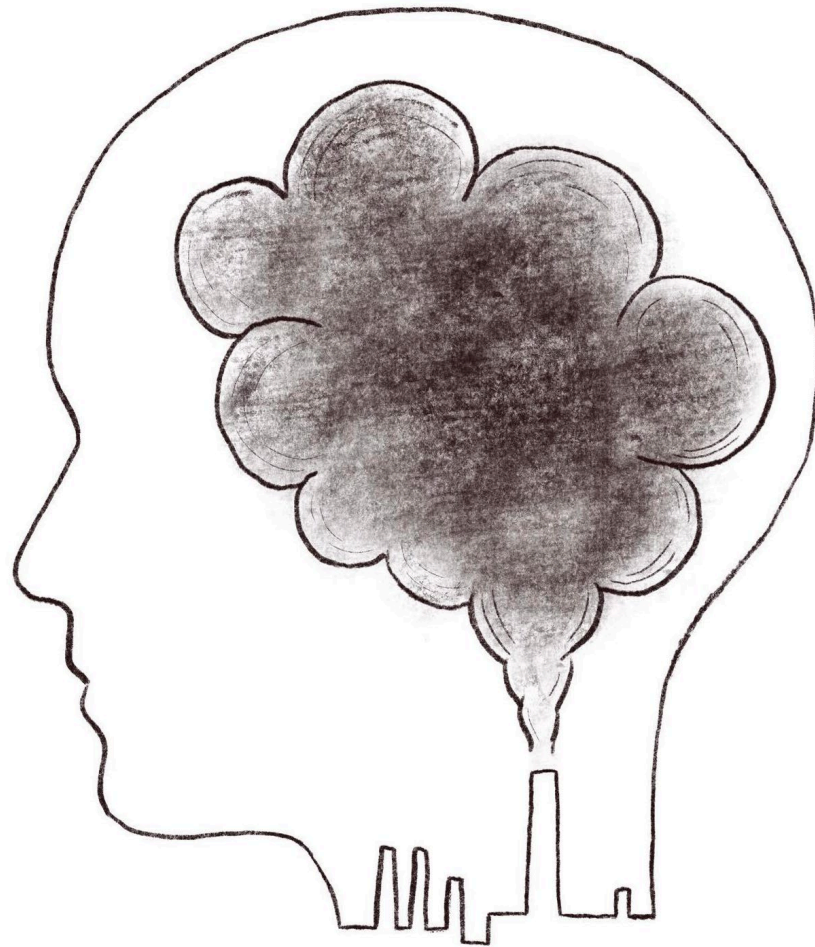




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Associations between high concentrations of air pollution and psychiatric emergency department visits during the COVID-19 pandemic: a register-based study

JENNY OLSSON
DEGREE PROJECT IN MEDICINE



THE SAHLGRENKA ACADEMY

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Degree Project in Medicine

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| Degree project: | 30 credits |
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Table of contents

| | |
|--------------------------------------------------------------------|-----------|
| Abbreviations | 4 |
| Abstract | 5 |
| Introduction | 7 |
| Acute psychiatry..... | 7 |
| Acute psychiatric care in Sweden | 8 |
| External factors affecting mental health | 8 |
| Air pollution and mental health | 8 |
| COVID-19 and mental health | 11 |
| Aim | 14 |
| Material and Methods | 15 |
| Study design..... | 15 |
| Study settings | 15 |
| Changes at the psychiatric unit during the COVID-19 pandemic | 16 |
| Data collection | 16 |
| PEV data | 16 |
| Air pollution data | 17 |
| Statistical methods | 18 |
| Student's contribution | 18 |
| Ethics | 19 |
| Results | 20 |
| Visits to the psychiatric emergency unit | 20 |
| Air pollution data | 21 |
| PEVs correlated to air pollution..... | 22 |
| Total visits at the emergency unit | 22 |
| Results by sex..... | 23 |
| Results by age | 24 |
| Results by outpatient status..... | 25 |
| Discussion | 27 |
| Air pollution and sex..... | 27 |
| Air pollution and age..... | 29 |
| Air pollution and outpatient status | 30 |
| Strengths and weaknesses | 31 |
| Conclusions | 33 |

| | |
|------------------------------------------------|-----------|
| Populärvetenskaplig sammanfattning..... | 34 |
| Acknowledgement | 36 |
| References | 37 |

Abbreviations

| | |
|----------|---------------------------------|
| COVID-19 | Coronavirus disease 2019 |
| CNS | Central Nervous System |
| PEV | Psychiatric Emergency Visit |
| PM | Particulate Matter |
| SUH | Sahlgrenska University Hospital |
| WHO | World Health Organization |

Abstract

Associations between high concentrations of air pollution and psychiatric emergency department visits during the COVID-19 pandemic: a register-based study

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Key words: Air pollution, Mental distress, Psychiatric disorders, COVID-19

Introduction / Background: Converging results has suggested a link between increased exposure to air pollution and acute exacerbation of mental disorders such as depression, substance abuse, psychotic disorders and even suicide. However, what happens to this association during a large societal change such as the COVID-19 pandemic, remains unknown.

Aim(s) / Objective(s): The aim of this study is to investigate the association between increased levels of particulate matter (PM) and number of visits to a psychiatric emergency department before and during the COVID-19 pandemic. Further, this study aims to identify if there are any specific risk groups who are more susceptible to the effects of air pollution by studying sex, age, and outpatient status.

Methods: Data on number of visits to the psychiatric emergency unit at Sahlgrenska University Hospital in Gothenburg was provided by hospital administration and compared to daily levels of PM₁₀ and PM_{2.5}. The data was analyzed statistically using a time-stratified case-crossover design.

Results: A significant association between exposure to PM₁₀ and PM_{2.5} and increasing number of visits to the psychiatric emergency department could be seen during the control period for day 0-1 post exposure for females and for patients with ongoing outpatient contact. Remaining results in this study did not reach statistical significance. However, a positive association could be seen numerically for several of the analyses. For males, the age groups

18-24 and >65 years and individuals without ongoing psychiatric outpatient contact, this association seemed to increase during the pandemic.

Conclusion(s) / Implication(s): Although not significant, several of the analyses indicate that there might be a positive association between increased levels of air pollution and number of visits to the psychiatric emergency department, and that this association changed during the pandemic. Additional studies on a larger population and for a longer period are needed to further explore how the pandemic has affected the suggested relationship between increased air pollution and mental illness.

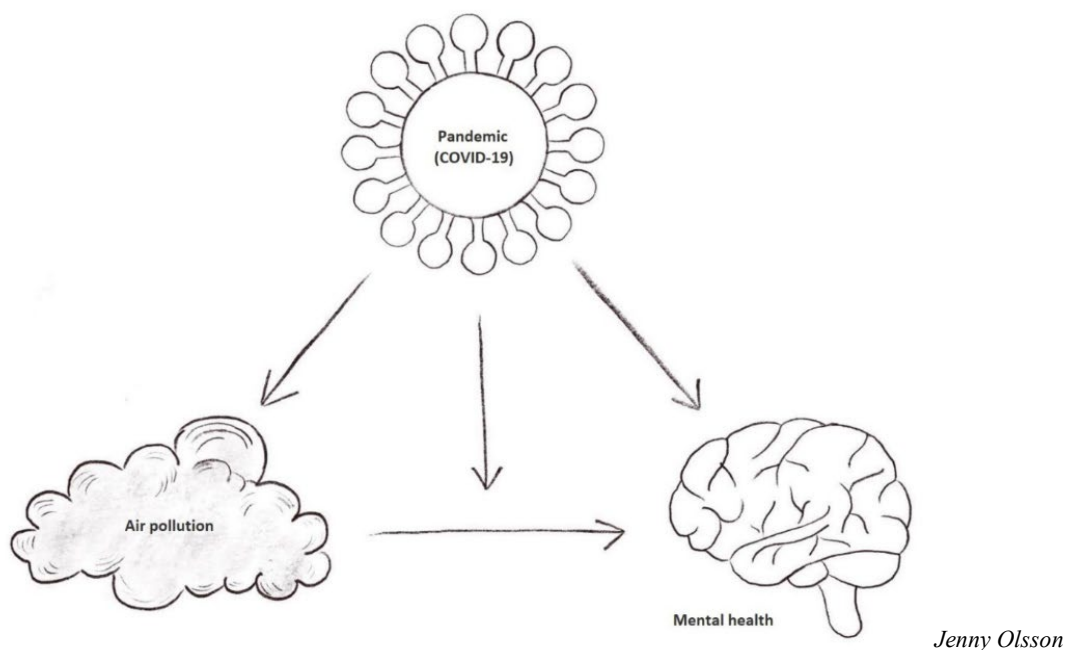


Figure 1. Schematic illustration of the suggested associations between air pollution, the COVID-19 pandemic and mental health.

Introduction

The global magnitude of mental illness is immense. Even though commonly highlighted by studies on the global burden of disease, research suggests that the overall burden of mental health problems remain underestimated. Psychiatric disorders and mental distress may severely influence individuals' life quality, potential and ability to contribute to society, and are important factors affecting our well-being (1).

Convergent evidence indicates possible associations between peoples' mental health and outer factors, such as environmental pollution and pandemics (like the ongoing Coronavirus disease 2019 (COVID-19) one). Recent research prior to the COVID-19 outbreak suggests a link between air pollution exposure and acute exacerbation of mental disorders, consequently leading to an increased number of visits to psychiatric emergency departments. However, how this association is affected by a large societal change that uncovers fragilities and weaknesses of our societal system, such as the COVID-19 pandemic, remains unknown.

Additional studies on the interactions between external environmental phenomena and mental illness may contribute to an extend our knowledge about psychiatric well-being, and further emphasize the need for global interventions to reduce environmental pollution and prevent pandemics (2). This study focuses on the association between exposure to air pollution and acute exacerbation of mental distress, with COVID-19 as a potential confounder.

Acute psychiatry

In recent decades, there has been an increased acknowledgement of the importance of mental health for human wellbeing and global development. Globally, it is estimated that about 1 in 5 people have a mental health condition. People with severe mental health illness die prematurely, and suicide is the second leading cause of death among 15-29-year-olds (3). The World Health Organization (WHO) includes mental health in the Sustainable Development Goals as part of Goal number 3, Good Health and Well-being (4). Despite progress in the understanding of psychiatric illness, people with acute mental health conditions often experience stigma and discrimination. Increased investment and research is required to increase our knowledge about mental illness, reduce stigmas and increase the access to quality mental health care (5).

Acute psychiatric care in Sweden

The Swedish National Board of Health and Welfare estimates that about 7-8% of Swedish 16-84-year-olds suffered from severe mental distress 2020 (6). In 2020, the total number of visits to psychiatric emergency departments in Sweden was 123.986, a decrease with 9.8% compared to 2019 when the number of total visits was 137.504 (7).

