Original papers

Association between the long-term exposure to air pollution and depression

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Abstract

Background. Air pollution has a negative influence on neurological and psychiatric disorders. However, findings concerning the impact of air pollution on depression remain inconclusive. A deeper insight into these associations is warranted.

Objectives. To evaluate the impact of long-term exposure to air pollution on the incidence of depression among residents of 13 counties in the Lower Silesia region of Poland.

Materials and methods. We used data on cases of depression from the National Health Fund (Narodowy Fundusz Zdrowia – NFZ) from 13 counties of Lower Silesia between January 1, 2010, and December 31, 2015. Patients with a confirmed diagnosis of depression were included. Data on air pollution levels were extracted from the Chief Inspectorate of Environmental Protection (Główny Inspektorat Ochrony Środowiska – GIOŚ), and demographic data were extracted from Statistics Poland (Główny Urząd Statystyczny – GUS).

Results. The percentage of people diagnosed with depression over the 6-year study period depended on the group of counties homogeneous in terms of air pollution exposure ($p < 0.001$). We showed statistically significant correlations between different depression diagnoses and exposure to air pollutants. Elevated concentration of airborne fine particles with a diameter less than 2.5 µm ($PM_{2.5}$) and carbon monoxide (CO), and low benzo(a)pyrene (BaP), sulfur dioxide (SO_2) and cadmium (Cd) levels were independent risk factors for major depressive episodes with psychotic symptoms (F32.3). There was a significant negative correlation between ozone (O_3) levels and depression incidence.

Conclusions. Regions with heavy air pollution had a higher incidence of depression. There is a significant association between the exposure to air pollutants and different depression diagnoses.

Key words: depression, air pollution, particulate matter, ozone, nitrogen oxides

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Background

Depression is a mental disorder that affects 264 million people worldwide, and is a major cause of disability.[1] Beck described depression as a combination of disturbed thinking, low mood and a negative perception of self, the surrounding world and the future.[2] Depression is associated with excess mortality[3] and increased suicide risk.[4] There are many risk factors for depression,[5] such as female gender, chronic illness, traumatic life events,[6] unemployment, lower education, a lack of physical activity, and limited social support.[7]

In recent years, there has been an increasing interest in the environmental risk factors for depression.[8] Lack of green spaces, poor quality of housing, chronic noise exposure, and air pollution are all strongly associated with risk of depression.[9] Both chronic stress[10] and gene–environment interactions[11] contribute to risk for psychiatric illnesses, such as depression. Neuroinflammation is one of the main pathogenic mechanisms implicated in depression.[12] A prominent environmental risk factor associated with neuroinflammation is air pollution.[13] The exposure to intense air pollution may disrupt metabolic processes and thus lead to inflammation.[14] For example, experimental studies have shown that high concentrations of air pollutants are associated with systemic inflammation and insulin resistance.[15,16]

Long-term exposure to certain air pollutants leads to low-grade inflammation.[17] In response, more anti-inflammatory cytokines are released, in turn causing immune tolerance. Chronic inflammation is also linked to the activation of the kynurenine (KYN) metabolic pathway of tryptophan, leading to the synthesis of various oxidant and immunomodulating molecules at the expense of the serotonin production.[18] These metabolites modulate the immune system towards low-grade inflammation, strengthening the vicious cycle of the immune response.[19] The KYN pathway plays a role in the pathogenesis of neurodegenerative and psychiatric diseases.[18] The levels of quinolinic acid (a toxin produced by KYN pathway) are increased in patients with major depression.[20] Moreover, experimental data indicate that one compound of air pollution, ozone (O_3), causes increased concentration of kynurenine.[21] These mechanisms could explain the adverse impact of air pollution on neuroinflammation and risk for mental illnesses.

Air pollution is a mixture of various particles and gases suspended in the air, such as particulate matter (coarse particles with an aerodynamic diameter between 2.5 μm and 10 μm (PM_{10}), fine particles with a diameter less than 2.5 μm ($PM_{2.5}$), and ultrafine particles with a diameter less than 0.1 μm ($PM_{0.1}$)), e.g., O_3, carbon monoxide (CO), sulfur dioxide (SO_2), nitrogen oxides (NO_x), nitrogen dioxide (NO_2), and polycyclic aromatic hydrocarbons (PAHs). Their main sources are anthropogenic emissions from traffic, industry and coal stoves.[22] The Lancet Commission highlighted that air pollution is one of the main environmental causes of disease and premature death.[23] It is estimated that 8.79 million people worldwide died prematurely in 2019.[24] Studies consistently indicate that increased mortality associated with exposure to air pollutants is largely due to cardiovascular and respiratory diseases.[14] The health impact of air pollutants has been broadened to include neurological and psychiatric disorders such as anxiety, depression and dementia.[25] Research on these associations is extremely important, since mental and neurological conditions are among the main causes of disability, including 30% of all strokes being related to air pollution.[26]

There are some proposed mechanisms whereby air pollutants can negatively affect the brain. For instance, particulate matter can reach the systemic circulation through the lungs or through olfactory neurons,[27] and directly interact with the brain.[28] Especially dangerous are ultrafine particles which, due to their small size and the toxic compounds bound to them, can cause pathophysiological alterations in the central nervous system.[28] Another mechanism is alveolar inflammation, which leads to the production of cytokines[29] that can penetrate the blood–brain barrier.[30] The exposure to air pollutants triggers the activation of the hypothalamic–pituitary–adrenal (HPA) axis and the release of stress hormones,[31] which is commonly associated with cardiovascular disease (CVD), type II diabetes mellitus, dementia, and depression.[32] These mechanisms can explain the negative effect of air pollution on the central nervous system and mental health.[33]

Findings on the impact of air pollution on depression remain inconclusive. Two meta-analyses confirmed that a long-term exposure to fine particles is associated with increased incidence of depression[34] and suicide risk.[35] Another study showed that $PM_{2.5}$ is significantly associated with the occurrence of depression for both long, and short-term exposure.[36] Long-term exposure to $PM_{2.5}$ and short-term exposure to PM_{10}, NO_2, SO_2, and CO, are risk factors for depression.[37] On the other hand, a meta-analysis of 22 studies showed a weaker relationship between air pollution and depression risk. This includes long-term exposure to $PM_{2.5}$, PM_{10} and NO_2, as well as short-term exposure to $PM_{2.5}$, PM_{10}, SO_2, O_3, and NO_2.[38] Moreover, current studies are based mostly on self-reports, and they do not specify the association between air pollution and the sub-diagnoses of depression.[34,37] No studies have examined the relationship between the exposure to air pollution and risk for depression with psychotic symptoms. There is also not enough evidence on long-term exposure to many different air pollutants and its impact on depression, especially at the sub-diagnosis level. Therefore, a deeper insight into these associations is important, and more data are needed to clarify the impact of air pollutants on depression risk.

Objectives

The aim of this study was to evaluate the impact of long-term exposure to air pollution on depression risk among residents of 13 counties in Lower Silesia (Poland).

Materials and methods

Data on depression cases used in the study were derived from the National Health Fund (Narodowy Fundusz Zdrowia – NFZ) from counties (Polish: powiat; Głogów, Jelenia Góra, Kłodzko, Legnica, Lubań, Oława, Oleśnica, Polkowice, Złotoryja, Zgorzelec, Wałbrzych, Świdnica, and Wrocław) pertaining the period between January 1, 2010, and December 31, 2015. The inclusion criteria were based on the International Classification of Diseases, 10th Revision (ICD-10) code diagnosis: F32 (depressive episode), F32.0 (mild depressive episode), F32.1 (moderate depressive episode), F32.2 (severe depressive episode without psychotic symptoms), F32.3 (severe depressive episode with psychotic symptoms), F33 (recurrent depressive disorder), F33.0 (recurrent depressive disorder, current episode mild), F33.1 (recurrent depressive disorder, current episode moderate), F33.2 (recurrent depressive disorder, current episode severe without psychotic symptoms), and F33.3 (recurrent depressive disorder, current episode severe with psychotic symptoms). In total, data on depression diagnoses were available for 318,779 individuals per study year. Data on air pollution levels were extracted from the Chief Inspectorate of Environmental Protection (Główny Inspektorat Ochrony Środowiska – GIOŚ) and covered the period from 2010 to 2015. Considered pollutants included: PM_{10}, $PM_{2.5}$, SO_2, NO_x, benzo(a)pyrene (BaP)(PM_{10}), O_3, CO, and NO_2. We used demographic data for the period 2010–2015 from Statistics Poland (Główny Urząd Statystyczny – GUS), including marriage and divorce rate, feminization rate, non-working population, working people, people >65 years old, medical help accessibility, beneficiaries of social welfare, unemployment, average salary, and total pollution emissions. Two statistical methods were used. Cluster analysis was used to distinguish between counties homogeneous in terms of air pollution. The 2nd method utilized all county data to perform univariate and multivariate regression analyses, and an analysis of variance (ANOVA). For multivariate and ANOVA analyses, data on marriage and divorce rate, feminization rate, non-working population, working people, people >65 years old, medical help accessibility, beneficiaries of social welfare, unemployment, average salary, total pollution emissions, and PM_{10}, $PM_{2.5}$, SO_2, NO_x, BaP(PM_{10}), O_3, CO, and NO_2 concentrations were used. For univariate analyses, we used depression rate and its associations with PM_{10}, $PM_{2.5}$, SO_2, NO_x, BaP(PM_{10}), O_3, CO, and NO_2 concentrations. The homogeneity of variance in the groups was verified using the Levene's test. In the case of unequal variances in the compared groups, the Welch's correction was applied. Normality of distribution was determined using the Kolmogorov–Smirnov and Shapiro–Wilk tests. For the construction of multivariate linear regression models, non-normal data were transformed using the Box–Cox method.

