the road surface, and precipitation. In Stockholm during the late winter and in connection with dry road surfaces, the contribution from studded tire wear can be 80% to 90% of the total PM_{10} levels. Meteorological data for the wind model were taken from a 50-mm mast in Högdalen in southern Stockholm and a 24-m mast outside Uppsala. The geographical distributions of air pollution levels were calculated with a Gaussian model at 2 m above open ground on a fixed grid of 250 × 250 m. In addition, a street canyon contribution was added for addresses in street segments with more than 3000 vehicles per day and multistory houses on one or both sides using the OSPM (operational street pollution model) street canyon model. To ensure that the modeled concentrations also include air pollution transported into the modeling domain from sources outside the Stockholm-Uppsala region, we added the daily mean concentrations of the respective species collected at strategically located rural monitoring sites outside Stockholm and Uppsala. Comparison of the calculated levels with measurements of daily mean values at a traffic monitoring site and 2 urban background sites (1 for BC resulted in R^2 values of 0.90 for PM_{10}, 0.97 for PM_{2.5}, 0.90 for BC, and 0.91 for NOx. We subsequently assigned the daily air pollution exposure preceding the case and control dates as long as 7 days (lag 0 to lag 7) to the cases as the main exposure.

Covariates

Demographic and COVID-19–related characteristics were derived from the questionnaire data of the BAMSE 24-year follow-up and the BAMSE COVID-19 follow-up. Demographic information including age, sex, educational level (university or elementary and/or high school), occupation (student, employed, or other), current smoking (yes or no), body mass index category (having overweight or not [calculated as weight in kilograms divided by height in meters squared], where overweight was defined as ≥25) were derived from the BAMSE 24-year follow-up (before the pandemic). Asthma is defined based on at least 2 of the 3 following criteria: (1) symptoms of wheezing in the last 12 months before the date of questionnaire follow-up; (2) ever having a physician’s diagnosis of asthma; and (3) asthma medicine used occasionally or regularly in the last 12 months. This definition has been developed by a panel of experts within the Mechanisms of the Development of Allergy consortium. In the present study, individuals fulfilling the asthma definition at any follow-up to 24 years were classified as having asthma.
Statistical Analysis

Data were analyzed from September 1 to December 31, 2021. We used a case-crossover study design widely used for analyzing short-term exposures for acute events, where each case serves as their own control at different periods, hence controlling for time-invariant (or slowly varying over time) individual confounding factors. We adopted the time-stratified strategy for control selection in which, for each case, 3 to 4 control days were selected as the same day of the week within the same calendar month and year as the case day (the day of the PCR test for each individual with SARS-CoV-2 infection). We fitted conditional logistic regression models to estimate the association between air pollution and the risk of SARS-CoV-2 infection. Air pollution exposure was modeled using linear terms in the main analysis. We also applied natural splines to investigate the exposure-response shapes. To estimate lagged associations, we applied distributed-lag models from lag 0 (day of the PCR test or control day) to lag 7 (7 days before PCR test or control) and imposed a quadratic polynomial constraint using the formula $\log[E(Y)] = \text{Covariate} + \lambda \text{Stratum} + \eta_0 W_0 + \ldots + \eta_d W_d$, where stratum is the time stratum in the time-stratified case-crossover design; $W_d$ was defined as weighted sums of the air pollution exposure variable and its lags, with $W_d = Z_1 + 2^d Z_2 + \ldots + q^d Z_q$ and $W_0 = Z_0 + Z_1 + \ldots + Z_q$, and the coefficient of $W_s$ will be the parameters of the polynomial distributed lags.

Separate single-pollutant models were established for PM$_{2.5}$, PM$_{10}$, BC, and NOx. We also repeated the analysis using cumulative air pollution exposures. Meteorological factors such as temperature and humidity were not adjusted because they were used as in-data in the daily air pollution modeling. Further, we examined interaction by sex, having overweight, asthma, smoking status, season, and self-reported COVID-19-related respiratory symptoms by adding exposure-modifier interaction terms into the model. In sensitivity analysis, we increased the maximum lag to 14 days. Relative risks (RRs) with corresponding 95% CIs were presented for an IQR increase in air pollution concentrations. All analyses were performed using R software, version 4.0.5 (R Foundation for Statistical Computing), with 2-sided $P < .05$ indicating statistical significance.