Psychiatric illness is more common among women than men in Sweden, and women are in contact with psychiatric care to a greater extent compared to men. Immigrants and refugees in Sweden suffer to a greater extent from mental illness, especially depression, sleep-related disorders, post-traumatic stress disorder, and suicidality. However, immigrants are less likely to seek acute psychiatric care (relatively to the proportion of individuals seeking psychiatric emergency units), possibly due to lack of knowledge regarding procedures, language difficulties or lack of faith in the healthcare system. (8)

External factors affecting mental health

Increasing evidence shows that external factors such as climate change, environmental pollution and pandemics have a negative effect on mental health. Suggested pathophysiological mechanisms include changes in the central nervous system (CNS) due to inflammatory processes, activation of the immune system, oxidative stress, damage to blood vessels and dysfunctions of neurotransmitters (9-12). Since the environment and human beings are complicated systems interacting in complex ways, it is difficult to establish a specific cause-effect relationship of these phenomena on mental health (13). Still, it seems that these naturally occurring events have similar consequences on individuals as well as collectivity regarding both health and socio-economic aspects (2).

Air pollution and mental health

Air pollution is one of the most common causes of morbidity and mortality in the world. In 2010, ambient particulate matter (PM) was considered the ninth leading risk factor to the global burden of disease (14). About 91% of the world's population live in places where the air quality exceed WHO limits, and low- and middle- income countries experience the highest burden (15).

A wealth of research has presented evidence of the negative effects of air pollution on somatic well-being. Air pollution has been linked to several different type of somatic diseases, including respiratory diseases (16) such as asthma (17), respiratory infections (18), lung cancer (19) and chronic obstructive pulmonary disease (20), as well as cardiovascular diseases such as ischemic heart disease and stroke (21, 22).

Air pollution defined

Air pollution is defined as a mixture of ambient particles, gases, organic compounds and metals. The term PM is used to describe liquid or solid airborne particles, where the most widely studied pollutants are PM_{2.5} and PM₁₀. PM is categorized according to their aerodynamic diameter, where PM_{2.5} includes particles smaller than 2,5 micrometers and PM₁₀ include particles smaller than 10 micrometers (23). The main source of PM emissions in cities is motor vehicles, contributing to more than 50% of total PM emissions (24). Other sources of PM emissions include biomass burning and industrial activities (25).

Acute effects of air pollution on mental health

In addition to its effects on somatic health, multiple studies have now shown that air pollution affects people's mental health negatively as well. Converging data based on self-reported measures reveals that air pollution decreases people's subjective experienced physiological health and life satisfaction (26). Associations between air pollution and increased annoyance and anxiety has been shown, as well as more severe psychiatric disorders such as depression (27), schizophrenia (28) and autism (29). Other studies indicates that air pollution may be a risk factor for substance abuse (30), non-suicidal self-harm (31) and suicide (32). Chronically, air pollution has even been shown to have a negative effect on cognitive function such as attention, memory, visuo-construction and verbal intelligence (33).

Another environmental factor contributing to mental distress is cigarette smoking. Studies has shown that cigarette smoking is associated to major depression, depressive symptoms and anxiety (34, 35), and that adults with any type of mental illness are more likely to have smoked than those with no mental illness (36).

A way of measuring the acute effects of air pollution on mental health is to compare fluctuations the number of visits to psychiatric emergency units, in this study referred to as *psychiatric*

emergency room visits (PEVs), with levels of environmental pollution. Converging results indicates that an increase in air pollutants is associated with a significant increase in PEVs, and the strongest evidence seems to be found for the association between the pollutants PM_{2.5} and PM₁₀ and PEVs. (37). This association seems to apply to all types of psychiatric conditions, including mood-related disorders, psychotic disorders (37), and substance use (30).

An epidemiological study on the acute effects of ambient air particle concentrations on mental health was performed at SUH, Gothenburg, in 2018. Daily monitored data on PM₁₀, ozone (O₃) and nitrogen dioxides (NO₂) were compared with PEVs using a case-crossover design. The results showed that visits increased with increasing levels of PM₁₀ during the warmer season in Sweden, implying that air pollution either exacerbates underlying psychiatric disorders or increases mental distress (38).

A similar study was performed at SUH in 2021, with focus on identifying risk groups susceptible to the acute psychological effects of air pollution. This study showed that exposure to PM₁₀ and PM_{2.5} may trigger acute exacerbating in mental health problems, results that aligned with the ones from the study achieved in 2018. The association applied for both males and females, with the distinction that females seemed to seek psychiatric care within the first days following air pollution exposure while males tended to seek a few days post exposure. A significant correlation between air pollution and acute exacerbation of mental illness could be seen among the age group 35-65 years, but not among individuals above 65 years old. Regarding outpatient status, it was noted that individuals with ongoing outpatient care tended to seek care in the first few days after exposure while those without ongoing outpatient contact care tended to seek care a few days after being exposed (39).

Pathophysiology

Several different pathophysiological pathways aiming to explain the correlation between air pollution and mental health has been proposed. One theory is based on the thought that air pollution leads to an accumulation of proinflammatory cytokines such A β 42 and α -synuclein, triggering neuroinflammation by causing an innate immune response in the brain (40). Another study conducted on mice proposes that exposure to airborne particulate matter leads to elevation of proinflammatory cytokines TNF α and IL1 β , causing a decreased dendritic spine density and dendritic branching in regions of the hippocampus (41). Further studies indicates that the effects of air pollution on the brain is due to an activation of the immune system in other parts of the

body, causing inflammatory mediators to circulate in the blood system and penetrating the brain tissue through the blood-brain barrier (42, 43).

Another theory suggests that the effects of air pollution on human behavior and well-being could be due to an increased stimulation of hormones rather than an activation of the immune system. This change in the hormonal balance is thought to be linked to activation of the hypothalamic-pituitary-adrenal axis, causing increased levels of glucocorticoid corticosterone and adrenocorticotrophic hormone in plasma (44). An association between activation of the hypothalamic-pituitary-adrenal axis and depressive behavior has been shown in several studies (45).

Additionally, research has shown that fine particulate matter such as air pollution causes cell cycle arrest and apoptosis among neurons and inhibits cell proliferation (46). The disruption of the cell cycle can be linked to degeneration of brain tissue (47). Further, air pollution has been shown to trigger oxidative stress and hydromethylation of DNA causing neurotoxicity, which has been linked to mental illness (46).

COVID-19 and mental health

The COVID-19 pandemic

As a newly emerged subtype, the highly pathogenic Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was first noted in November 2019 (48). The SARS-CoV-2 infection is transmitted by aerosols and/or droplets generated by sneezing and dry coughing by the infected individual, and causes the serious disease known as COVID-19 (49, 50). The clinical manifestations of COVID-19 are similar to other viral illnesses, and common symptoms include fever, dry coughing, shortness of breath and fatigue (51). Elderly (>60 years) and those with underlying medical conditions like hypertension, diabetes, obesity, malignancy, liver disease, or chronic respiratory or cardiovascular disease are at the highest risk of severe and critical disease (52).

SARS-CoV-2 was first noted in November 2019 in Wuhan, China. The WHO reported the first case of COVID-19 on December 31, 2019, and the virus outbreak was declared a global pandemic on March 11, 2020 (53). In May 2020, a total of almost 6.000.000 positive cases were registered globally, including over 360.000 death cases (52). As of September 2, 2021, the

WHO has announced that over 217.000.000 people have been diagnosed with COVID-19 and about 4.500.000 death cases has been caused by the disease (54).

Acute effects of COVID-19 on mental health

The rapid evolvement of the COVID-19 pandemic led to drastic alterations in people's everyday lives in multiple ways, including social life, work situation and private economy. The mass lockdowns and economic recessions, along with the fear and uncertainties associated with the virus outbreak, were predicted to lead to an increase in mental illness and number of suicides (55). Several studies described an increase in mental distress among the general population, as well as in health care workers (56). The prevalence of depressive symptoms was reported to increase significantly (57-59), as well as anxiety symptoms (60-62). Regarding symptoms of post-traumatic stress syndrome, the results in different studies varied remarkably from similar prevalence rates (63) to a notable increase during the pandemic (64).

Despite all the data pointing out COVID-19 has had a negative effect on the mental health of the population, reports from hospitals around the world shows a decrease in the number of PEVs (65-71). Additionally, studies report a similar decrease in psychiatric admissions to inpatient care during the pandemic (69, 72, 73). The underlying mechanisms explaining the decreased rates remain widely unknown, but it has been suggested that limitations in mobility and physical distancing due to fear of infection may have affected in which extent people seek acute psychiatric care (74).

Contradictory to the earlier predictions that mental illness would increase during the COVID-19 pandemic, another explanation to the decreasing number of visits to acute psychiatry departments could be that psychological distress in general has not escalated during the pandemic. Recent reports from The Public Health Agency of Sweden shows a decrease in the number of people seeking acute psychiatric care due to anxiety, symptoms of depression and stress, and fewer suicides in Sweden during the pandemic (75).

Air pollution during COVID-19

In addition to its health-related and economic consequences, the lockdown during the COVID-19 pandemic has had a notable impact on the environment (76). In spring and summer 2020, when the disease was declared a global pandemic, governments around the world introduced lockdown restrictions to ensure the safety of their citizens. Social distancing became a new norm, and people were urged to avoid international travel (77).

These type of measures were initiated to limit the exposure of COVID-19, and as a consequence reduced transportation, businesses, and industrial shutdowns led to a significant drop in greenhouse gas emissions (78). Air quality improved significantly, mainly because of the lower emissions of air pollutions such as carbon monoxide, nitrous oxide and carbon dioxide in industrial economies. Especially in countries with severe air pollution, such as China and India, it has been shown that the lockdown restrictions during COVID-19 led to a reduced environmental pollution. Most notable was the reduced concentrations of NO₂ and PM_{2.5}, the main pollutants related to traffic (79, 80).

In summary, increasing evidence indicates that air pollution has a notable impact on our mental health. However, there is a lack of studies looking at this relationship during larger societal changes, such as a global pandemic. Given the extensive consequences of both air pollution, the COVID-19 pandemic and mental illness, further studies investigating the associations between these are induced in order to broaden our knowledge about mental health and how to prevent psychiatric illness.

Highlighting the mental consequences of air pollution and pandemics can contribute to understanding the importance of global interventions to reduce climate change and air pollution, and to prevent pandemics. This study mainly focuses on how variations in air pollution levels affects physiological well-being, and if the earlier shown association between air pollution exposure and increased PEVs has remained during the COVID-19 pandemic.

Aim

This study aims to investigate the association between air pollution exposure and acute exacerbation of mental distress, with the COVID-19 pandemic as a confounding factor. More specifically, this study aims to answer the question:

“Can the association between fluctuations in concentrations of air pollution and daily visits to the psychiatric emergency unit at Sahlgrenska University Hospital still be seen during the COVID-19 pandemic?”

Based on this research question, the null-hypothesis hence is that there has not been any change in the association between PM and PEV during the COVID-19 pandemic.

Furthermore, this study aims to compare the effects of air pollution on mental health among different subgroups by studying the sex, age and whether there is an ongoing outpatient contact with the psychiatric health care or not.

Material and Methods

Study design

This is an administrative register-based epidemiological study on the association between PEVs and air pollution levels, statistically analyzed using a time-stratified case-crossover design.

Two different time periods of higher COVID-19 infection rates were defined as the first wave (10th of March to 14th of June 2020) and the second wave (26th of October to 31st of December 2020). Data from these periods were compared with data from corresponding time periods in previous years (2018-2019).