Results

Air pollution

Table 1 presents data on air pollutant levels. Cluster analysis was used to distinguish homogeneous counties in terms of air pollution. It was possible to reduce a whole set to the average of individual groups. The Euclidean distance was used as a dissimilarity measure. Based

Table 1. Average air pollutant levels (2010–2015) in 13 counties of Lower Silesia (Me (IQR))

County	$PM_{2.5}$ [μm/m^3]	PM_{10} [μm/m^3]	NO_2 [μm/m^3]	CO [μm/m^3]	Pb [μm/m^3]	SO_2 [μm/m^3]
Głogów	27.5 (1.1)	30.0 (7.5)	11.3 (2.3)	0.36 (0.10)	0.052 (0.021)	5.8 (1.5)
Jelenia Góra	27.2 (1.5)	44.8 (21.0)	15.7 (4.4)	0.45 (0.20)	0.033 (0.017)	10.4 (3.6)
Kłodzko	29.2 (1.4)	32.0 (5.6)	19.1 (4.6)	0.47 (0.02)	0.032 (0.007)	10.0 (2.7)
Legnica	26.7 (4.3)	34.1 (6.7)	22.6 (4.1)	0.47 (0.03)	0.049 (0.008)	7.6 (1.6)
Lubań	17.2 (1.6)	22.4 (4.4)	5.9 (1.8)	0.32 (0.00)	0.009 (0.008)	5.6 (2.1)
Oława	23.9 (1.1)	35.0 (6.7)	17.7 (2.0)	0.41 (0.04)	0.023 (0.004)	7.8 (0.2)
Oleśnica	24.2 (1.6)	31.3 (3.4)	18.8 (0.2)	0.41 (0.02)	0.030 (0.002)	7.1 (1.5)
Polkowice	22.4 (1.6)	29.4 (5.2)	10.4 (7.7)	0.38 (0.01)	0.025 (0.011)	6.5 (2.6)
Złotoryja	25.7 (1.8)	33.7 (3.5)	10.8 (3.7)	0.44 (0.05)	0.032 (0.002)	7.1 (1.2)
Zgorzelec	21.6 (4.8)	23.9 (12.3)	15.8 (9.8)	0.39 (0.05)	0.024 (0.005)	7.5 (1.8)
Wałbrzych	23.9 (2.0)	27.0 (5.1)	15.4 (2.4)	0.39 (0.08)	0.033 (0.015)	8.5 (3.0)
Świdnica	25.7 (2.6)	18.4 (12.2)	16.8 (1.8)	0.41 (0.07)	0.035 (0.004)	11.8 (1.9)
Wrocław	30.6 (1.6)	39.0 (9.5)	55.1 (10.6)	0.61 (0.15)	0.025 (0.009)	6.1 (0.9)
All	25.2 (4.7)	31.1 (8.7)	16.5 (7.6)	0.41 (0.09)	0.030 (0.014)	7.5 (2.9)

Me (IQR) – median and interquartile range; $PM_{2.5}$ – atmospheric aerosols with a diameter of not more than 2.5 μm (the average daily dust standard ≤25 μg/m^3 and average annual standard ≤10 μg/m^3); PM_{10} – a mixture of suspended dusts with a diameter ≤10 μg (the average daily dust standard ≤200 μg/m^3 and average annual standard ≤20 μg/m^3); NO_2 – nitrogen dioxide; CO – carbon monoxide; Pb – lead; SO_2 – sulfur dioxide.

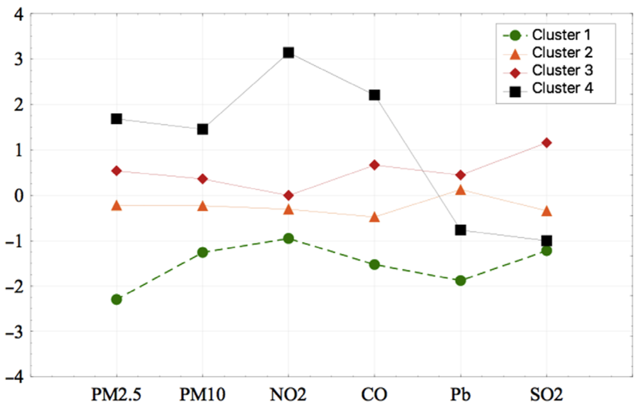


Fig. 1. Average values of pollution in 4 groups of counties (cluster 1 – Lubań county; cluster 2 – Głogów, Oława, Oleśnica, Polkowice, Złotoryja, Zgorzelec, and Wałbrzych counties; cluster 3 – Jelenia Góra, Kłodzko, Legnica, and Świdnica counties; cluster 4 – Wrocław county)

$PM_{2.5}$ – atmospheric aerosols with a diameter of not more than 2.5 μm (the average daily dust standard ≤25 μg/m^3 and average annual standard ≤10 μg/m^3); PM_{10} – a mixture of suspended dusts with a diameter ≤10 μg (the average daily dust standard ≤200 μg/m^3 and average annual standard ≤20 μg/m^3); NO_2 – nitrogen dioxide; CO – carbon monoxide; Pb – lead; SO_2 – sulfur dioxide.

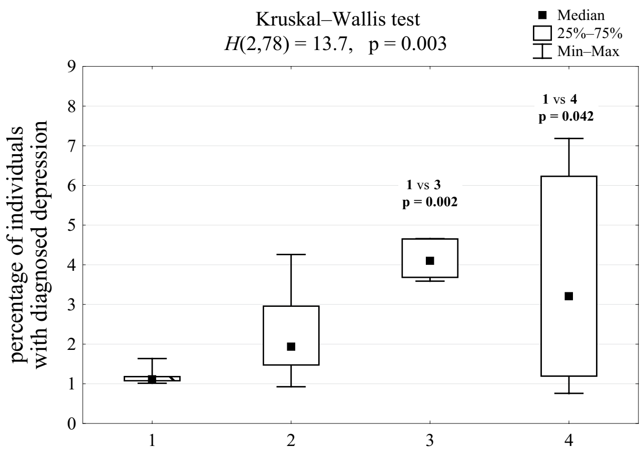


Fig. 2. Percentage of individuals with diagnosed depression in 4 groups of counties homogeneous in terms of air pollution, and results of the analysis of variance (ANOVA)

on the hierarchical structure of the set of counties, they were divided into 4 clusters homogeneous in terms of air pollution:

- cluster 1: Lubań county;
- cluster 2: Głogów, Oława, Oleśnica, Polkowice, Złotoryja, Zgorzelec, and Wałbrzych counties;
- cluster 3: Jelenia Góra, Kłodzko, Legnica, and Świdnica counties;
- cluster 4: Wrocław county.

A graph of average values (Fig. 1) for standardized air pollution parameters showed that the highest level of air pollution, except for lead (Pb) and SO_2, was recorded in the Wrocław county (cluster 4). The next most affected counties in terms of the level of air pollution were Jelenia Góra, Kłodzko, Legnica, and Świdnica (cluster 3). The lowest level of pollution was recorded in the Lubań county (cluster 1).

Depression cases

The number of people diagnosed with depression in 2010–2015 was compared between individual counties (Table 2). The structure index (percentage) of people diagnosed with depression in the next 6 years of observation did not change significantly ($p > 0.05$). However, this depended significantly ($p = 0.003$) on the group of counties homogeneous in terms of air pollution (Fig. 2). The average structure index of people diagnosed with depression between 2010 and 2015 across the 13 counties was 2.72 ±1.78% (women: 2.04 ±1.30%; men: 0.67 ±0.50%).

The linear relationships between depression diagnoses and air pollutant levels measured between 2010 and 2015 for all counties are summarized in Table 3. Since there were statistically significant correlations between the independent variables (predictors), the variance inflation factor (VIF) was estimated for each of them (Table 4). The strongest collinearity with PM_{10} was observed for NO_2 and NO_x (VIF > 10). Variables NO_2 and NO_x were excluded from the predictive model for estimating the depression rate. The concentration of PM_{10} ($r = 0.385$) and CO ($r = 0.344$) were significantly positively correlated with the frequency of severe depressive episodes with psychotic symptoms (F32.3). The concentration of O_3 was significantly negatively correlated with depression risk ($r = -0.283$). There were statistically significant correlations between different depression diagnoses and the following pollutants: $PM_{2.5}$ and F32 ($B = 0.303$), PM_{10} and F32, F32.0, F32.2, and F33; CO and F32, F32.0, F32.1, F32.2, F32.3, and F33; Pb(PM_{10}) and F32, F32.0, and F32.2; BaP(PM_{10}) and F32.0; arsenic (As)(PM_{10}) and F32, F32.0 and F32.2; and cadmium (Cd) (PM_{10}) and F32, F32.0 and F32.2. The O_3 levels were significantly negatively correlated with all depression diagnoses except F33.