Results

A total of 425 participants with positive SARS-CoV-2 PCR test results were identified within the BAMSE cohort from May 5, 2020, to March 31, 2021. The descriptive statistics of the background characteristics of included participants are presented in Table 1. The median age was 25.6 (IQR, 24.9-26.3) years; 229 (53.9%) were women and 196 (46.1%) were men. Comparison between the included samples and the BAMSE original cohort as well as the 24-year follow-up are presented in eTable 1 in Supplement 1.

The distribution of daily air pollution exposure is provided in Table 2, with a slightly higher median concentrations on the case days compared with those on control days (for PM$_{2.5}$, 4.4 [IQR, 2.6-6.8] μg/m$^3$ vs 3.8 [IQR, 2.4-5.9] μg/m$^3$; for PM$_{10}$, 7.7 [IQR, 4.6-11.3] μg/m$^3$ vs 6.6 [IQR, 4.5-10.4] μg/m$^3$; for BC, 0.3 [IQR, 0.2-0.5] μg/m$^3$ vs 0.2 [IQR, 0.2-0.4] μg/m$^3$; and for NOx, 8.2 [5.6-14.1] μg/m$^3$ vs 7.7 [IQR, 5.3-12.8] μg/m$^3$). Temporal variations of air pollution as well as the temperature during the study period are shown in eFigure 1 in Supplement 1. Concurrent estimates of PM$_{2.5}$, PM$_{10}$, and BC were highly correlated with each other (Spearman correlation index, 0.8-0.9) and moderately correlated with NOx (Spearman correlation index, 0.2-0.3) (eFigure 2 in Supplement 1).

Figure 1 shows the lag-specific associations between SARS-CoV-2 infection and short-term exposure to air pollution. We observed associations at lag 2 for PM$_{10}$ and PM$_{2.5}$ (RR, 1.07 [95% CI, 1.02-1.12] for both) and at lag 1 for BC (RR, 1.06 [95% CI, 1.00-1.12]). The risk of having an infection increased by 6.9% (95% CI, 2.0%-12.1%) per IQR increase in PM$_{10}$ exposure, by 6.8% (95% CI, 2.1%-11.8%) per IQR increase in PM$_{2.5}$ exposure, and by 5.8% (95% CI, 0.3%-11.6%) per IQR increase in BC exposure (eTable 2 in Supplement 1 gives numeric results). We did not observe associations for NOx (RR, 1.05 [95% CI, 0.97-1.12]) per IQR increase on lag 1. Using cumulative exposure generated a similar lag response but stronger effect size and wider 95% CIs (eTable 2 in Supplement 1). Extending the
maximum lag to 14 days did not alter the results (eTable 3 in Supplement 1). No significant effect size modification was found in subgroup analyses (eFigures 3-14 in Supplement 1). Spline regression shows that increasing air pollution exposure was associated with increased risk of SARS-CoV-2 infection, with a steeper curve at lower levels of PM$_{2.5}$, PM$_{10}$, and BC. For NOx, the increasing trend was less informative owing to a small number of observations at high NOx exposure levels (Figure 2).

Table 1. Characteristics of Participants With Positive Results of Polymerase Chain Reaction Testing for SARS-CoV-2