The chosen time periods were based on the evolution of the passage of events and public recommendations during the pandemic. The first cases of COVID-19 in Sweden were reported in February 2020, but it was not until the beginning of March 2020 that the Swedish Government and the Public Health Agency of Sweden decided to introduce suggested restrictions and more extensive information spreading. The virus outbreak was declared a global pandemic on 11th of March 2020 (81). During the set time periods, the Public Health Agency of Sweden recommended to “avoid all unnecessary visits to health care” (82).

Study settings

The SUH is one of the largest hospitals in the Northern Europe, serving an area of approximately a million adult inhabitants in the Gothenburg area. The Psychiatric emergency unit at the SUH is located at Östra Sjukhuset, Gothenburg. As part of the public welfare, any individual can seek acute psychiatric care here for a set fee, and psychiatric health care can be accessed by any person with a mental health problem. The psychiatric emergency room is open 24-hours all days, including holidays. The SUH Psychiatric Emergency Unit is available for anyone to visit, and you don't necessarily have to go through primary care first.

Upon arriving to the psychiatric emergency unit, the patient is initially evaluated by a psychiatric nurse, and then, if needed, by a psychiatrist. If necessary, acute psychiatric care is offered. The patient may then be referred to further outpatient care, either by primary care or

by specialized psychiatric clinics. Patients with milder mental health problems are offered psychosocial support or psychopharmacological treatment provided by general practitioners in primary care. More severe cases of psychiatric illness, such as bipolar disease, schizophrenia and major depressive disorder, are referred to specialist psychiatric care. If necessary, inpatient psychiatric care is given (83).

Changes at the psychiatric unit during the COVID-19 pandemic

The COVID-19 pandemic caused an abrupt change in the Swedish healthcare system, and the way psychiatric care services were provided changed drastically. Based on oral communication with clinically active staff at SUH, the pandemic had an extensive impact on both the psychiatric emergency room and inpatient care units as well as outpatient care.

At the psychiatric unit at Östra Sjukhuset, patients seeking acute psychiatric care were referred to a container outside the hospital building. Here, the patients were asked about any symptoms of COVID-19, and their body temperature was measured before they were allowed into the psychiatric emergency room. These arrangements were done in order to identify patients who could be infected with the SARS-Cov-2 virus, to prevent spreading of COVID-19 within the hospital.

Patients receiving inpatient care were not allowed to receive visitors except for exceptional cases. All health care workers had to wear protective equipment consisting of face masks and visors when interacting with patients, and some of the patient activity rooms were closed. A separate unit was implemented to provide care specifically for psychiatric patients that were simultaneously infected with COVID-19.

Data collection

PEV data

Data on PEVs was provided by management at SUH. All registered visits to the psychiatric emergency room by inhabitants in the Gothenburg area over 18 years of age was collected via an electronic patient file system (ELVIS) and provided by the hospital administration. Patients who were not registered in the in the city of Gothenburg were excluded from the study.

PEVs were measured as all visits registered by the staff at the psychiatric emergency unit, and hence some things are important to note. The same patient could seek care at the psychiatric emergency unit multiple time a day, and by the used measurement each occasion would count as a visit. There is also a possibility that some individuals entering the psychiatric emergency unit are not registered by the staff for some reason, either by mistake or, for example, if the staff immediately redirects the patient to another part of the healthcare system.

Air pollution data

Daily data on PM₁₀ and PM_{2.5} levels are available to the public via the Swedish Meteorological and Hydrological Institute (SMHI) website (<https://datavardluft.smhi.se/portal/concentrations-in-air>). Exposure data for any day can be downloaded as one hour mean values in µg/m³. This study uses measurements from the main station in Gothenburg, “*Femman Huset*”, located in a central urban part of the city (Figure 2). All available measurements during the set time period were gathered. The data was aggregated into 24-hour values for each day from midnight to midnight, and then the mean value for each day was calculated. Days where measurement was missing for 25% of hours or more were excluded from the study.

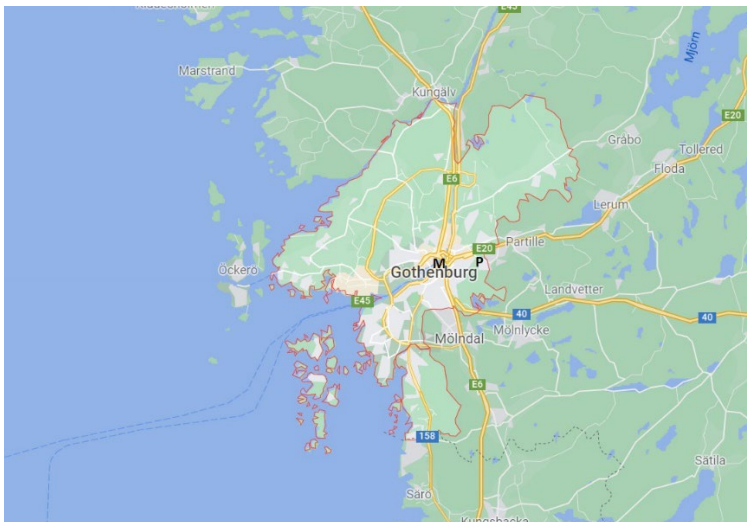


Figure 2. Map of the study area, Gothenburg Municipality. The locations of the air pollution measuring station (M) and the SUH psychiatric emergency unit (P) are indicated (Google Maps).

Statistical methods

The data were analyzed using a Distributed Lag Non-linear Model (DLNM) with a time-stratified case-crossover design. A distributed lag model was fitted so that effects seen on the day of the event (i.e., increased levels of PM₁₀ and PM_{2.5}) could be investigated, and delayed effects could be observed in the following days. The time stratified case crossover design (84) is a method where a day with a certain exposure, in this case PM air pollution, is considered a case, and days within the same strata (same weekday, same month, same year), but have lower PM levels are used as controls. The model inherently adjusts for weekday, a potential confounding factor, as number of emergency visits tend to be lower during weekends. The model also adjusts for annual fluctuations. In the final models, a quasipoisson distribution was considered more appropriate to account more unequal variance across the outcome variable distribution.

In the modelling procedure, a cross-basis was first specified, a function which allows for non-linear, and differentiated effects across values of the exposure, and the lagged values up to seven days. In this case, we fitted separate cross-bases for the control and covid-wave period.

The cross-bases were then introduced into separate Poisson regression models along with an indicator variable for covid-period and a variable indicating odd holidays. The model results estimate the effect of PM on the number of visits across the time-stratified strata. Finally, the model results were used to predict the relative risk (effect) associated with an increase in PM by 10 units, including a 95% confidence interval in the control period and the covid-wave respectively and these were plotted.

In the analysis, the study population was divided by different subgroups by sex, age and outpatient status.

Student's contribution

The background research and writing of the thesis paper has been conducted by the student. The student has also, with guidance of the supervisors, compiled the provided data on daily PEVs and PM. The student received help with the statistical analyzes from co-supervisor Hanne Krage Carlsen. The results were evaluated and analyzed by the student together with the supervisors.

Ethics

This study adheres to the Hawaii declaration and to ethical principles. Ethical approval from the ethical committee was granted (2020-04222). Every person included in the study was anonymous, and no identifiable data was managed.

Results

Visits to the psychiatric emergency unit

The total number of PEVs for the control period was 27.779. For the total time period defined as *pandemic*, including the first wave (10th of Mars 2020 to 14th of June 2020) and the second wave (26th of October to 31st of December), there was a total of 4.105 PEVs. The mean value of daily registered visits was 14.5 for the control period and 12.0 for the pandemic period, resulting in a decrease with 17.2% daily visits during the pandemic. Time series for daily counts of PEVs is plotted in figure 3.

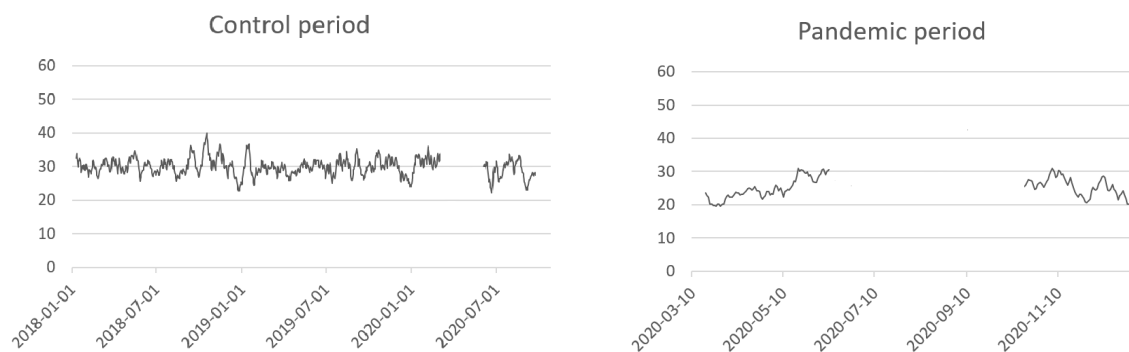


Figure 3. Daily visits to the SUH psychiatric emergency unit during the control period and the pandemic period.

In table 1, descriptive data with information about specific daily counts by sex, age and outpatient status can be found. For both sexes, all age groups and both outpatient status categories, the number of mean daily visits decreased during the pandemic compared to the control period. As the table shows, the patients with no ongoing psychiatric outpatient contact showed most distinct decrease, with a 23.5% decrease in PEVs during the pandemic.

Table 1. Descriptive statistics for daily number of visits to the psychiatric emergency unit for the different subgroups.

| | Control (n = 938 days) | Pandemic (n = 158 days) | p-value |
|--------------------------------------|-----------------------------------|------------------------------------|----------------|
| Total | | | <0.001 |
| Mean (SD) | 29.8 (6.7) | 24.7 (6.6) | |
| Range | 12-50 | 11-41 | |
| Females | | | <0.001 |
| Mean (SD) | 14.5 (4.3) | 12.0 (4.1) | |
| Range | 3-28 | 2-26 | |
| Males | | | <0.001 |
| Mean (SD) | 15.4 (4.3) | 12.8 (4.0) | |
| Range | 3-31 | 4-25 | |
| Age: 18-24 years | | | <0.001 |
| Mean (SD) | 4.7 (2.3) | 3.7 (2.0) | |
| Range | 0-13 | 0-10 | |
| Age: 25-64 years | | | <0.001 |
| Mean (SD) | 22.0 (5.5) | 18.3 (5.3) | |
| Range | 6-45 | 7-35 | |
| Age: >65 years | | | 0.001 |
| Mean (SD) | 3.2 (1.9) | 2.7 (1.6) | |
| Range | 0-9 | 0-8 | |
| Ongoing outpatient contact | | | 0.011 |
| Mean (SD) | 12.7 (4.0) | 11.7 (4.0) | |
| Range | 2-28 | 4-23 | |
| No ongoing outpatient contact | | | <0.001 |
| Mean (SD) | 17.0 (4.7) | 13.0 (4.0) | |
| Range | 5-32 | 4-23 | |

Air pollution data

In table 2, data on daily levels of PM₁₀ and PM_{2.5} during the control period and the pandemic period can be seen, as well as on missed days and the highest and lowest measured values. The daily mean concentration of PM₁₀ was 12.8 during the control period, and 12.6 during the pandemic period. Corresponding values for PM_{2.5} was 6.8 during the control period and 6.2 during the pandemic period. In figure 4, daily mean values of PM₁₀ and PM_{2.5} from the control period and the pandemic period are plotted according to day of the year.