Mathematical model of the occurrence of major depressive episodes with psychotic symptoms (F32.3)

The percentage of people diagnosed with a F32.3 in all counties was 0.23 ±0.19%. Table 5 presents the results of uni- and multivariate regression analyses of predictors associated with the risk for F32.3. The $PM_{2.5}$, CO, BaP, SO_2, and Cd levels were independently associated with the occurrence of F32.3. The formula for evaluating the structure index of F32.3 can be expressed as:

$$F32.3 = -403.4 + 10.8 \times PM_{2.5} + 379.8 \times CO + 24.1 \times Ni - 5.33 \times BaP - 6.44 \times SO_2 + 25.8 \times Cd$$

$$R = 0.803;\ F\ (\text{degrees of freedom (df)}: 7{,}70) = 18.2;\ p < 0.001$$

Table 2. Basic statistics (IQR) of the structure (‰) of depression diagnosis in 13 counties in 2010–2015

County	Percentage of people diagnosed with depression (ICD-10)					
	F32.0	F32.1	F32.2	F32.3	F33	F34
Głogów	6.1 (1.5)	1.2 (0.6)	4.2 (1.6)	0.2 (0.2)	0.1 (0.1)	10.6 (4.2)
Jelenia Góra	11.8 (5.4)	5.0 (3.4)	8.9 (4.9)	0.4 (0.4)	0.3 (0.3)	10.4 (2.2)
Kłodzko	2.8 (0.7)	0.5 (0.1)	0.6 (0.1)	0.1 (0.1)	0.1 (0.1)	1.4 (0.6)
Legnica	5.9 (1.1)	6.5 (1.8)	15.4 (6.2)	0.4 (0.1)	0.6 (0.3)	6.1 (1.5)
Lubań	2.0 (1.3)	0.7 (0.6)	1.8 (1.6)	0.2 (0.1)	0.1 (0.1)	2.3 (0.3)
Oława	1.2 (0.3)	1.0 (0.2)	1.2 (0.8)	0.1 (0.1)	0.2 (0.2)	3.5 (2.8)
Oleśnica	0.9 (0.7)	0.7 (0.2)	0.7 (0.3)	0.1 (0.0)	0.0 (0.0)	2.6 (0.7)
Polkowice	1.1 (0.4)	3.9 (1.2)	3.9 (2.7)	0.1 (0.1)	0.0 (0.0)	3.3 (2.3)
Złotoryja	1.3 (1.0)	0.9 (0.4)	4.0 (1.3)	0.1 (0.2)	0.1 (0.0)	3.4 (1.1)
Zgorzelec	5.9 (1.8)	1.1 (0.5)	1.5 (0.9)	0.2 (0.1)	0.2 (0.1)	3.6 (0.7)
Wałbrzych	4.4 (0.3)	4.8 (0.5)	5.4 (1.0)	0.5 (0.1)	0.4 (0.0)	4.5 (0.3)
Świdnica	2.3 (1.2)	0.7 (0.6)	1.3 (0.3)	0.1 (0.0)	0.0 (0.0)	3.8 (0.5)
Wrocław	3.3 (1.4)	4.6 (1.7)	4.4 (2.2)	0.4 (0.1)	0.4 (0.2)	4.9 (0.3)
Cluster 1	2.0 (1.3)	0.7 (0.6)	1.8 (1.6)	0.2 (0.1)	0.1 (0.1)	2.3 (0.3)
Cluster 2	1.6 (4.0)	1.1 (2.4)	2.9 (3.3)	0.2 (0.2)	0.1 (0.2)	3.7 (1.9)
Cluster 3	3.3 (1.4)	4.6 (1.7)	4.4 (2.2)	0.4 (0.1)	0.4 (0.2)	4.9 (0.3)
Cluster 4	4.9 (4.1)	2.1 (5.5)	3.6 (11.3)	0.2 (0.3)	0.1 (0.4)	4.8 (5.7)
All	3.1 (3.9)	1.3 (3.5)	3.1 (4.1)	0.2 (0.3)	0.1 (0.3)	4.0 (2.4)

IQR – interquartile range; ICD-10 – International Classification of Diseases, 10th Revision; F32.0 – mild depressive episode; F32.1 – moderate depressive episode; F32.2 – severe depressive episode without psychotic symptoms; F32.3 – severe depressive episode with psychotic symptoms; F33 – recurrent depressive disorders; F34 – persistent mood disorders.

Table 3. Values of Pearson's correlation coefficients between air pollution and indices of the structure of depressive episodes in all 13 analyzed counties

Air pollutants	F32	F32.0	F32.1	F32.2	F32.3	F33	F34
$PM_{2.5}$	**0.303**	0.204	0.198	0.152	0.222	0.197	**0.281**
PM_{10}	**0.341**	**0.277**	0.198	0.211	**0.385**	**0.328**	**0.291**
CO	**0.326**	**0.226**	**0.260**	**0.234**	**0.344**	**0.330**	0.102
Pb	**0.327**	**0.270**	0.213	**0.352**	0.117	0.157	**0.431**
SO_2	−0.040	0.171	−0.093	−0.064	−0.057	0.013	0.032
BaP	0.039	**0.269**	−0.060	−0.004	0.067	−0.052	0.071
O_3	**−0.412**	**−0.264**	−0.296	**−0.288**	**−0.283**	−0.166	**−0.375**
As	**0.433**	**0.295**	0.215	**0.513**	0.158	0.218	**0.491**
Cd	**0.241**	**0.237**	0.124	**0.267**	0.073	0.218	**0.293**
Ni	0.091	0.065	0.017	0.004	0.091	0.163	0.092

Values in bold are statistically significant. BaP – benzo(a)pyrene; $PM_{2.5}$ – atmospheric aerosols with a diameter of not more than 2.5 µm (the average daily dust standard ≤25 µg/m^3 and average annual standard ≤10 µg/m^3); PM_{10} – a mixture of suspended dusts with a diameter ≤10 µg (the average daily dust standard ≤200 µg/m^3 and average annual standard ≤20 µg/m^3); CO – carbon monoxide; Pb – lead; SO_2 – sulfur dioxide; O_3 – ozone; As – arsenic; Cd – cadmium; Ni – nickel.

Table 4. Results of the collinearity analysis (variance inflation factor (VIF) values) of independent variables

Predictors	$PM_{2.5}$	PM_{10}	NO_2	CO	Pb	SO_2	NO_x	BaP	O_3	As	Cd	Ni
VIF	8.44	3.21	**27.55**	4.26	2.99	2.73	**20.81**	3.07	8.62	3.36	4.57	3.41

Values in bold are statistically significant. BaP – benzo(a)pyrene; NO_x – nitrogen oxides; $PM_{2.5}$ – atmospheric aerosols with a diameter of not more than 2.5 µm (the average daily dust standard ≤25 µg/m^3 and average annual standard ≤10 µg/m^3); PM_{10} – a mixture of suspended dusts with a diameter ≤10 µg (the average daily dust standard ≤200 µg/m^3 and average annual standard ≤20 µg/m^3); NO_2 – nitrogen dioxide; CO – carbon monoxide; Pb – lead; SO_2 – sulfur dioxide; O_3 – ozone; As – arsenic; Cd – cadmium; Ni – nickel.

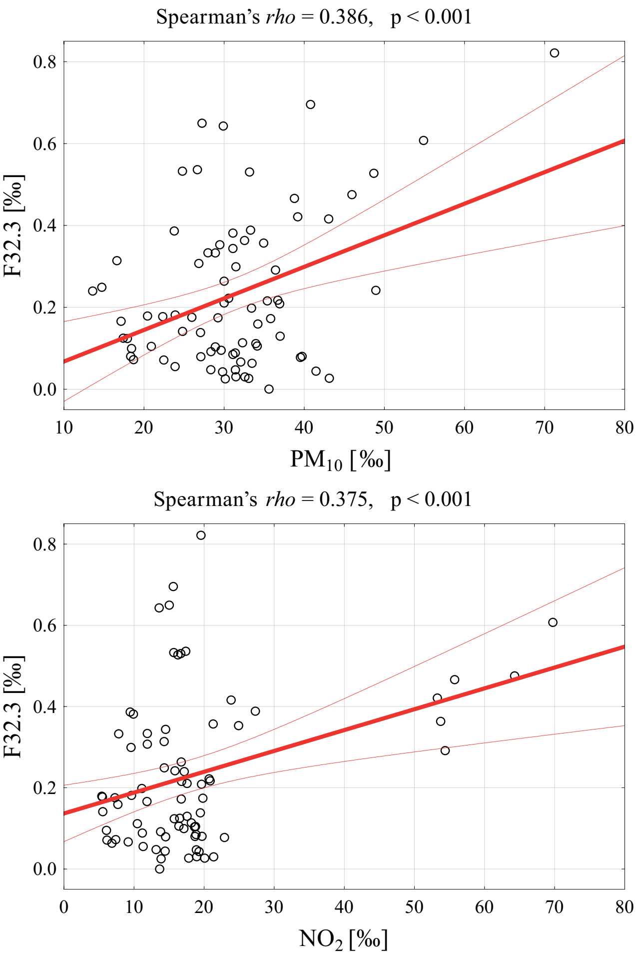


Fig. 3. Scatterplots showing reported cases of depression with psychotic symptoms (F32.3) and coarse particles with an aerodynamic diameter between 2.5 μm and 10 μm (PM_{10}) and nitrogen dioxide (NO_2) concentrations

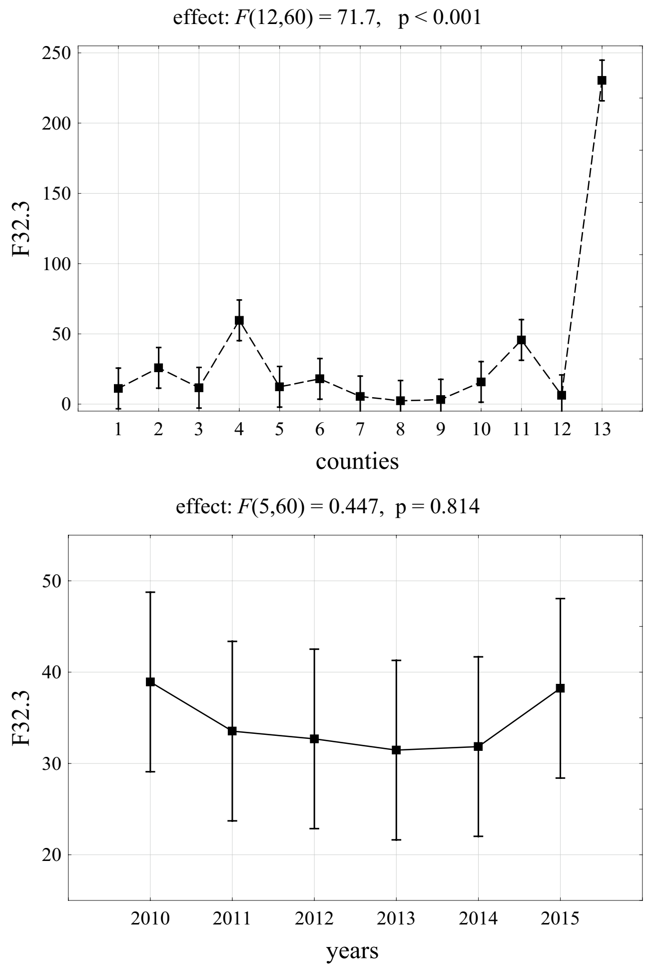


Fig. 4. F-ratio of the analysis of variance (ANOVA) concerning depression with psychotic symptoms (F32.3) ratio