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Participant data (N = 425)$^a$</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex</strong></td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>229/425 (53.9)</td>
</tr>
<tr>
<td>Men</td>
<td>196/425 (46.1)</td>
</tr>
<tr>
<td><strong>Age, median (IQR), y</strong></td>
<td>25.6 (24.9-26.3)</td>
</tr>
<tr>
<td><strong>Educational level attained</strong></td>
<td></td>
</tr>
<tr>
<td>University</td>
<td>115/345 (33.3)</td>
</tr>
<tr>
<td>Elementary or high school</td>
<td>230/345 (66.7)</td>
</tr>
<tr>
<td><strong>Occupation</strong></td>
<td></td>
</tr>
<tr>
<td>Student</td>
<td>164/345 (47.5)</td>
</tr>
<tr>
<td>Employed</td>
<td>154/345 (44.6)</td>
</tr>
<tr>
<td>Other</td>
<td>27/345 (7.8)</td>
</tr>
<tr>
<td><strong>Current smoking</strong></td>
<td>79/345 (22.9)</td>
</tr>
<tr>
<td>Having overweight</td>
<td>61/278 (21.9)</td>
</tr>
<tr>
<td>Having asthma</td>
<td>126/408 (30.9)</td>
</tr>
<tr>
<td><strong>COVID-19–related characteristic</strong></td>
<td></td>
</tr>
<tr>
<td>Any symptoms (any of the below)</td>
<td>107/200 (53.5)</td>
</tr>
<tr>
<td>Fever</td>
<td>76/144 (52.8)</td>
</tr>
<tr>
<td>Cough</td>
<td>81/145 (55.9)</td>
</tr>
<tr>
<td>Sore throat</td>
<td>78/144 (54.2)</td>
</tr>
<tr>
<td>Loss of taste or smell</td>
<td>70/146 (47.9)</td>
</tr>
<tr>
<td>Runny nose</td>
<td>115/146 (78.8)</td>
</tr>
<tr>
<td>Nasal congestion</td>
<td>96/146 (65.7)</td>
</tr>
<tr>
<td>Breathing difficulties</td>
<td>37/145 (25.5)</td>
</tr>
<tr>
<td>COVID-19 cases in household</td>
<td>81/142 (57.0)</td>
</tr>
<tr>
<td>Regularly meeting people during pandemic</td>
<td>147/200 (73.5)</td>
</tr>
<tr>
<td>Use of public transportation during pandemic</td>
<td>62/200 (31.0)</td>
</tr>
</tbody>
</table>

$^a$ Unless otherwise indicated, data are expressed as number/total number (%). The total number is smaller for some variables owing to missing data.

Table 2. Distribution of Daily Air Pollution Exposure Levels on Case Days and Control Days

<table>
<thead>
<tr>
<th>Exposure</th>
<th>Mean (range), μg/m$^3$</th>
<th>Median (IQR [difference]), μg/m$^3$</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Case days</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PM$_{10}$</td>
<td>8.8 (1.1-53.7)</td>
<td>7.7 (4.6-11.3) [6.7]</td>
</tr>
<tr>
<td>PM$_{2.5}$</td>
<td>5.0 (0.8-23.8)</td>
<td>4.4 (2.6-6.8) [4.2]</td>
</tr>
<tr>
<td>BC</td>
<td>0.3 (0.1-1.5)</td>
<td>0.3 (0.2-0.5) [0.3]</td>
</tr>
<tr>
<td>NOx</td>
<td>11.5 (1.5-65.6)</td>
<td>8.2 (5.6-14.1) [8.5]</td>
</tr>
<tr>
<td><strong>Control days</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PM$_{10}$</td>
<td>8.4 (1.3-54.6)</td>
<td>6.6 (4.5-10.4) [5.9]</td>
</tr>
<tr>
<td>PM$_{2.5}$</td>
<td>4.6 (0.7-26.1)</td>
<td>3.8 (2.4-5.9) [3.5]</td>
</tr>
<tr>
<td>BC</td>
<td>0.3 (0.03-1.5)</td>
<td>0.2 (0.2-0.4) [0.2]</td>
</tr>
<tr>
<td>NOx</td>
<td>11.0 (1.4-98.7)</td>
<td>7.7 (5.3-12.8) [7.5]</td>
</tr>
</tbody>
</table>

Abbreviations: BC, black carbon; NOx, nitrogen oxides; PM$_{2.5}$, particulate matter with diameter ≤2.5 μm; PM$_{10}$, particulate matter with diameter ≤10 μm.
Discussion

To our knowledge, this is the first report of individual-level, short-term exposure to air pollution associated with SARS-CoV-2 infection among young adults. Our case-crossover analysis based on data from a population-based cohort found an association between daily PM$_{2.5}$, PM$_{10}$, and BC exposure and a positive PCR test result (i.e., having an infection). For each IQR increase in PM$_{2.5}$, PM$_{10}$, and BC daily concentrations, the risk increased significantly by approximately 6% to 7%. No significant interaction was found, suggesting a general association of acute air pollution exposure with SARS-CoV-2 infection.