Table 2. Descriptive statistics for daily concentrations of PM₁₀ and PM_{2.5}.

| | Control | Pandemic | p-value |
|-------------------------|----------------|-----------------|----------------|
| PM₁₀ | | | 0.677 |
| Mean (SD) | 12.8 | 12.6 | |
| Range | 1.5-74.7 | 2.8-36.8 | |
| Days missed | 44 | 3 | 0.758 |
| PM_{2.5} | | | 0.125 |
| Mean (SD) | 6.8 | 6.2 | |
| Range | 0.7-35.0 | 0.6-25.0 | |
| Days missed | 44 | 3 | 0.758 |

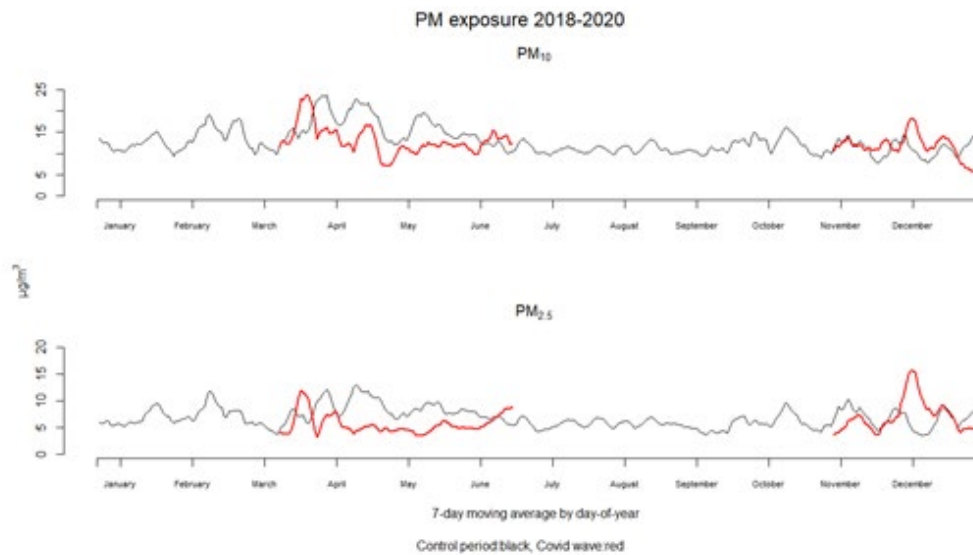


Figure 4. Time series plots for the daily mean concentrations of air pollutants PM_{10} and $PM_{2.5}$ during 2018-2020, plotted as 7-day moving average by day-of-year. Control period is marked as black and COVID waves are marked as red.

PEVs correlated to air pollution

In figure 5, the total number of daily PEVs is plotted against measured levels of PM_{10} and $PM_{2.5}$ for the same day, for both the control period and the pandemic period. From unadjusted regression analysis, the estimated association between same-day values of $PM_{2.5}$ and PEV was 0.019 ($p=0.904$) during the pandemic, and 0.022 ($p=0.665$) during the control period. The estimates for PM_{10} were 0.029 ($p=0.756$) during the pandemic and 0.058 ($p=0.010$) during the control period.

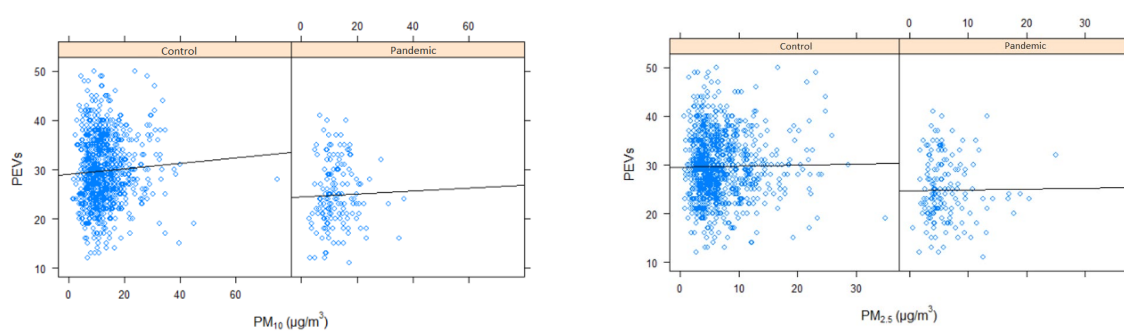


Figure 5. Total daily visits to the psychiatric emergency room during the control period and the pandemic period, plotted against measured levels of PM_{10} and $PM_{2.5}$ with a best-fit line.

Total visits at the emergency unit

For the total count of PEVs, no statistically significant correlation between higher levels of PM_{10} and $PM_{2.5}$ and an increased risk of seeking acute psychiatric care could be seen. The results in figure 6

presents the total relative risk of seeking the psychiatric emergency unit with every $10 \mu\text{g}/\text{m}^3$ increase in PM_{10} and $\text{PM}_{2.5}$ on the same day and 1-7 days lagged exposures.

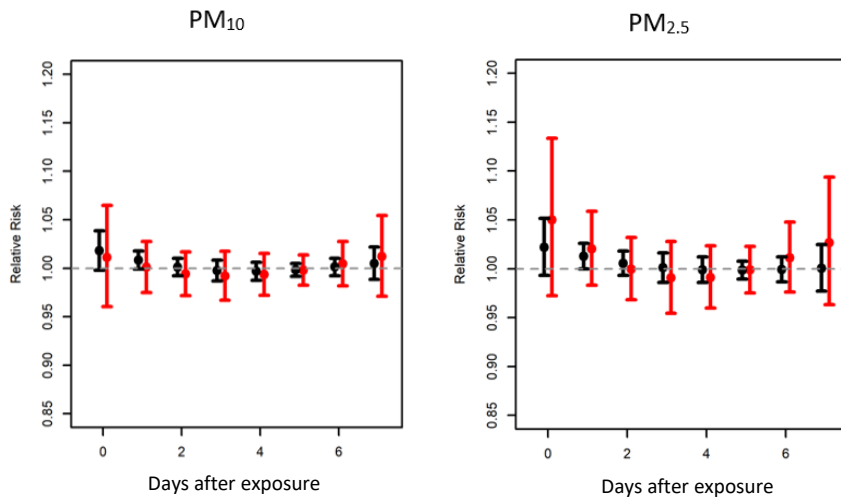


Figure 6. Total relative risk of seeking the psychiatric emergency unit with every $10 \mu\text{g}/\text{m}^3$ increase in PM_{10} and $\text{PM}_{2.5}$ on the same day as well as on 1-7 days lagged exposures, with a 95% confidence interval. Control period: black, pandemic period: red.

Results by sex

In figure 7 and 8, the relative risk of females and males seeking acute psychiatric care when exposed to increasing air pollution levels can be seen.

For females, a significant correlation could be seen day 1 after exposure for both PM_{10} and $\text{PM}_{2.5}$ for the control period. For the pandemic period, there was no significant correlation for any lag.

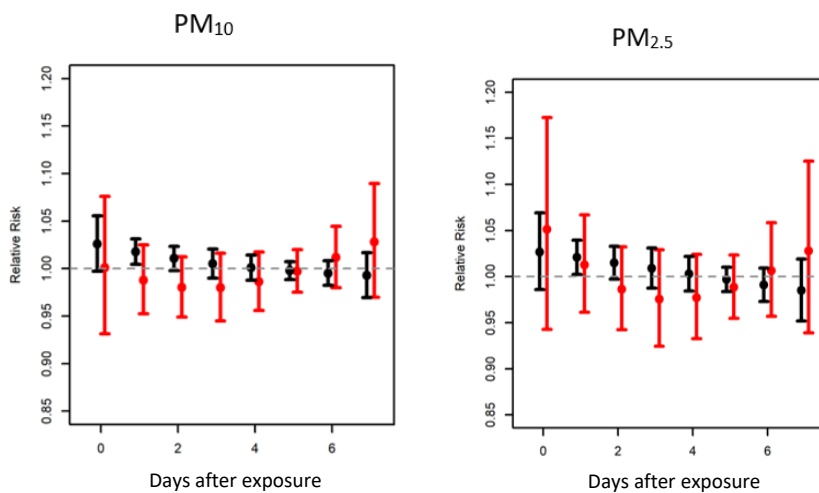


Figure 7. Relative risk of females seeking the psychiatric emergency unit with every $10 \mu\text{g}/\text{m}^3$ increase in PM_{10} and $\text{PM}_{2.5}$ on the same day as well as on 1-7 days lagged exposures, with a 95% confidence interval. Control period: black, pandemic period: red.

For males, no significant correlation could be seen for either PM₁₀ and PM_{2.5} for both the control period and the pandemic period.

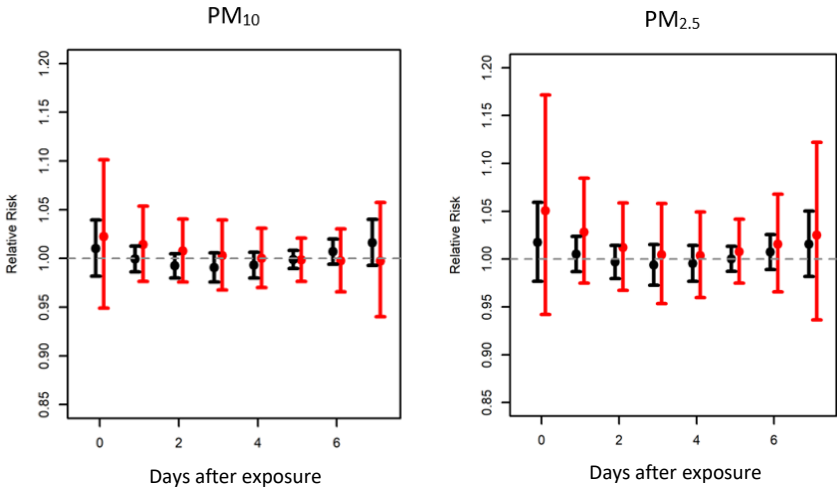


Figure 8. Relative risk of males seeking the psychiatric emergency unit with every 10 µg/m³ increase in PM₁₀ and PM_{2.5} on the same day as well as on 1-7 days lagged exposures, with a 95% confidence interval. Control period: black, pandemic period: red.

Results by age

The relative risk of seeking acute psychiatric care when exposed to increased levels of air pollution for individuals aged 18-24, 25-64 and >65 years care can be seen in figure 9-11. No significant correlation could be seen for PM₁₀ and PM_{2.5} for any of the age groups, for the control period as well as the pandemic period.