Table 5. Values of univariate and multivariate regression analyses between air pollution and the occurrence of severe depressive episodes with psychotic symptoms (F.32.3)

Risk factors (F32.3 occurrence predictors)	Univariate analysis		Multivariate analysis	
	b	p-value	β	p-value
$PM_{2.5}$	11.04	<0.001	**10.8**	**<0.001**
PM_{10}	–0.42	0.614	0.06	0.918
CO	409.0	<0.001	**379.8**	**<0.001**
Pb	154.7	0.775	538.2	0.775
SO_2	–7.36	0.014	**–6.44**	**0.019**
BaP	–5.42	0.002	**–5.33**	**0.002**
O_3	2.09	0.188	1.95	0.160
As	–0.85	0.702	–0.01	0.682
Cd	–47.2	0.192	**–54.4**	**0.039**
Ni	25.7	0.089	**24.1**	**0.040**

Multivariate regression statistics: R^2adj. = 0.609, F(7, 70) = 18.2, p < 0.001, SE = 38.3. SE – standard error; b – linear regression coefficient; β – standardized regression coefficient. Values in bold are statistically significant. BaP – benzo(a)pyrene; $PM_{2.5}$ – atmospheric aerosols with a diameter of not more than 2.5 μm (the average daily dust standard ≤25 μg/m^3 and average annual standard ≤10 μg/m^3); PM_{10} – a mixture of suspended dusts with a diameter ≤10 μg (the average daily dust standard ≤200 μg/m^3 and average annual standard ≤20 μg/m^3); CO – carbon monoxide; Pb – lead; SO_2 – sulfur dioxide; O_3 – ozone; As – arsenic; Cd – cadmium; Ni – nickel.

The positive values of the regression coefficients indicated the effects of increased $PM_{2.5}$, CO, Ni, and Cd on the occurrence of F32.3. All structural parameters of the model were statistically significant ($p < 0.05$), and the model fit was satisfactory ($p < 0.001$). In order to avoid the pseudoreplication problem, and since the measurements of depression rates were taken in each county annually, the correlation analysis in consecutive individual years between air pollution and the occurrence of F32.3 was performed. The PM_{10} correlated significantly with the F32.3 diagnosis in 2010 (rho = 0.560, $p < 0.05$), and both PM_{10} and NO_2 concentrations were linked to this diagnosis across all years (rho = 0.386, $p < 0.001$; rho = 0.375, $p < 0.001$; Table 6; Fig. 3,4).

Analysis including demographic and social data

Over the entire analyzed period, the percentage of diagnosed cases of depression was stable at a level of 2.7 ±1.8%. The analyzed database lacked information on the depression incidence in the Wałbrzych county in 2010–2012. The missing data were supplemented with average values.

Table 6. Correlation analysis in consecutive individual years between air pollution and the occurrence of severe depressive episodes with psychotic symptoms (F32.3)

Year	PM_{10} compared to F32.3	NO_2 compared to F32.2
2010	**rho = 0.560 p < 0.05**	rho = 0.407 p > 0.05
2011	rho = –0.044 p > 0.05	rho = –0.077 p > 0.05
2012	rho = 0.440 p > 0.05	rho = 0.198 p > 0.05
2013	rho = 0.104 p > 0.05	rho = 0.473 p > 0.05
2014	rho = 0.544 p > 0.05	rho = 0.401 p > 0.05
2015	rho = 0.429 p > 0.05	rho = 0.099 p > 0.05
All	rho = 0.386 p < 0.001	rho = 0.375 p < 0.001

Values in bold are statistically significant. PM_{10} – a mixture of suspended dusts with a diameter ≤10 µg (the average daily dust standard ≤200 µg/m^3 and average annual standard ≤20 µg/m^3); NO_2 – nitrogen dioxide.

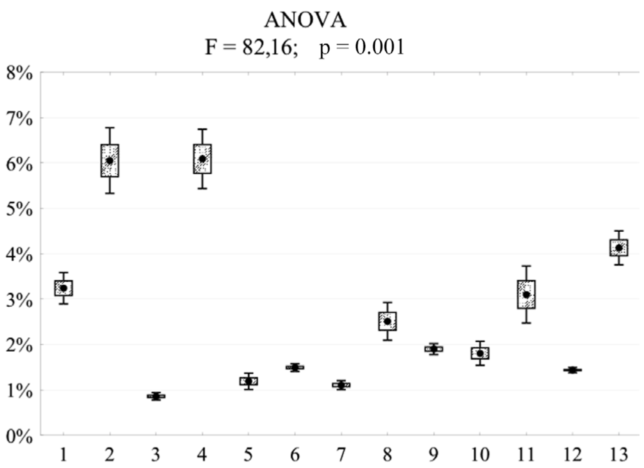


Fig. 5. Percentage of diagnosed depression cases in 2010–2015 in 13 counties of Lower Silesia and the result of the analysis of variance (ANOVA)

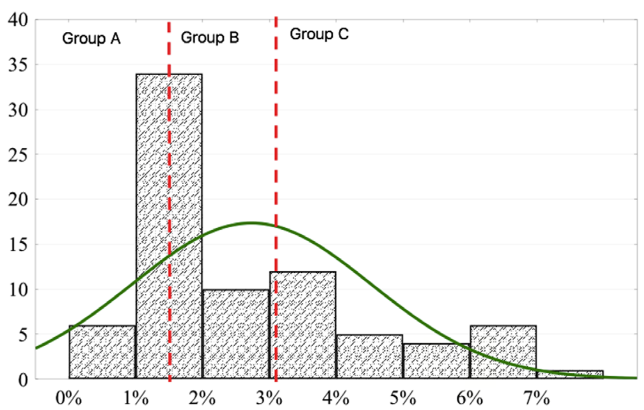


Fig. 6. Histogram of the percentage of depression cases against the normal distribution, the results of normality tests, and the adopted division. Kolmogorov–Smirnov test: d = 0.193, p < 0.01; Lilliefors test: p < 0.01; Shapiro–Wilk test: W = 0.866, p < 0.00001

Basic demographic data concerning depression cases (2010–2015) across the 13 counties of Lower Silesia are summarized in Table 6 and Table 7. Statistically significant differences were observed between depression incidence in individual counties (Fig. 5) (p < 0.001). The highest incidence of depression was recorded in Jelenia Góra (2) and Legnica (4) counties (6.1%), while the lowest in Kłodzko (0.9%) and Oleśnica (1.1%) counties.. Table 8 shows the results of ANOVA concerning depression cases and Table 9 displays the results of post-hoc test (Turkey's test).

The distribution of depression cases was non-normal (Fig. 6). The analyzed counties were classified into 3 groups: group A – depression rate below 1.5% (Kłodzko, Lubań, Oleśnica, and Świdnica counties); group B – depression rate of 1.5–3.1% (Oława, Polkowice, Złotoryja, and Zgorzelec counties); group C – depression rate over 3.1% (Głogów, Jelenia Góra, Legnica, Wałbrzych, and Wrocław counties) (Fig. 7). In group C, a high percentage of diagnosed depression cases was associated with higher concentrations of PM_{10} and $PM_{2.5}$, as well as lower O_3 concentrations. The level of BaP did not differ significantly between

Table 7. Statistics of the percentage of diagnosed depression cases in 2010–2015 in 13 counties of Lower Silesia and the results of ANOVA

Years	Mean ±SD	Me (Q1–Q3)	Min–Max	Result of the test
2010	2.5 ±1.5	1.8 (1.5–3.7)	0.8–7.2	F = 0.29 df = 5 p = 0.868
2011	2.4 ±1.5	1.6 (1.4–3.6)	0.8–5.1	
2012	2.7 ±1.8	1.8 (1.4–3.9)	0.8–6.2	
2013	2.8 ±2.0	2.1 (1.5–3.5)	0.9–6.9	
2014	3.0 ±2.1	2.1 (1.5–4.3)	0.8–7.2	
2015	3.0 ±2.0	2.2 (1.3–3.9)	1.0–6.9	
Counties				
Głogów	3.2 ±0.4	3.3 (3.0–3.6)	2.5–3.6	F = 88.6 df = 12 p < 0.001
Jelenia Góra	6.1 ±0.9	6.0 (5.3–6.9)	4.9–7.2	
Kłodzko	0.9 ±0.1	0.8 (0.8–0.9)	0.8–1.0	
Legnica	6.1 ±0.8	6.4 (5.1–6.7)	5.1–6.9	
Lubań	1.2 ±0.2	1.1 (1.1–1.2)	1.0–1.6	
Oława	1.5 ±0.1	1.5 (1.4–1.5)	1.4–1.7	
Oleśnica	1.1 ±0.1	1.1 (1.0–1.2)	0.9–1.3	
Polkowice	2.5 ±0.5	2.8 (1.9–2.9)	1.8–3.0	
Złotoryja	1.9 ±0.2	1.9 (1.8–2.0)	1.6–2.1	
Zgorzelec	1.8 ±0.3	1.8 (1.5–2.1)	1.5–2.2	
Wałbrzych*	3.5 ±0.7	3.9 (3.9–4.0)	2.4–4.3	
Świdnica	1.4 ±0.1	1.4 (1.4–1.5)	1.3–1.5	
Wrocław	4.1 ±0.5	4.1 (3.7–4.7)	3.6–4.7	
All (n = 78)	2.7 ±1.8	1.9 (1.4–3.9)	0.8–7.2	–

* missing data for 2010–2012 have been replaced with averages; ANOVA – analysis of variance; M – arithmetic mean; SD – standard deviation; Me – median (50%); Q1 – lower quartile (25%); Q3 – upper quartile (75%); df – degrees of freedom; Min – the smallest value; Max – the largest value. The differences between the percentages of diagnosed depression cases in 2010–2015 in all counties turned out to be statistically insignificant (Fig. 1; p > 0.05).