Our results are consistent with those of previous ecological studies in several countries and regions indicating that areas with poorer air quality are more likely to have more infections, although the effect sizes and lag-time window of air pollution are heterogeneous between studies. A recent meta-analysis including 35 observational studies found that the COVID-19 incidence was associated with short-term exposure to PM$_{2.5}$ (RR, 1.003 [95% CI, 1.002-1.004] per 1-μg/m$^3$ increase) and PM$_{10}$ (RR, 1.005 [95% CI, 1.003-1.008] per 1-μg/m$^3$ increase), which is somewhat smaller than the effect size observed in the present study, although the differences in study design, target population, exposure distribution, and statistical methods preclude a direct comparison with our findings. Typically, previous ecological studies used a time-series study design and generalized additive model to quantify the association, which may be limited by the autocorrelation of air pollution concentrations over time and group- and population-level exposure. By using an

Figure 1. Lag-Specific Relative Risks (RRs) for SARS-CoV-2 Infection Associated With per-IQR Increase in Air Pollution Exposure

A. Particulate matter ≤2.5 μm  
B. Particulate matter ≤10 μm  
C. Black carbon  
D. Nitrogen oxides

A lag of 0 is the day of sampling for polymerase chain reaction testing (case days) and the days 7, 14, 21, and 28 days apart (control days), whereas a lag of 1 is the previous day and so forth. Curved line indicates RR; shaded areas, 95% CIs.
individual-level case-crossover design and distributed-lag model, our study overcomes these limitations and shows an acute association of air pollution with SARS-CoV-2 infection. Moreover, our data add to the body of evidence that the association between air pollution and SARS-CoV-2 infection also exists in young adults because no previous short-term studies focused on this subpopulation or reported interaction by age.

In this study, we observed a shorter lag-response association between air pollution and SARS-CoV-2 infection (the association of PM$_{2.5}$ and PM$_{10}$ exposure peaks on lag day 2, and BC exposure peaks on lag day 1) because the median incubation period was approximately 5 days. In addition, recent literature suggests that transmission of SARS-CoV-2 is more likely to be related to indoor settings rather than the outdoor environment. In Wuhan, China, a study found that only 2 of 7324 COVID-19 cases could be linked to transmission in an outdoor environment. In Ireland, only 262 of 232164 cases were linked to transmission in outdoor environment reported by the Health Protection Surveillance Centre. In Italy, a study found that the viral particle concentrations were very low in ambient air samples. Taken together, we speculate that increased levels of short-term air pollution play a role in manifesting the disease (symptoms) for those who have been infected with the virus.

Figure 2. Exposure Response Curves Using Natural Splines With 3 Degrees of Freedom for the Association of Short-term Air Pollution Exposure and SARS-CoV-2 Infection

A lag of 0 is the day of sampling for polymerase chain reaction testing (case days) and the days 7, 14, 21, and 28 days apart (control days), whereas a lag of 1 is the previous day and so forth. The exposure time window for air pollutants was lag 3 for particulate matter with diameter of 2.5 μm or less (PM$_{2.5}$) and particulate matter with diameter of 10 μm or less (PM$_{10}$), lag 1 for black carbon (BC), and lag 0 for nitrogen oxides (NOx). Curved line indicates RR; shaded areas, 95% CIs.
rather than contributing to the transmission of the virus. Short-term exposure to air pollution can affect airway inflammation and oxidative stress, whereas absorbed air pollutants may cause deep lung irritation and immunomodulation of the host response to infection, possibly worsening the severity of existing infection. Previously, Kogevinas et al also found that long-term exposure to air pollution was not associated with SARS-CoV-2 infection (measured by antibody levels in blood samples) per se but was associated with severity after infection (based on hospitalizations and self-reported symptoms) in a Spanish cohort. More mechanistic studies are needed to examine this hypothesis.