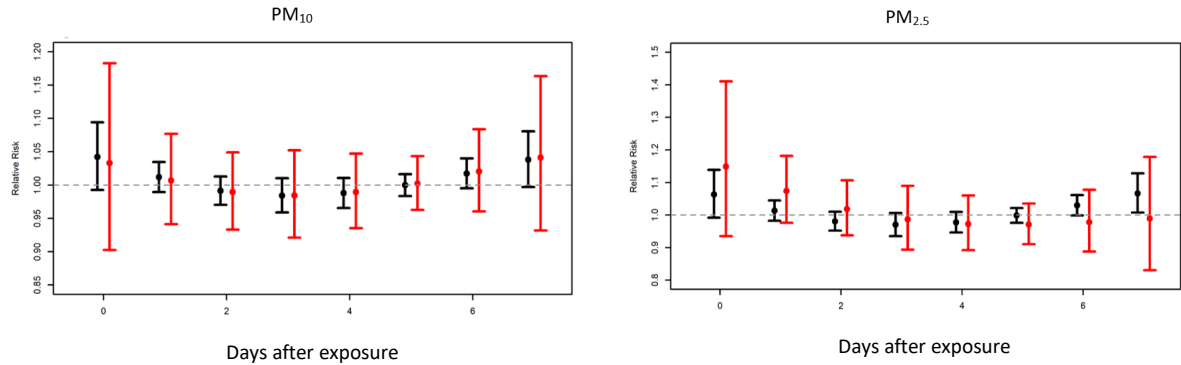


Figure 9. Relative risk of seeking the psychiatric emergency unit with every 10 µg/m³ increase in PM₁₀ and PM_{2.5} on the same day as well as on 1-7 days lagged exposures, for ages 18-24, with a 95% confidence interval. Control period: black, pandemic period: red.

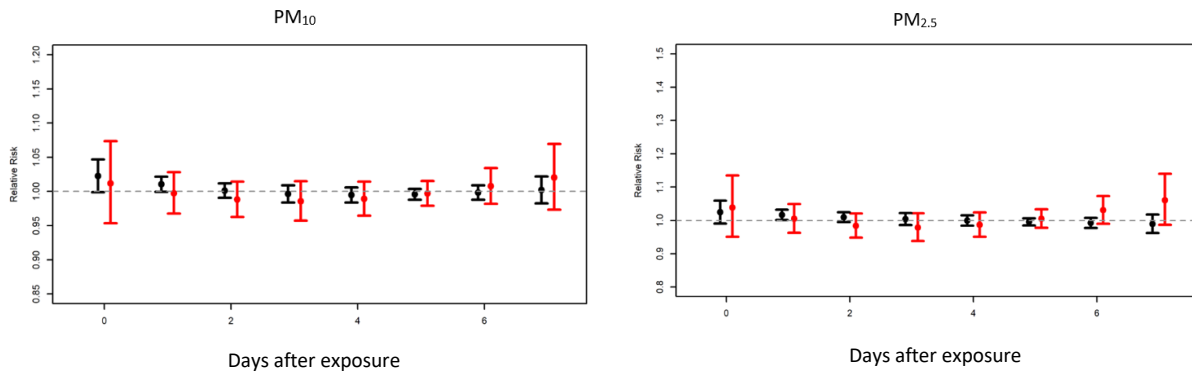


Figure 10. Relative risk of seeking the psychiatric emergency unit with every $10 \mu\text{g}/\text{m}^3$ increase in PM_{10} and $\text{PM}_{2.5}$ on the same day as well as on 1-7 days lagged exposures, for ages 25-64, with a 95% confidence interval. Control period: black, pandemic period: red.

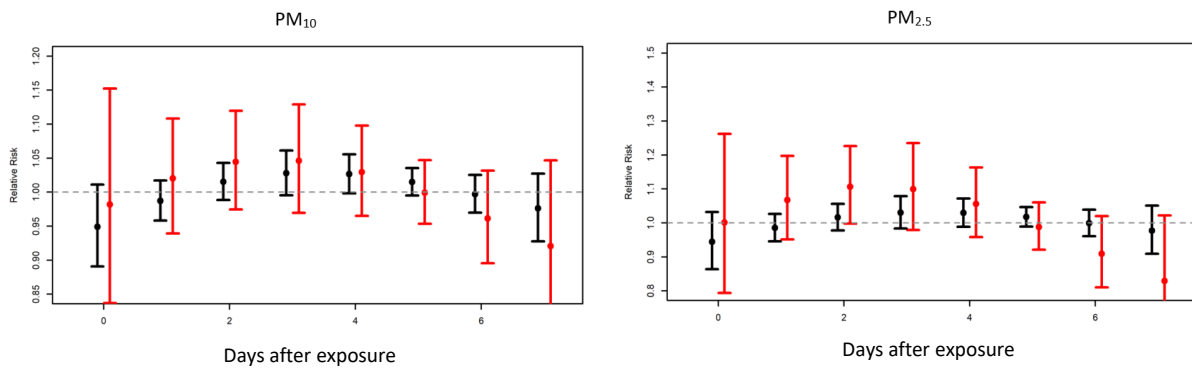


Figure 11. Relative risk of seeking the psychiatric emergency unit with every $10 \mu\text{g}/\text{m}^3$ increase in PM_{10} and $\text{PM}_{2.5}$ on the same day as well as on 1-7 days lagged exposures for patients >65 years, with a 95% confidence interval. Control period: black, pandemic period: red.

Results by outpatient status

Patients with ongoing psychiatric outpatient contact showed a significant association on early lags for both PM_{10} and $\text{PM}_{2.5}$ during the control period, as can be seen in figure 12. For the pandemic period, no significant correlation could be seen for either PM_{10} or $\text{PM}_{2.5}$.

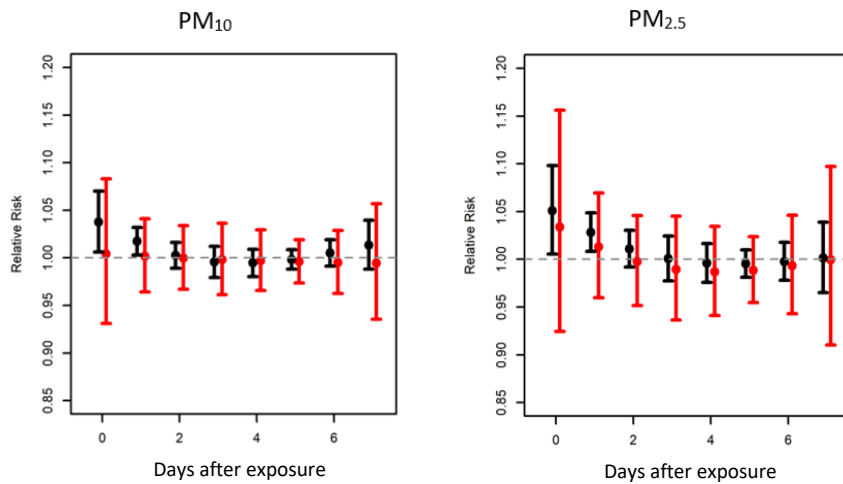


Figure 12. Relative risk of individuals with ongoing outpatient psychiatric contact seeking the psychiatric emergency unit with every $10 \mu\text{g}/\text{m}^3$ increase in PM_{10} and $\text{PM}_{2.5}$ on the same day as well as on 1-7 days lagged exposures, with a 95% confidence interval. Control period: black, pandemic period: red.

As can be seen in figure 13, no significant correlation could be seen for either PM_{10} or $\text{PM}_{2.5}$ for patients without ongoing psychiatric outpatient contact.

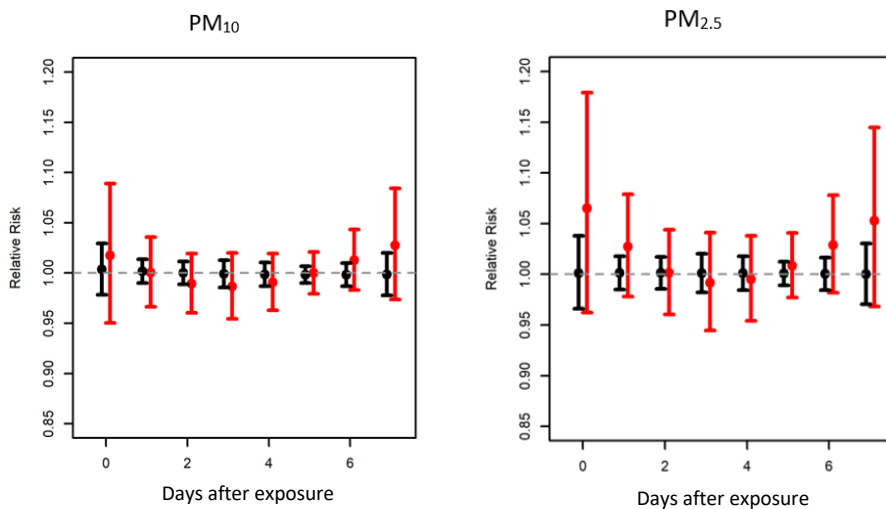


Figure 13. Relative risk of individuals without ongoing outpatient psychiatric contact seeking the psychiatric emergency unit with every $10 \mu\text{g}/\text{m}^3$ increase in PM_{10} and $\text{PM}_{2.5}$ on the same day as well as on 1-7 days lagged exposures, with a 95% confidence interval. Control period: black, pandemic period: red.

Discussion

Except for the significant association seen for day 0-1 post exposure for females and patients with ongoing psychiatric outpatient care during the control period, the analyses in this study did not reach significance. However, majority of the results implied that a positive relation might exist, with varying distinctness among the different subgroups. These findings may support the hypotheses from existing studies within the same area, suggesting that air pollution exposure could cause an acute exacerbation of mental distress (38, 39). Since none of the results for the pandemic period were significant, no sure conclusion can be drawn concerning if the association between air pollution and PEVs changed during the pandemic. Hence, it is important to bear in mind that all discussions regarding this are highly speculative.

For the total visits, no distinct change in seeking pattern correlated to air pollution levels could be seen during the pandemic. When studying the specific subgroups however, variations could be seen in the possible association for some of the categories. For example, the association for females and patients with ongoing outpatient psychiatric contact seemed to rather go down than up. For other subgroups, like the age groups 18-24 and >65 years and patients without ongoing outpatient psychiatric contact, the association appeared to increase during the pandemic period. The results for each subgroup are discussed more thoroughly in the paragraphs below.

Air pollution and sex

Previous studies evaluating the harmful consequences of increased air pollution rates has reported that females seem to be more susceptible to the effects of air pollution exposure compared to males (85-91). However, a study performed by Muhsin et al. at SUH, Gothenburg, earlier in 2021 reported that both sexes had a significantly higher risk of seeking acute psychiatric care when exposed to higher concentrations of air pollution with similar risk estimates (39). The fact that ambient particles have a greater deposition in females compared to men has been discussed a possible explanation to females being more susceptible to air pollution than males (92). Another suggested explanation is that females have smaller airways and slightly greater airway reactivity than males, why dose-response relations may be easier detected in females (93).

This study has been unable to demonstrate a significant correlation between air pollution exposure and acute exacerbation of mental distress among both males and females for the pandemic period. Still, a positive association can be seen in the early lags for both sexes, especially for PM_{2.5}. Even if not statistically significant in this study, one can still argue that these results reflect the trends seen in earlier reports.

In contrast to earlier findings, however, the association to both PM_{2.5} and PM₁₀ seemed to be more distinct among males than females. Since this difference has not been found elsewhere, and since the results in this study has not shown significance, caution must be applied when interpreting these findings. Additional studies with a larger sample size are needed in order to further investigate possible gender-based differences in vulnerability to air pollution in this geographical area.

Muhsin et al. (2021) reports in their study that females seemed to seek psychiatric care within the first days after air pollution exposure, while males tended to seek help a few days after exposure. In contrast to this, this study found no obvious difference in lagging in the seek pattern between the sexes.