Table 8. The results of ANOVA concerning depression cases

Effect	SS	df	MS	F	p-value
Constant	52563	1	92564	295	**<0.001**
Years	701	5	140	0.45	0.814
Countries	270075	12	22506	71.7	**<0.001**
Error	18821	60	314	–	–

R^2adj. = 0.917, F(17, 60) = 50.8, p < 0.001. ANOVA – analysis of variance; SS – sums of squares; df – degrees of freedom; MS – mean squares. Values in bold are statistically significant.

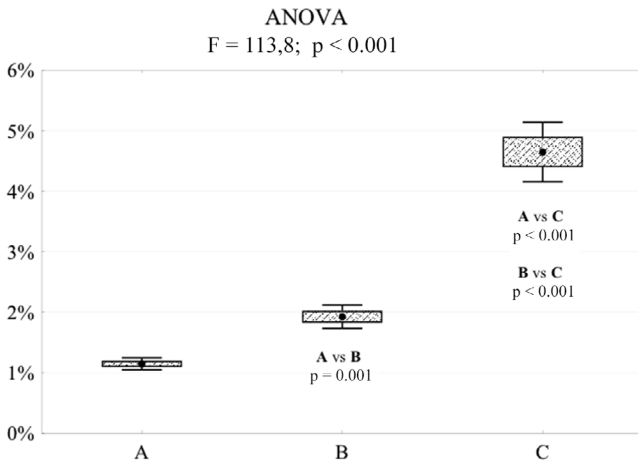


Fig. 7. Percentage of depression diagnosed in 2010–2015 in 3 groups of counties and the result of the analysis of variance (ANOVA) and post hoc tests (Tukey's test)

the individual counties. The average values of pollutants in groups of counties differing in the severity of diagnosed depression are summarized in Table 10 and Table 11, as well as Fig. 8.

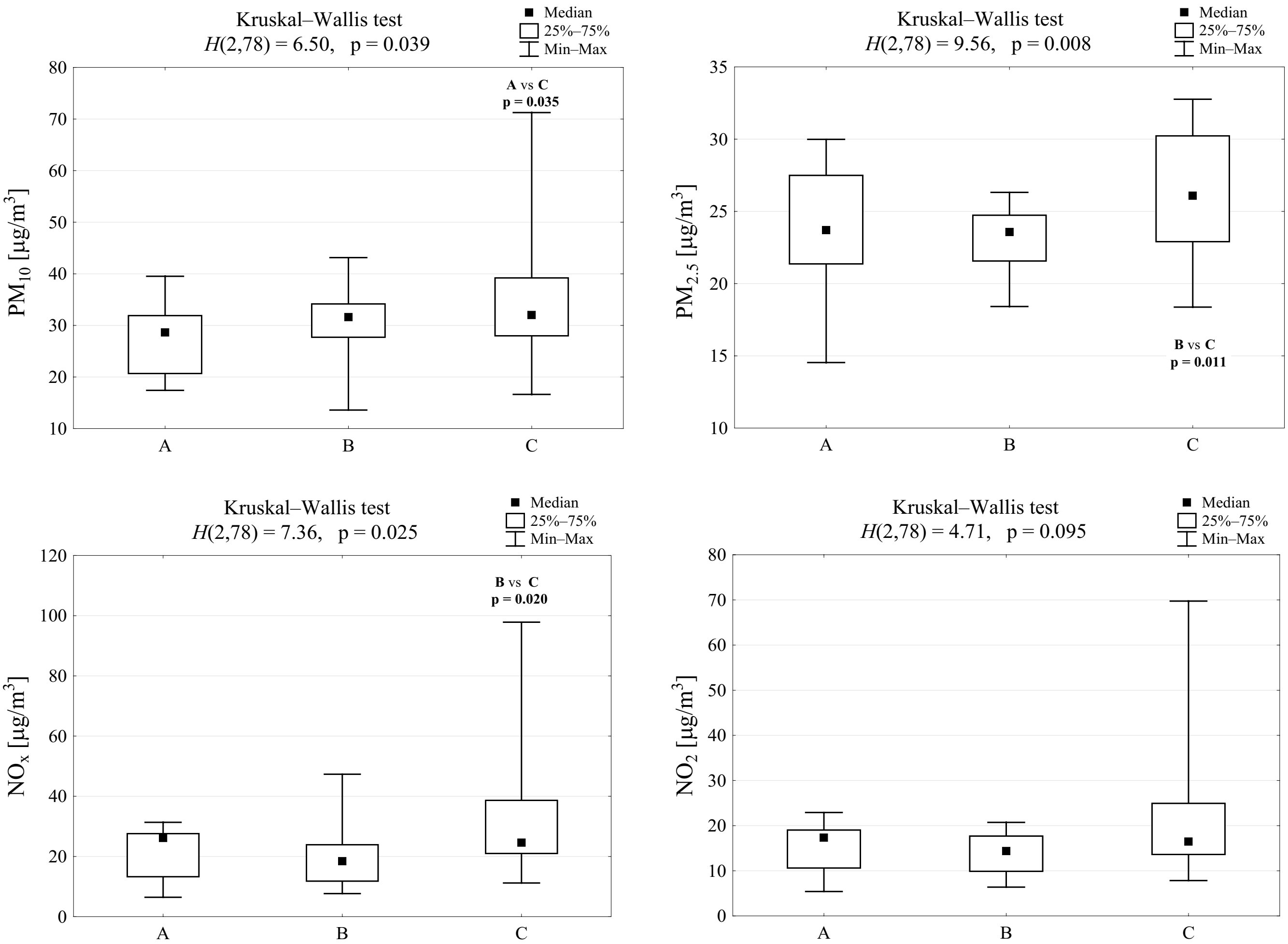
In counties with the highest percentage of diagnosed depression, there were significantly higher emissions of gaseous pollutants (1000 t/year/km²) (p = 0.003), SO_2 (p = 0.011), NO_x (p = 0.002), CO (p = 0.001), and CO_2 (p = 0.003), as well as concentrations of PM_{10} (p = 0.039), $PM_{2.5}$ (p = 0.008) and NO_x (p = 0.025). The O_3 levels were significantly inversely correlated with depression (p < 0.001; Table 10,11, Fig. 8).

In order to determine the independent predictors of depression incidence, univariate and multivariate linear regression analyses were performed (Table 12). Univariate regression analysis showed that PM_{10} and $PM_{2.5}$ concentrations, as well as divorces (per 1000 inhabitants), demographic burden, demographic dependency rate for the elderly, percentage of people >65 years old, feminization rate, outpatient clinics per 1000 population, doctors (total working staff) per 10,000 population, number of beds in hospitals in relation to the population, working people rate, emission of gaseous pollutants, and average monthly gross salary were significantly positively correlated with the incidence of depression. On the other hand, O_3 concentration, the number of marriages and the number of beneficiaries of social welfare were significantly negatively correlated with depression risk. Multivariate regression analysis showed that O_3 concentration, demographic burden, feminization rate, number of doctors, number of hospital beds in relation to the population, number of employed people per 1000 population, and average monthly gross salary were independent predictors of the depression rate. Increased O_3 concentrations were significantly associated with a lower depression risk (p = 0.004).

Table 9. Results of multiple comparisons (post hoc) with Tukey's test: Głogów compared to Jelenia Góra (3.2% compared to 6.1%; p < 0.001) and Głogów compared to Polkowice (3.2% compared to 2.5%; p = 0.261)

Counties	Multiple comparison results (Tukey's test)												
	Głogów M = 3.2	Jelenia Góra M = 6.1	Kłodzko M = 0.9	Legnica M = 6.1	Lubań M = 1.2	Oława M = 1.5	Oleśnica M = 1.1	Polkowice M = 2.5	Złotoryja M = 1.9	Zgorzelec M = 1.8	Wałbrzych M = 3.5	Świdnica M = 1.4	Wrocław M = 4.1
Głogów	–	**0.000**	**0.000**	**0.000**	**0.000**	**0.000**	**0.000**	0.261	**0.000**	**0.000**	0.998	**0.000**	0.068
Jelenia Góra	**0.000**	–	**0.000**	1.000	**0.000**	**0.000**	**0.000**	**0.000**	**0.000**	**0.000**	**0.000**	**0.000**	**0.000**
Kłodzko	**0.000**	**0.000**	–	**0.000**	0.989	0.478	0.999	**0.000**	**0.014**	**0.038**	**0.000**	0.623	**0.000**
Legnica	**0.000**	1.000	**0.000**	–	**0.000**	**0.000**	**0.000**	**0.000**	**0.000**	**0.000**	**0.000**	**0.000**	**0.000**
Lubań	**0.000**	**0.000**	0.989	**0.000**	–	0.995	1.000	**0.001**	0.305	0.525	**0.000**	0.999	**0.000**
Oława	**0.000**	**0.000**	0.478	**0.000**	0.995	–	0.962	**0.018**	0.947	0.993	**0.000**	1.000	**0.000**
Oleśnica	**0.000**	**0.000**	0.999	**0.000**	1.000	0.962	–	**0.000**	0.161	0.322	**0.000**	0.989	**0.000**
Polkowice	0.261	**0.000**	**0.000**	**0.000**	**0.001**	**0.018**	**0.000**	–	0.536	0.314	**0.020**	**0.009**	**0.000**
Złotoryja	**0.000**	**0.000**	**0.014**	**0.000**	0.305	0.947	0.161	0.536	–	1.000	**0.000**	0.877	**0.000**
Zgorzelec	**0.000**	**0.000**	**0.038**	**0.000**	0.525	0.993	0.322	0.314	1.000	–	**0.000**	0.974	**0.000**
Wałbrzych	0.998	**0.000**	**0.000**	**0.000**	**0.000**	**0.000**	**0.000**	**0.020**	**0.000**	**0.000**	–	**0.000**	0.538
Świdnica	**0.000**	**0.000**	0.623	**0.000**	0.999	1.000	0.989	**0.009**	0.877	0.974	**0.000**	–	**0.000**
Wrocław	0.068	**0.000**	**0.000**	**0.000**	**0.000**	**0.000**	**0.000**	**0.000**	**0.000**	**0.000**	0.538	**0.000**	–

M – arithmetic mean. Values in bold are statistically significant.