We did not observe any interaction of the observed association between air pollution and SARS-CoV-2 infection by sex, smoking, or having overweight, asthma, or COVID-19–related respiratory symptoms. This outcome could be explained in part by the general effects of ambient air pollution. However, the present outcome based on registry data was influenced by test-seeking behaviors, whereas a large proportion of young adults were asymptomatic or with mild symptoms after infection, and therefore the included participants with infection were not representative of the general young adult population. Outcome assessment that can capture all individuals with current or past infection (such as measurement of antibody levels) is needed to investigate the potential effect size modifier in the future study.

Strengths and Limitations
The main strengths of our study include the time-stratified case-crossover design that controlled for time-invariant confounding factors (eg, population density, lifestyle factors), ascertainment of cases based on PCR testing results from the national register of infectious diseases, application of a distributed-lag model that assesses the acute and delayed effect size of exposure, use of high-resolution spatiotemporal air pollution modeling to estimate exposure on an individual level, and ability to perform subgroup analysis based on selected characteristics. Potential limitations include exposure misclassification given that we estimated exposure to outdoor air pollution, whereas information on microclimatic differences in exposure or time-activity patterns (eg, time spent in traffic and indoors) was not available. In addition, we investigated predisposition factors in a relatively small group of participants with only mild to moderate disease, which limited the statistical power. Owing to the high correlations between air pollutants, we did not test the 2-pollutant model to assess the independence of each pollutant. We were also unable to exclude the existence of residual time-varying confounding factors. Further individual-level studies with a larger sample size, preferably from different geographical regions, are needed to verify the association between short-term air pollution and SARS-CoV-2 infection.

Conclusions
The findings of this case-crossover study of Swedish young adults with air pollution exposure and SARS-CoV-2 infection suggest that residential short-term exposure to air pollution was associated with increased risk of having positive PCR test results for SARS-CoV-2 infection. These findings support the broad public health benefits of reducing ambient air pollution levels.
Author Affiliations: Institute of Environmental Medicine, Karolinska Institutet, Stockholm, Sweden (Yu, Bellander, Bergström, Georgelis, Ljungman, Pershagen, Gruzieva); Centre for Occupational and Environmental Medicine, Region Stockholm, Stockholm, Sweden (Bellander, Bergström, Georgelis, Pershagen, Gruzieva); Medical Diagnostics Karolinska, Karolinska University Hospital, Stockholm, Sweden (Dillner); SLB-analys, Environment and Health Administration, Stockholm, Sweden (Eneroth, Engardt); Department of Clinical Sciences and Education, Karolinska Institutet, Södersjukhuset, Stockholm, Sweden (Kull, Melén); Department of Pediatrics, Sachs Children’s Hospital, Stockholm, Sweden (Kull, Melén); Department of Cardiology, Danderyd Hospital, Stockholm, Sweden (Ljungman); Department of Epidemiology, Lazio Regional Health Service, Rome, Italy (Stafoggia).

Author Contributions: Drs Yu and Gruzieva had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Drs Melén and Gruzieva contributed equally to the study.

Concept and design: Yu, Georgelis, Ljungman, Stafoggia, Melén, Gruzieva.

Acquisition, analysis, or interpretation of data: Yu, Bellander, Bergström, Dillner, Eneroth, Engardt, Kull, Pershagen, Melén, Gruzieva.

Drafting of the manuscript: Yu, Eneroth, Gruzieva.

Critical revision of the manuscript for important intellectual content: All authors.

Statistical analysis: Yu, Bellander, Eneroth.

Obtained funding: Bergström, Georgelis, Melén, Gruzieva.

Administrative, technical, or material support: Bergström, Kull, Ljungman, Melén.

Supervision: Melén, Gruzieva.

Air quality modeling: Engardt.

Conflict of Interest Disclosures: Dr Georgelis reported receiving personal fees from Region Stockholm during the conduct of the study and outside the submitted work. Dr Gruzieva reported receiving grants from the Swedish Research Council for Health, Working Life and Welfare Funding for generation of air pollution data and to cover salary during the conduct of the study. No other disclosures were reported.