When comparing the association between air pollution and PEVs before and during the COVID-19 pandemic, the seeking pattern seemed to remain consistent for both males and females. Based on figure 7 and 8, the association on females seem to have been less during the pandemic for PM₁₀ and not very dramatically changed for PM_{2.5}. For males, the association rather increased during the pandemic, similarly for both PM₁₀ and PM_{2.5}.

These results need to be interpreted with caution since they are not significant, but one can still speculate in why the numerical results suggests that the association for females seemed to reduce while the associations for males tended towards not being changed. There is an infinite number of possible explanations to this, but one participating factor could be that women due to traditional gender roles stayed at home taking care of the home, children and sick relatives to a greater extent than men during the pandemic (94), and therefore were less exposed to ambient air pollution.

Air pollution and age

Several previous studies have reported that elderly (>65 years) seem to be more susceptible to the effects of air pollution on somatic and mental health compared to younger age groups (85, 86, 95-98). One suggested theory to explain this is that there are differences in pharmacokinetics between older and younger adults, and that older people often have an increased particle deposition in their airways due to age-related and pathological changes in the respiratory system (99). Another explanation could be that older people have a decreased capacity of compensating for the negative effects of environmental pollutants on their bodies (100).

In contrast to the earlier reports, Muhsin et al. (2021) only found a significant correlation between exposure to air pollution and increased visits to the psychiatric emergency among 35-65 years old. No significant association could be seen for individuals above the age of 65. However, this study points out that this could be due to a type 2 error, considering the particularly low number of visits to the psychiatric emergency department for that specific age group.

In this study, no significant correlation could be seen for any of the age groups. However, some differences in trends could be noted. For individuals aged 18-24 years, a positive association could be seen for the earlier lags for both PM₁₀ and PM_{2.5}, with similar numerical values for both the control period and the pandemic period. Contrary to what was described by Mushin et al. (2021), no obvious positive association was found in this study for the age group 25-64, for either period. For individuals >65 years however, a positive trend in the association could be seen on lag 2-4 for both PM₁₀ and PM_{2.5}. This association seemed to increase numerically during the pandemic period, especially for PM_{2.5}.

Apart from the physiological differences, the amount of air pollution exposure could explain the difference in risk during the pandemic. It has been shown that older people spend more time outdoors, increasing the time they are exposed to ambient particles in the air (101, 102). It is possible that elderly, bound by stricter social restrictions during the pandemic, spent even more taking walks and being outdoors. This, among with other factors, could influence the extent of the effects of air pollution.

Air pollution and outpatient status

In earlier studies, the difference between how rising air pollution levels affects patients with ongoing psychiatric outpatient contacts compared to patients without ongoing contact has not been as widely studied as differences in sex and age. Previous research has rather focused on how the effects of air pollution varies within specific diagnoses, a factor that this study did not investigate. However, Muhsin et al. (2021) showed that patients with an ongoing psychiatric outpatient contact tended to seek acute psychiatric care on the first few days post air pollution exposure, while patients without ongoing outpatient contact seemed to show an increased search pattern on later lags.

In this study, patients with ongoing outpatient contact showed a significant association during the control period on day zero and one after exposure for both PM₁₀ and PM_{2.5}. For the pandemic period, the association seemed to follow a similar pattern, but none of the lags during this period reached significance. The association rather seemed to go down than up during the pandemic period compared to the control period, a finding that could have multiple explanation.

One possible reason could be that patients with ongoing outpatient status avoided going to the psychiatric emergency room at the hospital because of the pandemic situation, and chose to make contact with their existing psychiatric contact in non-physical ways. For example, the alternative to talk to medical staff over telephone or video link were more widespread during the pandemic period than before, an option that could be more accessible to individuals that already had an ongoing contact with the health care system.

For patients with no ongoing psychiatric outpatient contact, no distinct association between air pollution exposure and risk of seeking the psychiatric emergency could be seen for PM₁₀. For PM_{2.5} however, the relationship differed between the control period and the pandemic period. During the control period no association could be identified, but for the pandemic period the results numerically tended to increase for the early lags as well as the later lags. Even if these results did not show significance, this distinction could point towards a possible change in seeking pattern correlated to air pollution exposure during the pandemic.

Strengths and weaknesses

A major limitation of this study is the length of the studied periods. By the time this study was performed, data on air pollution was only available until 31st of December 2020. Optimally the pandemic period would include periods of restrictions during 2021 as well but had to be limited to 2020 due to lack of available data. Further, the time chosen as control period was longer than the pandemic period, which could affect the results. Another factor limiting the study is that data only was collected from one hospital. Further studies with longer studied periods and data from different hospitals within the region are needed to provide more reliable results.

Further, a limitation of this study is how the number of PEVs was measured. All registered visits to the psychiatric emergency room were counted as a PEV, meaning that the same person could seek multiple times a day and each visit would be counted as a separate visit. It is also possible that some patients visiting the psychiatric emergency were not correctly registered for some reason, leading to a misleading result for the total PEVs. Another limitation is that this study did not consider the diagnosis registered for each patient. It is therefore possible that not all the registered PEVs were actual psychiatric emergency patients, and that some none-acute or somatic issues could have been included in the analyses.

Another source of weakness is that this study did not measure individual exposure to air pollution. The measured values of PM were all taken from Femman Huset in the central part of Gothenburg, and all individuals were assumed to be exposed to the same levels. In addition, individuals suffering from mental illness tend to isolate and stay inside, and therefore may not be as exposed to ambient air pollution as others. However, to use central measuring stations are standard in many studies on the effects of air pollution.

Even if further studies including multiple hospitals is needed to fully explore the effects of air pollution on mental health, one of the strengths of this study is that is conducted at one of Scandinavia's largest psychiatric emergency departments with an average of 13.000 visits per year. Since Gothenburg is an urban area and the second largest city in Sweden, it is a valuable location to study the effects of air pollution.

Another strength is the choice of statistical method. In a case-crossover study design, each individual serves as his or her own control, reducing the risk of confounding factors affecting

the results. Further, this statistical design allows controlling for holidays, seasonality and day of the week, factors that otherwise influence the number of visits to psychiatric emergencies.

Conclusions

Air pollution and pandemics are naturally occurring phenomena facing the world, with consequences for both individuals and collectivity. The main aim of this study was to examine the earlier observed association between exposure to air pollution and acute exacerbation of mental distress, and to see if this association changed during the COVID-19 pandemic. Majority of the analyses in this study did not reach statistically significant results, which is important to bear in mind when drawing any type of conclusions from the findings. Additional studies are needed to further investigate the relations between air pollution, pandemics and mental illness.

Although not significant, several of the analyses point towards that there might be a positive relationship between increased levels of air pollution and a higher number of visits to the psychiatric emergency department. This association did not change distinctly during the pandemic period for the total count of visits, but for some of the studied subgroups the relationship seems to have altered. For females and patients with ongoing outpatient psychiatric contact the association seemed to decrease, while it seemed to increase for individuals between 18-24 years and >65 years, and for patients without ongoing outpatient contact.

Even though far from reaching a clear conclusion, these observations may help us understand how external factors as air pollution and pandemics affect mental health, and how these factors interfere with each other. Increased knowledge of the various effects of air pollution exposure and viral outbreaks can contribute to highlighting the importance of eco-health and planetary health on human well-being, and emphasizes the need to coordinate actions to achieve better human health and environmental outcomes.

Populärvetenskaplig sammanfattning

Luftföroreningars påverkan på psykisk ohälsa före och under COVID-19

| | |
|-----------------------|-------------------------------------------------------|
| Författare: | Jenny Olsson |
| Examensarbete: | 30 hp |
| Program: | Läkarprogrammet |
| År: | 2021 |
| Handledare: | Steinn Steingrimsson, Hanne Krage Carlsen |
| Nyckelord: | Luftföroreningar, Psykisk ohälsa, Psykiatri, COVID-19 |

Att luftföroreningar är farligt för hälsan är välkänt, men på senare tid har forskning pekat mot att luftföroreningar även kan påverka vårt psykiska välmående. Studier som gjorts runt om i världen har kunnat visa att ökade halter av luftföroreningar leder till att fler människor söker till psykiatriska akutmottagningar, något som kan ses som ett mått på akut psykisk ohälsa. Även i Göteborg har liknande studier gjorts, där forskare kunnat visa att sambandet mellan luftföroreningar och ökat antal besök till psykiatriakuten finns även där.

Nyligen gjordes ytterligare en studie vid Östra sjukhuset i Göteborg, denna gång för att se om sambandet mellan luftföroreningar och psykisk ohälsa ändrats under den pågående COVID-19-pandemin. Halten av föroreningar i luften för varje dag samlades in från SMHI och jämfördes med antalet besök till psykiatriakuten för en period före och en period under pandemin.

Resultaten som framkom i studien var inte tillräckligt starka för att kunna ses som vetenskapligt bevisade, men pekade ändå mot att luftföroreningar kan påverka vår psykiska hälsa. Om det skett någon förändring i detta samband under pandemin var inte heller helt klarlagt, men vissa tendenser tycktes kunna ses. När man kollade på det totala antalet besök till psykiatriakuten verkade sambandet inte ha ändrats något nämnvärt, men för vissa grupper kunde en antydning till förändring ses. Det verkade framför allt som att patienter utan pågående kontakt med psykiatri sedan tidigare blev mer benägna att söka psykiatriakuten när det var mer föroreningar i luften under pandemin, liksom individer över 65 år och de av manligt kön.

Luftföroreningars negativa påverkan på psykisk hälsa kan bidra till att uppmärksamma vikten av att minska luftföroreningarna i världen. Kunskapen om hur vi påverkas psykiskt av miljöföroreningar och pandemier är även viktig för att öka förståelsen om vilka faktorer som

kan påverka psykisk ohälsa, och kan bidra till framtida forskning inom ämnet. Författarna till studien är dock tydliga med att fler studier under längre perioder behövs innan man kan dra några säkra slutsatser utifrån resultaten.