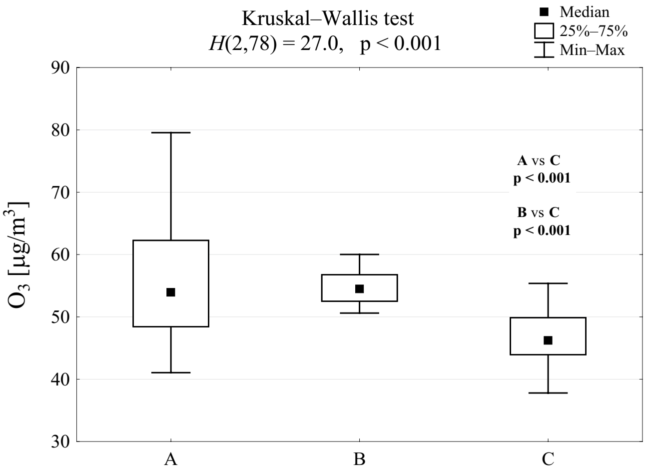


Fig. 8. The concentration of coarse particles with an aerodynamic diameter between 2.5 µm and 10 µm (PM_{10}), fine particles with a diameter less than 2.5 µm ($PM_{2.5}$), nitrogen dioxide (NO_2), nitrogen oxides (NO_x), and ozone (O_3) measured in 2010–2015 in 3 groups of counties and the results of the Kruskal–Wallis test

Discussion

We showed that depression is associated with long-term exposure to higher concentrations of PM_{10}, $PM_{2.5}$ and NO_x, and high emissions of SO_2, NO_x, CO, and CO_2. Other studies have reported similar results. For example, research using the National Health Insurance Database demonstrated a positive association between $PM_{2.5}$ and depression risk for both 1-year and 4-year exposure.[39] Other studies also found this relationship for periods of 1 year,[40] 2 years and 5 years.[41] In terms of PM_{10} long-term exposure, a positive relationship was found over a 1-year time period.[42] A study by Vert et al. supports these results for both PM fractions.[43] However, there was also a negative association for PM_{10}.[44] Furthermore, only a few studies evaluated the relationship between depression and NO_x. These studies consistently suggest a positive correlation between depression and long-term exposure to NO_2 and NO_x.[43,45]

Table 10. Comparison of the features characterizing the counties of Lower Silesia in groups differing in the occurrence of depression

Parameter	Group A	Group B	Group C	p-value
Percentage of depression [%]	1.1 (0.4)	1.9 (0.5)	4.3 (2.0)	**<0.001**[a]
PM_{10} [μg/m^3]	28.6 (11.2)	31.6 (6.5)	32.0 (11.2)	**0.010**[b]
BaP [μg/m^3]	7.9 (10.7)	4.8 (3.6)	5.6 (3.4)	0.229[b]
O_3 [μg/m^3]	54.0 (13.8)	54.5 (4.3)	46.2 (5.9)	**<0.001**[b]
$PM_{2.5}$ [μg/m^3]	23.7 (6.1)	23.6 (3.2)	26.1 (7.3)	**0.002**[b]
D1. Marriages (per 1000 inhabitants)	5.1 (0.7)	5.2 (0.9)	4.7 (1.0)	**0.009**[b]
D2. Divorces (per 1000 inhabitants)	2.0 (0.4)	1.8 (0.3)	2.3 (0.3)	**<0.001**[b]
D3. Demographic burden: non-working age population per 100 working age population	55.3 (3.4)	53.6 (3.4)	57.5 (5.1)	**<0.001**[b]
D4. Demographic dependency rate for the elderly	19.8 (3.2)	17.6 (3.3)	23.2 (6.1)	**<0.001**[b]
D5. Percentage of people aged 65 and over in the total population	14.2 (2.1)	12.7 (2.2)	16.6 (3.8)	**<0.001**[b]
D6. Feminization rate	107 (2)	104 (2)	112 (3)	**<0.001**[b]
D7. Outpatient clinics for 10,000 population	4.0 (1.0)	4.0 (1.0)	5.0 (1.0)	**<0.001**[b]
D8. Medical advice to the population	4.3 (0.9)	4.2 (0.8)	4.0 (0.5)	**0.008**[b]
D9. Total advice (in thousands)	536 (345)	288 (160)	413 (112)	**0.004**[b]
D10. Beneficiaries of social welfare per 10,000 population	744 (192)	784 (276)	584 (250)	**<0.001**[b]
D11. Doctors working according to the basic workplace per 10,000 population	13.4 (4.4)	12.7 (7.4)	24.4 (6.9)	**<0.001**[b]
D12. Doctors (total working staff) per 10,000 population	31.2 (15.5)	26.8 (11.5)	50.4 (16.4)	**<0.001**[b]
D13. Social welfare homes	2.0 (3.5)	1.0 (1.0)	2.0 (2.0)	**0.014**[b]
D14. Inhabitants of social welfare homes (including branches) per 1000 population	3.0 (2.0)	1.0 (2.5)	2.0 (1.0)	**<0.001**[b]
D15. Hospital beds to population (%)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	**<0.001**[b]
D16. Registered unemployment rate	16.1 (9.6)	12.0 (9.0)	10.2 (6.3)	**<0.001**[b]
D17. Working people per 1000 population	167 (45)	250 (198)	284 (74)	**<0.001**[b]
D18. Average monthly gross salaries	3187 (374)	3487 (401)	3580 (639)	**<0.001**[b]
D19. Average monthly gross salaries in relation to the national average (Poland = 100)	82 (6)	91 (6)	88 (12)	**<0.001**[b]

[a] – significance level of the Pearson χ^2 test, [b] – significance level of the Kruskal–Wallis test. Values in bold are statistically significant. BaP – benzo(a) pyrene; $PM_{2.5}$ – atmospheric aerosols with a diameter of not more than 2.5 μm (the average daily dust standard ≤25 μg/m^3 and average annual standard ≤10 μg/m^3); PM_{10} – a mixture of suspended dusts with a diameter ≤10 μg (the average daily dust standard ≤200 μg/m^3 and average annual standard ≤20 μg/m^3); O_3 – ozone.

Table 11. Comparison of the characteristics of the groups of counties in Lower Silesia in terms of pollutant emissions per 1 km^2 of land in counties with different rates of depression

Parameter Percentage of depression	Group A 1.1 (0.4)	Group B 1.9 (0.5)	Group C 4.3 (2.0)	p-value
Z1. Emission of gaseous pollutants (1000 t/year/km^2)	4530 (8864)	14732 (483176)	64755 (58043)	**0.003**
Z2. SO_2	0.14 (0.32)	0.27 (7.14)	1.22 (3.46)	**0.011**
Z3. NO_x	0.06 (0.11)	0.32 (4.61)	0.65 (1.46)	**0.002**
Z4. CO	0.19 (0.11)	0.42 (0.68)	0.57 (0.56)	**0.001**
Z5. CO_2	45.0 (88.1)	146.5 (4820.8)	644.5 (576.1)	**0.003**

p-value is significance level of the Kruskal–Wallis test. Values in bold are statistically significant. NO_x – nitrogen oxides; SO_2 – sulfur dioxide; CO – carbon monoxide; CO_2 – carbon dioxide.

We have observed a negative association between long-term exposure to O_3 and depression, which contradicts some of the previous results.[41] However, some studies found no relationship between O_3 levels and depressive symptoms.[46] Volatile organic compounds and NO_x are precursors to O_3 formation,[47] and photochemical processes which depend on sunlight play a key role.[48] This can explain our results, since sunlight exposure[49] and vitamin D_3 production[50] have a preventive impact on depression. The O_3 exposure and its health effects are more complicated, and possibly threshold-like.[51] Finally, our study showed the important correlation between NO_x, NO_2 and depression risk, and these pollutants are known to decrease O_3 production.[52]

We showed that high levels of $PM_{2.5}$, CO, and low BaP, SO_2 and Cd concentrations are independent risk factors for depressive episodes with psychotic symptoms (F32.3). To the best of our knowledge, there is no available research on this topic. However, some researchers

Table 12. Values of univariate and multivariate regression coefficients between the depression rate and risk factors