Funding/Support: This study was supported by grant FORTE 2017-01146 from the Swedish Research Council for Health, Working Life and Welfare (Dr Gruzieva); BAMSE (Children, Allergy Milieu, Stockholm, Epidemiology [in Swedish]) is supported by the Swedish Research Council, the Swedish Heart-Lung Foundation, and Region Stockholm (Medical Training and Research Agreement and Centre for Occupational and Environmental Medicine).

Role of the Funder/Sponsor: The funders had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Group Information: A complete list of the BAMSE COVID-19 Study Group nonauthor collaborators appears in Supplement 2.

Additional Contributions: Beatrice Säll, MS, Christer Johansson, PhD, and Jenny Lindvall, PhD, SLB-analys, Environment and Health Administration, Stockholm, Sweden, contributed to the completion of air quality modeling, for which they did not receive any compensation.

REFERENCES


**SUPPLEMENT 1.**

eTable 1. Characteristics of BAMSE Subjects Identified as SARS-CoV-2 Infection Cases From SmiNet, Participants of COVID-19 Follow-up, and 24-Year Follow-up

eTable 2. Lag-Specific Relative Risks for SARS-CoV-2 Infection Associated With per-IQR Increase in Short-term Air Pollution Exposure Using Single-Day Lag and Cumulative Lag

eTable 3. Lag-Specific Relative Risks for SARS-CoV-2 Infection Associated With per-IQR Increase in Short-term Air Pollution Exposure From Lag 0 to Lag 14

eFigure 1. Daily Variation of Modelled Air Pollutants and Observed Temperature at the SITE of the Urban Background Station in Central Stockholm Torkel Knutssonsgatan During the Study Period

eFigure 2. Correlation (Spearman) Matrix Between Air Pollutants and Temperature in Different Time Windows

eFigure 3. Lag-Specific Relative Risks for SARS-CoV-2 Infection Associated With per-IQR Increase in Short-term Air Pollution Exposure Stratified by Sex

eFigure 4. Lag-Specific Relative Risks for SARS-CoV-2 Infection Associated With per-IQR Increase in Short-term Air Pollution Exposure Stratified by Asthma

eFigure 5. Lag-Specific Relative Risks for SARS-CoV-2 Infection Associated With per-IQR Increase in Short-term Air Pollution Exposure Stratified by Smoking Status

eFigure 6. Lag-Specific Relative Risks for SARS-CoV-2 Infection Associated With per-IQR Increase in Short-term Air Pollution Exposure Stratified by Having Overweight
eFigure 7. Lag-Specific Relative Risks for SARS-CoV-2 Infection Associated With per-IQR Increase in Short-term Air Pollution Exposure Stratified by Season

eFigure 8. Lag-Specific Relative Risks for SARS-CoV-2 Infection Associated With per-IQR Increase in Short-term Air Pollution Exposure Stratified by Self-reported Fever

eFigure 9. Lag-Specific Relative Risks for SARS-CoV-2 Infection Associated With per-IQR Increase in Short-term Air Pollution Exposure Stratified by Self-reported Cough

eFigure 10. Lag-Specific Relative Risks for SARS-CoV-2 Infection Associated With per-IQR Increase in Short-term Air Pollution Exposure Stratified by Self-reported Sore Throat

eFigure 11. Lag-Specific Relative Risks for SARS-CoV-2 Infection Associated With per-IQR Increase in Short-term Air Pollution Exposure Stratified by Self-reported Sense of Taste and Smell

eFigure 12. Lag-Specific Relative Risks for SARS-CoV-2 Infection Associated With per-IQR Increase in Short-term Air Pollution Exposure Stratified by Self-reported Nasal Congestion

eFigure 13. Lag-Specific Relative Risks for SARS-CoV-2 Infection Associated With per-IQR Increase in Short-term Air Pollution Exposure Stratified by Self-reported Sniffle

eFigure 14. Lag-Specific Relative Risks for SARS-CoV-2 Infection Associated With per-IQR Increase in Short-term Air Pollution Exposure Stratified by Self-reported Breathing Difficulty

SUPPLEMENT 2.
Nonauthor Collaborators