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References

1. Vigo D, Thornicroft G, Atun R. Estimating the true global burden of mental illness. *Lancet Psychiatry*. 2016;3(2):171-8.
2. Marazziti D, Cianconi P, Mucci F, Foresi L, Chiarantini I, Della Vecchia A. Climate change, environment pollution, COVID-19 pandemic and mental health. *Sci Total Environ*. 2021;773:145182.
3. Bachmann S. Epidemiology of Suicide and the Psychiatric Perspective. *International Journal of Environmental Research and Public Health*. 2018;15(7):1425.
4. WHO. Sustainable Development Goals (SDGs) 2021 [Available from: https://www.who.int/health-topics/sustainable-development-goals#tab=tab_1].
5. WHO. Mental Health 2021 [Available from: https://www.who.int/health-topics/mental-health#tab=tab_1].
6. Public Health Agency of Sweden. Statistik psykisk hälsa 2021 [updated June 2, 2021. Available from: <https://www.folkhalsomyndigheten.se/livsvillkor-levnadsvanor/psykisk-halsa-och-suicidprevention/statistik-psykisk-halsa/>].
7. National Board of Health and Welfare. Patientregistret 2021 [updated June 15, 2021. Available from: <https://www.socialstyrelsen.se/statistik-och-data/register/alla-register/patientregistret/>].
8. Bäärnhielm S, Sundvall M. Clinical challenges in cultural psychiatry – searching for meaning, searching for methods†. *Nordic Journal of Psychiatry*. 2018;72(sup1):S9-S12.
9. Costa LG, Cole TB, Dao K, Chang Y-C, Coburn J, Garrick JM. Effects of air pollution on the nervous system and its possible role in neurodevelopmental and neurodegenerative disorders. *Pharmacology & Therapeutics*. 2020;210:107523.
10. Chan JF, Zhang AJ, Yuan S, Poon VK, Chan CC, Lee AC, et al. Simulation of the Clinical and Pathological Manifestations of Coronavirus Disease 2019 (COVID-19) in a Golden Syrian Hamster Model: Implications for Disease Pathogenesis and Transmissibility. *Clin Infect Dis*. 2020;71(9):2428-46.
11. Paniz-Mondolfi A, Bryce C, Grimes Z, Gordon RE, Reidy J, Lednicky J, et al. Central nervous system involvement by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). *Journal of Medical Virology*. 2020;92(7):699-702.
12. Steardo L, Steardo L, Verkhatsky A. Psychiatric face of COVID-19. *Translational Psychiatry*. 2020;10(1).
13. Torres JM, Casey JA. The centrality of social ties to climate migration and mental health. *BMC Public Health*. 2017;17(1):600.
14. Lim SS, Vos T, Flaxman AD, Danaei G, Shibuya K, Adair-Rohani H, et al. A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. *The Lancet*. 2012;380(9859):2224-60.
15. WHO. Air pollution [Available from: https://www.who.int/health-topics/air-pollution#tab=tab_1].
16. Carlsen HK, Nyberg F, Torén K, Segersson D, Olin AC. Exposure to traffic-related particle matter and effects on lung function and potential interactions in a cross-sectional analysis of a cohort study in west Sweden. *BMJ Open*. 2020;10(10):e034136.
17. Young MT, Sandler DP, DeRoo LA, Vedal S, Kaufman JD, London SJ. Ambient air pollution exposure and incident adult asthma in a nationwide cohort of U.S. women. *Am J Respir Crit Care Med*. 2014;190(8):914-21.
18. Kurt OK, Zhang J, Pinkerton KE. Pulmonary health effects of air pollution. *Curr Opin Pulm Med*. 2016;22(2):138-43.
19. Xing YF, Xu YH, Shi MH, Lian YX. The impact of PM2.5 on the human respiratory system. *J Thorac Dis*. 2016;8(1):E69-74.
20. Kelly FJ, Fussell JC. Air pollution and airway disease. *Clin Exp Allergy*. 2011;41(8):1059-71.
21. Franklin BA, Brook R, Arden Pope C, 3rd. Air pollution and cardiovascular disease. *Curr Probl Cardiol*. 2015;40(5):207-38.

22. Brook RD, Franklin B, Cascio W, Hong Y, Howard G, Lipsett M, et al. Air pollution and cardiovascular disease: a statement for healthcare professionals from the Expert Panel on Population and Prevention Science of the American Heart Association. *Circulation*. 2004;109(21):2655-71.
23. Lu JG. Air pollution: A systematic review of its psychological, economic, and social effects. *Curr Opin Psychol*. 2020;32:52-65.
24. Srimuruganandam B, Shiva Nagendra SM. Source characterization of PM10 and PM2.5 mass using a chemical mass balance model at urban roadside. *Science of The Total Environment*. 2012;433:8-19.
25. Reizer M, Juda-Rezler K. Explaining the high PM10 concentrations observed in Polish urban areas. *Air Quality, Atmosphere & Health*. 2016;9(5):517-31.
26. Orru K, Orru H, Maasikmets M, Hendrikson R, Ainsaar M. Well-being and environmental quality: Does pollution affect life satisfaction? *Quality of Life Research*. 2016;25(3):699-705.
27. Vert C, Sánchez-Benavides G, Martínez D, Gotsens X, Gramunt N, Cirach M, et al. Effect of long-term exposure to air pollution on anxiety and depression in adults: A cross-sectional study. *Int J Hyg Environ Health*. 2017;220(6):1074-80.
28. Pedersen CB, Raaschou-Nielsen O, Hertel O, Mortensen PB. Air pollution from traffic and schizophrenia risk. *Schizophr Res*. 2004;66(1):83-5.
29. Volk HE, Lurmann F, Penfold B, Hertz-Picciotto I, McConnell R. Traffic-Related Air Pollution, Particulate Matter, and Autism. *JAMA Psychiatry*. 2013;70(1):71.
30. Szyszkowicz M, Thomson EM, Colman I, Rowe BH. Ambient air pollution exposure and emergency department visits for substance abuse. *PLOS ONE*. 2018;13(6):e0199826.
31. Liu W, Sun H, Zhang X, Chen Q, Xu Y, Chen X, et al. Air pollution associated with non-suicidal self-injury in Chinese adolescent students: A cross-sectional study. *Chemosphere*. 2018;209:944-9.
32. Kim C, Jung SH, Kang DR, Kim HC, Moon KT, Hur NW, et al. Ambient Particulate Matter as a Risk Factor for Suicide. *American Journal of Psychiatry*. 2010;167(9):1100-7.
33. Chen JC, Schwartz J. Neurobehavioral effects of ambient air pollution on cognitive performance in US adults. *Neurotoxicology*. 2009;30(2):231-9.
34. Audrain-McGovern J, Rodriguez D, Kassel JD. Adolescent smoking and depression: evidence for self-medication and peer smoking mediation. *Addiction*. 2009;104(10):1743-56.
35. Patton GC, Carlin JB, Coffey C, Wolfe R, Hibbert M, Bowes G. Depression, anxiety, and smoking initiation: a prospective study over 3 years. *Am J Public Health*. 1998;88(10):1518-22.
36. Lipari RN, Van Horn S. Smoking and Mental Illness Among Adults in the United States. *The CBHSQ Report*. Rockville (MD): Substance Abuse and Mental Health Services Administration (US); 2013. p. 1-.
37. Kim SH, Shin SD, Song KJ, Ro YS, Kong SY, Kim J, et al. Association between ambient PM2.5 and emergency department visits for psychiatric emergency diseases. *The American Journal of Emergency Medicine*. 2019;37(9):1649-56.
38. Oudin A, Åström DO, Asplund P, Steingrímsson S, Szabo Z, Carlsen HK. The association between daily concentrations of air pollution and visits to a psychiatric emergency unit: a case-crossover study. *Environ Health*. 2018;17(1):4.
39. Muhsin HA, Steingrímsson S, Oudin A, Åström DO, Carlsen HK. Air pollution and increased number of psychiatric emergency room visits: A case-crossover study for identifying susceptible groups. *Environ Res*. 2021;204(Pt A):112001.
40. Calderón-Garcidueñas L, Solt AC, Henríquez-Roldán C, Torres-Jardón R, Nuse B, Herritt L, et al. Long-term Air Pollution Exposure Is Associated with Neuroinflammation, an Altered Innate Immune Response, Disruption of the Blood-Brain Barrier, Ultrafine Particulate Deposition, and Accumulation of Amyloid β -42 and α -Synuclein in Children and Young Adult. *Toxicologic Pathology*. 2008;36(2):289-310.
41. Fonken LK, Xu X, Weil ZM, Chen G, Sun Q, Rajagopalan S, et al. Air pollution impairs cognition, provokes depressive-like behaviors and alters hippocampal cytokine expression and morphology. *Mol Psychiatry*. 2011;16(10):987-95, 73.

42. Kido T, Tamagawa E, Bai N, Suda K, Yang H-HC, Li Y, et al. Particulate Matter Induces Translocation of IL-6 from the Lung to the Systemic Circulation. *American Journal of Respiratory Cell and Molecular Biology*. 2011;44(2):197-204.
43. Eeden SFV, Hogg JC. SYSTEMIC INFLAMMATORY RESPONSE INDUCED BY PARTICULATE MATTER AIR POLLUTION: THE IMPORTANCE OF BONE-MARROW STIMULATION. *Journal of Toxicology and Environmental Health, Part A*. 2002;65(20):1597-613.
44. Thomson EM, Vladisavljevic D, Mohottalage S, Kumarathasan P, Vincent R. Mapping acute systemic effects of inhaled particulate matter and ozone: multiorgan gene expression and glucocorticoid activity. *Toxicol Sci*. 2013;135(1):169-81.
45. Pariante CM. Why are depressed patients inflamed? A reflection on 20 years of research on depression, glucocorticoid resistance and inflammation. *Eur Neuropsychopharmacol*. 2017;27(6):554-9.
46. Wei H, Feng Y, Liang F, Cheng W, Wu X, Zhou R, et al. Role of oxidative stress and DNA hydroxymethylation in the neurotoxicity of fine particulate matter. *Toxicology*. 2017;380:94-103.
47. Wang W, Bu B, Xie M, Zhang M, Yu Z, Tao D. Neural cell cycle dysregulation and central nervous system diseases. *Prog Neurobiol*. 2009;89(1):1-17.
48. Bryner J. 1st known case of coronavirus traced back to November in China 2020 [Available from: <https://www.livescience.com/first-case-coronavirus-found.html>].
49. Salian VS, Wright JA, Vedell PT, Nair S, Li C, Kandimalla M, et al. COVID-19 Transmission, Current Treatment, and Future Therapeutic Strategies. *Molecular Pharmaceutics*. 2021;18(3):754-71.
50. Atzrodt CL, Maknojia I, McCarthy RDP, Oldfield TM, Po J, Ta KTL, et al. A Guide to COVID-19: a global pandemic caused by the novel coronavirus SARS-CoV-2. *The FEBS Journal*. 2020;287(17):3633-50.
51. Zhou P, Yang X-L, Wang X-G, Hu B, Zhang L, Zhang W, et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. *Nature*. 2020;579(7798):270-3.
52. Adil MT, Rahman R, Whitelaw D, Jain V, Al-Taan O, Rashid F, et al. SARS-CoV-2 and the pandemic of COVID-19. *Postgraduate Medical Journal*. 2021;97(1144):110-6.
53. WHO. 2019-nCoV outbreak is an emergency of international concern 2020 [Available from: <https://www.euro.who.int/en/health-topics/health-emergencies/international-health-regulations/news/news/2020/2/2019-ncov-outbreak-is-an-emergency-of-international-concern>].
54. WHO. WHO Coronavirus (COVID-19) Dashboard 2021 [Available from: <https://covid19.who.int/>].
55. Hao F, Tan W, Jiang L, Zhang L, Zhao X, Zou Y, et al. Do psychiatric patients experience more psychiatric symptoms during COVID-19 pandemic and lockdown? A case-control study with service and research implications for immunopsychiatry. *Brain, Behavior, and Immunity*. 2020;87:100-6.
56. Hossain MM, Tasnim S, Sultana A, Faizah F, Mazumder H, Zou L, et al. Epidemiology of mental health problems in COVID-19: a review. *F1000Res*. 2020;9:636.
57. Huang Y, Zhao N. Generalized anxiety disorder, depressive symptoms and sleep quality during COVID-19 outbreak in China: a web-based cross-sectional survey. *Psychiatry Research*. 2020;288:112954.
58. Lei L, Huang X, Zhang S, Yang J, Yang L, Xu M. Comparison of Prevalence and Associated Factors of Anxiety and Depression Among People Affected by versus People Unaffected by Quarantine During the COVID-19 Epidemic in Southwestern China. *Medical Science Monitor*. 2020;26.
59. Mazza C, Ricci E, Biondi S, Colasanti M, Ferracuti S, Napoli C, et al. A Nationwide Survey of Psychological Distress among Italian People during the COVID-19 Pandemic: Immediate Psychological Responses and Associated Factors. *International Journal of Environmental Research and Public Health*. 2020;17(9):3165.
60. Ahmed MZ, Ahmed O, Aibao Z, Hanbin S, Siyu L, Ahmad A. Epidemic of COVID-19 in China and associated Psychological Problems. *Asian Journal of Psychiatry*. 2020;51:102092.