Risk factor	Univariate analysis		Multivariate analysis	
	b	p-value	β	p-value
PM_{10} [μg/m^3]	0.065	**0.002**	0.005	0.739
$PM_{2.5}$ [μg/m^3]	0.140	**0.007**	−0.115	0.080
O_3 [μg/m^3]	−0.089	**<0.001**	**−0.082**	**0.004**
BaP [μg/m^3]	0.017	0.738	–	–
D1. Marriages (per 1000 inhabitants)	−0.821	**0.013**	−0.027	0.932
D2. Divorces (per 1000 inhabitants)	3.023	**<0.001**	0.305	0.580
D3. Demographic burden: non-working age population per 100 working age population	0.208	**<0.001**	**−0.213**	**0.004**
D4. Demographic dependency rate for the elderly	0.234	**<0.001**	0.123	0.302
D5. Percentage of people aged 65 and over in the total population	0.365	**<0.001**	0.458	0.718
D6. Feminization rate	0.328	**<0.001**	**0.378**	**<0.001**
D7. Outpatient clinics per 10,000 population	0.384	**0.027**	−0.054	0.758
D8. Medical advice to the population	0.001	0.127	–	–
D9. Total advice (in thousands)	0.004	0.054	–	–
D10. Beneficiaries of social welfare per 10,000 population	−0.003	**0.002**	−0.001	0.588
D11. Doctors working according to the basic workplace per 10,000 population	0.091	**<0.001**	**0.158**	**0.014**
D12. Doctors (total working staff) per 10,000 population	0.039	**<0.001**	−0.043	0.130
D13. Social welfare homes	0.030	0.668	–	–
D14. Inhabitants of social welfare homes (including branches) per 1000 population	−0.294	0.094	–	–
D15. Hospital beds to population (%)	0.001	**0.019**	**−0.001**	**<0.001**
D16. Registered unemployment rate	−0.001	0.434	–	–
D17. Working people per 1000 population	0.010	**<0.001**	**0.007**	**0.001**
D18. Average monthly gross salaries	0.001	**0.013**	**0.003**	**0.001**
D19. Average monthly gross salaries in relation to the national average (Poland = 100)	0.054	**0.026**	**−0.130**	**0.008**
Z1. Emission of gaseous pollutants (1000 t/year/km^2)	0.860	**<0.001**	0.001	0.324
Z2. SO_2	−0.001	0.429	–	–
Z3. NO_x	−0.001	0.489	–	–
Z4. CO	0.001	0.120	–	–
Z5. CO_2	0.001	0.475	–	–

b – linear regression coefficient; β – standardized regression coefficient. Values in bold are statistically significant. BaP – benzo(a)pyrene; $PM_{2.5}$ – atmospheric aerosols with a diameter of not more than 2.5 μm (the average daily dust standard ≤25 μg/m^3 and average annual standard ≤10 μg/m^3); PM_{10} – a mixture of suspended dusts with a diameter ≤10 μg (the average daily dust standard ≤200 μg/m^3 and average annual standard ≤20 μg/m^3); O_3 – ozone; NO_x – nitrogen oxides; SO_2 – sulfur dioxide; CO – carbon monoxide; CO_2 – carbon dioxide.

attempted to find a connection between air pollution and depression severity. Pun et al. showed that $PM_{2.5}$ levels are positively associated with depressive symptom severity.[36] On the other hand, Wang et al. found no relationship between depressive symptoms and both long- and short-term exposure to air pollutants.[13] Similarly, there is very little evidence regarding psychotic symptoms and air pollution. An analysis using machine learning found a connection between schizophrenia emergency room admissions and ambient $PM_{2.5}$,[53] which was confirmed by Gao et al.[54]

A multivariate analysis of demographic and pollution data showed that the number of hospital beds, number of welfare recipients, number of employed people, and the average monthly gross salary were all related to the incidence of depression. These results are inconsistent with other studies, which demonstrated that welfare recipients are more likely to suffer from depression.[55] However, our results could represent reverse causality. For instance, we showed a positive correlation between depression and the number of hospital beds in the region, which could result from the fact that people with depression are more frequently hospitalized.[13] Similarly, employment status and depression rates could be related to workplace conditions, burnout, stress, and bullying,[56] which also translate into monthly salary. Depression accounts for up to 46% of days lost due to illness; therefore, it is more often diagnosed among the working population.[56,57] However, in our study, data concerning employment were not available.

Limitations

Results of our analyses based on 318,779 cases showed that there is a positive association between air pollutant levels and the risk of depression. However, these results should be interpreted cautiously, because, as an observational study, despite being useful in explaining the exposure to an outcome, they carry out the risk of possible reverse causality or undetected bias.[58] Other limitations are related to the use of semi-individual data, and potential underestimation of the prevalence of depression due to social stigmatization related to this diagnosis.[59] Nevertheless, because of the large and standardized sample size, our study provides new insights into the relationship between air pollutant exposure and depression.

The analyzed database lacked information on depression incidence for the Wałbrzych county in 2010–2012. Since regression analysis was used, even if a strong correlation is evident, it does not imply causation. Moreover, some risk factors found in our study could simply reflect the indirect effects of other risk factors. Finally, it is crucial to remember that air pollutant concentrations depend on many variables, such as the direction and speed of the wind, atmospheric stability, solar radiation, or geography.[60] This can cause spatial and temporal variations of pollutants levels, reaching dramatic changes, even over the course of several hours. Moreover, the stress response in the human population is extremely heterogeneous.[61] Age, gender, existing disease status, and psychosocial stressors play a potential role in the biological response to air pollutants. Given the numerous risk factors of depression, demonstrating the impact of air pollution on depressive disorders is difficult. Therefore, obtaining large-scale data on depression cases, and relating this to demographic and pollution information can help in identifying environmental risk factors, which could be potentially modifiable.

Conclusions

Heavy air pollution is associated with a higher incidence of depression, while O_3 levels were linked to the lower rate of depression. Elevated concentration of airborne $PM_{2.5}$, as well as CO, and low BaP, SO_2 and Cd levels are independent risk factors for the occurrence of major depressive episodes with psychotic symptoms (F32.3). A high percentage of people with depression could be related to higher concentrations of PM_{10} and $PM_{2.5}$, lower O_3 concentrations and higher emissions of gaseous pollutants, such as SO_2, NO_x, CO, and CO_2.

The incidence of depression was associated with high concentrations of PM_{10} and $PM_{2.5}$, as well as divorce rate per 1000 inhabitants, demographic burden, demographic dependency rate for the elderly, percentage of people >65 years old, feminization rate, outpatient clinics per 1000 population, doctors (total working staff) per 10,000 population, the number of hospital beds in relation to the population, working people rate, emission of gaseous pollutants, and average monthly gross salary. On the other hand, O_3 concentration, the number of marriages, and the number of welfare beneficiaries were negatively correlated with depression risk. The independent predictors of depression were: O_3 concentration, demographic burden, feminization rate, number of doctors, number of hospital beds in relation to the population, number of employed people per 1000 population, and the average monthly gross salary.

Availability of data and material

Data on air pollution are available on the website of the Chief Inspectorate of Environmental Protection: http://powietrze.gios.gov.pl/pjp/current. Demographic data are available on the website of the Statistics Poland: https://stat.gov.pl/.

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References

1. World Health Organization. Depression. https://www.who.int/news-room/fact-sheets/detail/depression. Accessed January 3, 2021.
2. King R. Book Review: *Cognitive Therapy of Depression*. Aaon Beck, John Rush, Brian Shaw, Gary Emery. New York: Guilford, 1979. *Aust N Z J Psychiatry*. 2002;36(2):272–275. doi:10.1046/j.1440-1614.2002.t01-4-01015.x
3. Walker ER, McGee RE, Druss BG. Mortality in mental disorders and global disease burden implications: A systematic review and meta-analysis [published correction appears in: *JAMA Psychiatry*. 2015;72(7):736] [published correction appears in: *JAMA Psychiatry*. 2015;72(12):1259]. *JAMA Psychiatry*. 2015;72(4):334. doi:10.1001/jamapsychiatry.2014.2502
4. Briley M, Lépine JP. The increasing burden of depression. *Neuropsychiatr Dis Treat*. 2011;7(Suppl 1):3–7. doi:10.2147/NDT.S19617
5. Otte C, Gold SM, Penninx BW, et al. Major depressive disorder. *Nat Rev Dis Primers*. 2016;2(1):16065. doi:10.1038/nrdp.2016.65
6. Jackson JC, Pandharipande PP, Girard TD, et al. Depression, post-traumatic stress disorder, and functional disability in survivors of critical illness in the BRAIN-ICU study: A longitudinal cohort study. *Lancet Respir Med*. 2014;2(5):369–379. doi:10.1016/S2213-2600(14)70051-7
7. Köhler CA, Evangelou E, Stubbs B, et al. Mapping risk factors for depression across the lifespan: An umbrella review of evidence from meta-analyses and Mendelian randomization studies. *J Psychiatr Res*. 2018;103:189–207. doi:10.1016/j.jpsychires.2018.05.020
8. Li F, Liu X, Zhang D. Fish consumption and risk of depression: A meta-analysis. *J Epidemiol Community Health*. 2016;70(3):299–304. doi:10.1136/jech-2015-206278
9. Rautio N, Filatova S, Lehtiniemi H, Miettunen J. Living environment and its relationship to depressive mood: A systematic review. *Int J Soc Psychiatry*. 2018;64(1):92–103. doi:10.1177/0020764017744582
10. Ross JA, Gliebus G, Van Bockstaele EJ. Stress induced neural reorganization: A conceptual framework linking depression and Alzheimer's disease. *Prog Neuropsychopharmacol Biol Psychiatry*. 2018;85:136–151. doi:10.1016/j.pnpbp.2017.08.004
11. Januar V, Saffery R, Ryan J. Epigenetics and depressive disorders: A review of current progress and future directions. *Int J Epidemiol*. 2015;44(4):1364–1387. doi:10.1093/ije/dyu273
12. Campos ACP, Antunes GF, Matsumoto M, Pagano RL, Martinez RCR. Neuroinflammation, pain and depression: An overview of the main findings. *Front Psychol*. 2020;11:1825. doi:10.3389/fpsyg.2020.01825