61. Gao J, Zheng P, Jia Y, Chen H, Mao Y, Chen S, et al. Mental health problems and social media exposure during COVID-19 outbreak. *PLOS ONE*. 2020;15(4):e0231924.
62. Wang Y, Di Y, Ye J, Wei W. Study on the public psychological states and its related factors during the outbreak of coronavirus disease 2019 (COVID-19) in some regions of China. *Psychology, Health & Medicine*. 2021;26(1):13-22.
63. Zhang Y, Ma ZF. Impact of the COVID-19 Pandemic on Mental Health and Quality of Life among Local Residents in Liaoning Province, China: A Cross-Sectional Study. *International Journal of Environmental Research and Public Health*. 2020;17(7):2381.
64. Wang H, Xia Q, Xiong Z, Li Z, Xiang W, Yuan Y, et al. The psychological distress and coping styles in the early stages of the 2019 coronavirus disease (COVID-19) epidemic in the general mainland Chinese population: A web-based survey. *PLOS ONE*. 2020;15(5):e0233410.
65. Montalbani B, Bargagna P, Mastrangelo M, Sarubbi S, Imbastro B, De Luca GP, et al. The COVID-19 Outbreak and Subjects With Mental Disorders Who Presented to an Italian Psychiatric Emergency Department. *J Nerv Ment Dis*. 2021;209(4):246-50.
66. Ambrosetti J, Macheret L, Folliet A, Wullschleger A, Amerio A, Aguglia A, et al. Impact of the COVID-19 Pandemic on Psychiatric Admissions to a Large Swiss Emergency Department: An Observational Study. *International Journal of Environmental Research and Public Health*. 2021;18(3):1174.
67. Hoyer C, Ebert A, Szabo K, Platten M, Meyer-Lindenberg A, Kranaster L. Decreased utilization of mental health emergency service during the COVID-19 pandemic. *European Archives of Psychiatry and Clinical Neuroscience*. 2021;271(2):377-9.
68. Gonçalves-Pinho M, Mota P, Ribeiro J, Macedo S, Freitas A. The Impact of COVID-19 Pandemic on Psychiatric Emergency Department Visits – A Descriptive Study. *Psychiatric Quarterly*. 2021;92(2):621-31.
69. Kim HK, Carvalho AF, Gratzer D, Wong AHC, Gutzin S, Husain MI, et al. The Impact of COVID-19 on Psychiatric Emergency and Inpatient Services in the First Month of the Pandemic in a Large Urban Mental Health Hospital in Ontario, Canada. *Front Psychiatry*. 2021;12:563906.
70. Butler M, Delvi A, Mujic F, Broad S, Pauli L, Pollak TA, et al. Reduced Activity in an Inpatient Liaison Psychiatry Service During the First Wave of the COVID-19 Pandemic: Comparison With 2019 Data and Characterization of the SARS-CoV-2 Positive Cohort. *Front Psychiatry*. 2021;12:619550.
71. Gómez-Ramiro M, Fico G, Anmella G, Vázquez M, Sagué-Vilavella M, Hidalgo-Mazzei D, et al. Changing trends in psychiatric emergency service admissions during the COVID-19 outbreak: Report from a worldwide epicentre. *J Affect Disord*. 2021;282:26-32.
72. Clerici M, Durbano F, Spinogatti F, Vita A, de Girolamo G, Micciolo R. Psychiatric hospitalization rates in Italy before and during COVID-19: did they change? An analysis of register data. *Ir J Psychol Med*. 2020;37(4):283-90.
73. Boldrini T, Girardi P, Clerici M, Conca A, Creati C, Di Cicilia G, et al. Consequences of the COVID-19 pandemic on admissions to general hospital psychiatric wards in Italy: Reduced psychiatric hospitalizations and increased suicidality. *Prog Neuropsychopharmacol Biol Psychiatry*. 2021;110:110304.
74. Ferrando SJ, Klepacz L, Lynch S, Shahar S, Dornbush R, Smiley A, et al. Psychiatric emergencies during the height of the COVID-19 pandemic in the suburban New York City area. *J Psychiatr Res*. 2021;136:552-9.
75. Torkelsson A-C. FHM: Inget bakslag för psykiska hälsan i pandemins spår 2021 [Available from: <https://lakartidningen.se/aktuellt/nyheter/2021/09/fhm-inget-bakslag-for-psykiska-halsan-i-pandemins-spar/#>].
76. Loh HC, Looi I, Ch'Ng ASH, Goh KW, Ming LC, Ang KH. Positive global environmental impacts of the COVID-19 pandemic lockdown: a review. *GeoJournal*. 2021.
77. Bashir MF, Ma B, Shahzad L. A brief review of socio-economic and environmental impact of Covid-19. *Air Qual Atmos Health*. 2020:1-7.
78. Zambrano-Monserrate MA, Ruano MA. Has air quality improved in Ecuador during the COVID-19 pandemic? A parametric analysis. *Air Quality, Atmosphere & Health*. 2020;13(8):929-38.

79. Chen C, Liu C, Chen R, Wang W, Li W, Kan H, et al. Ambient air pollution and daily hospital admissions for mental disorders in Shanghai, China. *Sci Total Environ*. 2018;613-614:324-30.
80. Agarwal A, Kaushik A, Kumar S, Mishra RK. Comparative study on air quality status in Indian and Chinese cities before and during the COVID-19 lockdown period. *Air Qual Atmos Health*. 2020:1-12.
81. Public Health Agency of Sweden. När hände vad under pandemin? 2021 [updated October 7, 2021. Available from: <https://www.folkhalsomyndigheten.se/smittskydd-beredskap/utbrott/aktuella-utbrott/covid-19/folkhalsomyndighetens-arbete-med-covid-19/nar-hande-vad-under-pandemin/>].
82. Public Health Agency of Sweden. Covid-19 2020 [Available from: <https://www.folkhalsomyndigheten.se/the-public-health-agency-of-sweden/>].
83. Hadlaczky G, Stefenson A, Wasserman D. The state of psychiatry in Sweden. *Int Rev Psychiatry*. 2012;24(4):356-62.
84. Gasparrini A, Armstrong B, Kenward MG. Distributed lag non-linear models. *Stat Med*. 2010;29(21):2224-34.
85. Franklin M, Zeka A, Schwartz J. Association between PM2.5 and all-cause and specific-cause mortality in 27 US communities. *J Expo Sci Environ Epidemiol*. 2007;17(3):279-87.
86. Kan H, London SJ, Chen G, Zhang Y, Song G, Zhao N, et al. Season, sex, age, and education as modifiers of the effects of outdoor air pollution on daily mortality in Shanghai, China: The Public Health and Air Pollution in Asia (PAPA) Study. *Environ Health Perspect*. 2008;116(9):1183-8.
87. Sunyer J, Jarvis D, Gotschi T, Garcia-Esteban R, Jacquemin B, Aguilera I, et al. Chronic bronchitis and urban air pollution in an international study. *Occup Environ Med*. 2006;63(12):836-43.
88. Brunekreef B, Janssen NA, de Hartog J, Harssema H, Knape M, van Vliet P. Air pollution from truck traffic and lung function in children living near motorways. *Epidemiology*. 1997;8(3):298-303.
89. Liu G, Sun B, Yu L, Chen J, Han B, Li Y, et al. The Gender-Based Differences in Vulnerability to Ambient Air Pollution and Cerebrovascular Disease Mortality: Evidences Based on 26781 Deaths. *Glob Heart*. 2020;15(1):46.
90. Kim H, Noh J, Noh Y, Oh SS, Koh SB, Kim C. Gender Difference in the Effects of Outdoor Air Pollution on Cognitive Function Among Elderly in Korea. *Front Public Health*. 2019;7:375.
91. Luginaah IN, Fung KY, Gorey KM, Webster G, Wills C. Association of ambient air pollution with respiratory hospitalization in a government-designated "area of concern": the case of Windsor, Ontario. *Environ Health Perspect*. 2005;113(3):290-6.
92. Kim CS, Hu SC. Regional deposition of inhaled particles in human lungs: comparison between men and women. *J Appl Physiol* (1985). 1998;84(6):1834-44.
93. Yunginger JW, Reed CE, O'Connell EJ, Melton LJ, 3rd, O'Fallon WM, Silverstein MD. A community-based study of the epidemiology of asthma. Incidence rates, 1964-1983. *Am Rev Respir Dis*. 1992;146(4):888-94.
94. Silveira Campos L, Brigagão de Oliveira M, Peixoto Caldas JM. COVID 19: sexual vulnerabilities and gender perspectives in Latin America. *Health Care Women Int*. 2020;41(11-12):1207-9.
95. Tong L, Li K, Zhou Q. Season, sex and age as modifiers in the association of psychosis morbidity with air pollutants: A rising problem in a Chinese metropolis. *Sci Total Environ*. 2016;541:928-33.
96. Zeka A, Zanobetti A, Schwartz J. Individual-level modifiers of the effects of particulate matter on daily mortality. *Am J Epidemiol*. 2006;163(9):849-59.
97. Shumake KL, Sacks JD, Lee JS, Johns DO. Susceptibility of older adults to health effects induced by ambient air pollutants regulated by the European Union and the United States. *Aging Clin Exp Res*. 2013;25(1):3-8.
98. Simoni M, Baldacci S, Maio S, Cerrai S, Sarno G, Viegi G. Adverse effects of outdoor pollution in the elderly. *J Thorac Dis*. 2015;7(1):34-45.

99. Lippmann M, Frampton M, Schwartz J, Dockery D, Schlesinger R, Koutrakis P, et al. The U.S. Environmental Protection Agency Particulate Matter Health Effects Research Centers Program: a midcourse report of status, progress, and plans. *Environ Health Perspect.* 2003;111(8):1074-92.
100. Geller AM, Zenick H. Aging and the environment: a research framework. *Environ Health Perspect.* 2005;113(9):1257-62.
101. Williams R, Suggs J, Creason J, Rodes C, Lawless P, Kwok R, et al. The 1998 Baltimore Particulate Matter Epidemiology-Exposure Study: part 2. Personal exposure assessment associated with an elderly study population. *J Expo Anal Environ Epidemiol.* 2000;10(6 Pt 1):533-43.
102. Williams R, Suggs J, Zweidinger R, Evans G, Creason J, Kwok R, et al. The 1998 Baltimore Particulate Matter Epidemiology-Exposure Study: part 1. Comparison of ambient, residential outdoor, indoor and apartment particulate matter monitoring. *J Expo Anal Environ Epidemiol.* 2000;10(6 Pt 1):518-32.