13. Wang Y, Eliot MN, Koutrakis P, et al. Ambient air pollution and depressive symptoms in older adults: Results from the MOBILIZE Boston study. *Environ Health Perspect*. 2014;122(6):553–558. doi:10.1289/ehp.1205909
14. Brook RD, Newby DE, Rajagopalan S. Air pollution and cardiometabolic disease: An update and call for clinical trials. *Am J Hypertens*. 2018;31(1):1–10. doi:10.1093/ajh/hpx109
15. Sun Q, Yue P, Deiuliis JA, et al. Ambient air pollution exaggerates adipose inflammation and insulin resistance in a mouse model of diet-induced obesity. *Circulation*. 2009;119(4):538–546. doi:10.1161/CIRCULATIONAHA.108.799015
16. Lodovici M, Bigagli E. Oxidative stress and air pollution exposure. *J Toxicol*. 2011;2011:1–9. doi:10.1155/2011/487074
17. Liu K, Cao H, Li B, et al. Long-term exposure to ambient nitrogen dioxide and ozone modifies systematic low-grade inflammation: The CHCN-BTH study. *Int J Hyg Environ Health*. 2022;239:113875. doi:10.1016/j.ijheh.2021.113875
18. Tanaka M, Vécsei L. Monitoring the kynurenine system: Concentrations, ratios or what else? *Adv Clin Exp Med*. 2021;30(8):775–778. doi:10.17219/acem/139572
19. Tanaka M, Tóth F, Polyák H, Szabó Á, Mándi Y, Vécsei L. Immune influencers in action: Metabolites and enzymes of the tryptophan–kynurenine metabolic pathway. *Biomedicines*. 2021;9(7):734. doi:10.3390/biomedicines9070734
20. Ogyu K, Kubo K, Noda Y, et al. Kynurenine pathway in depression: A systematic review and meta-analysis. *Neurosci Behav Rev*. 2018; 90:16–25. doi:10.1016/j.neubiorev.2018.03.023
21. Rose M, Filiatreault A, Guénette J, Williams A, Thomson EM. Ozone increases plasma kynurenine–tryptophan ratio and impacts hippocampal serotonin receptor and neurotrophic factor expression: Role of stress hormones. *Environ Res*. 2020;185:109483. doi:10.1016/j.envres.2020.109483
22. Thomson EM, Breznan D, Karthikeyan S, et al. Contrasting biological potency of particulate matter collected at sites impacted by distinct industrial sources. *Part Fibre Toxicol*. 2016;13(1):65. doi:10.1186/s12989-016-0176-y
23. Landrigan PJ, Fuller R, Acosta NJR, et al. The Lancet Commission on pollution and health [published correction appears in: *Lancet*. 2018;391(10119):430]. *Lancet*. 2018;391(10119):462–512. doi:10.1016/S0140-6736(17)32345-0
24. Lelieveld J, Klingmüller K, Pozzer A, et al. Cardiovascular disease burden from ambient air pollution in Europe reassessed using novel hazard ratio functions. *Eur Heart J*. 2019;40(20):1590–1596. doi:10.1093/eurheartj/ehz135
25. Thomson EM. Air pollution, stress, and allostatic load: Linking systemic and central nervous system impacts. *J Alzheimers Dis*. 2019; 69(3):597–614. doi:10.3233/JAD-190015
26. Feigin VL, Roth GA, Naghavi M, et al. Global burden of stroke and risk factors in 188 countries, during 1990–2013: A systematic analysis for the Global Burden of Disease Study 2013. *Lancet Neurol*. 2016; 15(9):913–924. doi:10.1016/S1474-4422(16)30073-4
27. Doty RL. The olfactory vector hypothesis of neurodegenerative disease: Is it viable? *Ann Neurol*. 2008;63(1):7–15. doi:10.1002/ana.21327
28. Elder A, Gelein R, Silva V, et al. Translocation of inhaled ultrafine manganese oxide particles to the central nervous system [published correction appears in: *Environ Health Perspect*. 2006;114(8):1178]. *Environ Health Perspect*. 2006;114(8):1172–1178. doi:10.1289/ehp.9030
29. Nel A. Air pollution-related illness: Effects of particles [published correction appears in: *Science*. 2005;309(5739):1326]. *Science*. 2005; 308(5723):804–806. doi:10.1126/science.1108752
30. Genc S, Zadeoglulari Z, Fuss SH, Genc K. The adverse effects of air pollution on the nervous system. *J Toxicol*. 2012;2012:1–23. doi:10.1155/2012/782462
31. Hajat A, Diez Roux AV, Castro-Diehl C, et al. The association between long-term air pollution and urinary catecholamines: Evidence from the multi-ethnic study of atherosclerosis. *Environ Health Perspect*. 2019;127(5):057007. doi:10.1289/EHP3286
32. Thomson EM. Air pollution, stress, and allostatic load: Linking systemic and central nervous system impacts. *J Alzheimers Dis*. 2019;69(3): 597–614. doi:10.3233/JAD-190015
33. Chen C, Nakagawa S. Planetary health and the future of human capacity: The increasing impact of planetary distress on the human brain. *Challenges*. 2018;9(2):41. doi:10.3390/challe9020041
34. Braithwaite I, Zhang S, Kirkbride JB, Osborn DPJ, Hayes JF. Air pollution (particulate matter) exposure and associations with depression, anxiety, bipolar, psychosis and suicide risk: A systematic review and meta-analysis. *Environ Health Perspect*. 2019;127(12):126002. doi:10.1289/EHP4595
35. Davoudi M, Barjasteh-Askari F, Amini H, et al. Association of suicide with short-term exposure to air pollution at different lag times: A systematic review and meta-analysis. *Sci Total Environ*. 2021;771:144882. doi:10.1016/j.scitotenv.2020.144882
36. Pun VC, Manjourides J, Suh H. Association of ambient air pollution with depressive and anxiety symptoms in older adults: Results from the NSHAP Study. *Environ Health Perspect*. 2017;125(3):342–348. doi:10.1289/EHP494
37. Zeng Y, Lin R, Liu L, Liu Y, Li Y. Ambient air pollution exposure and risk of depression: A systematic review and meta-analysis of observational studies. *Psychiatry Res*. 2019;276:69–78. doi:10.1016/j.psychres.2019.04.019
38. Fan SJ, Heinrich J, Bloom MS, et al. Ambient air pollution and depression: A systematic review with meta-analysis up to 2019. *Sci Total Environ*. 2020;701:134721. doi:10.1016/j.scitotenv.2019.134721
39. Kim KN, Lim YH, Bae HJ, Kim M, Jung K, Hong YC. Long-term fine particulate matter exposure and major depressive disorder in a community-based urban cohort. *Environ Health Perspect*. 2016;124(10):1547–1553. doi:10.1289/EHP192
40. Lin H, Guo Y, Kowal P, et al. Exposure to air pollution and tobacco smoking and their combined effects on depression in six low- and middle-income countries. *Br J Psychiatry*. 2017;211(3):157–162. doi:10.1192/bjp.bp.117.202325
41. Kioumourtzoglou MA, Power MC, Hart JE, et al. The association between air pollution and onset of depression among middle-aged and older women. *Am J Epidemiol*. 2017;185(9):801–809. doi:10.1093/aje/kww163
42. Kim J, Kim H. Demographic and environmental factors associated with mental health: A cross-sectional study. *Int J Environ Res Public Health*. 2017;14(4):431. doi:10.3390/ijerph14040431
43. Vert C, Sánchez-Benavides G, Martínez D, 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):1074–1080. doi:10.1016/j.ijheh.2017.06.009
44. Zijlema WL, Wolf K, Emeny R, et al. The association of air pollution and depressed mood in 70,928 individuals from four European cohorts. *Int J Hyg Environ Health*. 2016;219(2):212–219. doi:10.1016/j.ijheh.2015.11.006
45. Altuğ H, Fuks KB, Hüls A, et al. Air pollution is associated with depressive symptoms in elderly women with cognitive impairment. *Environ Int*. 2020;136:105448. doi:10.1016/j.envint.2019.105448
46. Szyszkowicz M, Rowe B, Colman I. Air pollution and daily emergency department visits for depression. *Int J Occup Med Environ Health*. 2009;22(4):355–362. doi:10.2478/v10001-009-0031-6
47. Pollack IB, Ryerson TB, Trainer M, et al. Airborne and ground-based observations of a weekend effect in ozone, precursors, and oxidation products in the California South Coast Air Basin. *J Geophys Res Atmos*. 2012;117(D21):D00V05. doi:10.1029/2011JD016772
48. Tan Z, Lu K, Jiang M, et al. Exploring ozone pollution in Chengdu, southwestern China: A case study from radical chemistry to O3-VOC-NOx sensitivity. *Sci Total Environ*. 2018;636:775–786. doi:10.1016/j.scitotenv.2018.04.286
49. Kim SY, Bang M, Wee JH, et al. Short- and long-term exposure to air pollution and lack of sunlight are associated with an increased risk of depression: A nested case-control study using meteorological data and national sample cohort data. *Sci Total Environ*. 2021;757:143960. doi:10.1016/j.scitotenv.2020.143960
50. Penckofer S, Kouba J, Byrn M, Estwing Ferrans C. Vitamin D and depression: Where is all the sunshine? *Issues Ment Health Nurs*. 2010; 31(6):385–393. doi:10.3109/01612840903437657
51. Zhao T, Markevych I, Standl M, et al. Short-term exposure to ambient ozone and inflammatory biomarkers in cross-sectional studies of children and adolescents: Results of the GINIplus and LISA birth cohorts. *Environ Pollut*. 2019;255:113264. doi:10.1016/j.envpol.2019.113264
52. Gao W, Tie X, Xu J, et al. Long-term trend of O_3 in a mega City (Shanghai), China: Characteristics, causes, and interactions with precursors. *Sci Total Environ*. 2017;603–604:425–433. doi:10.1016/j.scitotenv.2017.06.099

53. Lary DJ, Lary T, Sattler B. Using machine learning to estimate global $PM_{2.5}$ for environmental health studies. *Environ Health Insights*. 2015; 9(Suppl 1):41–52. doi:10.4137/EHI.S15664
54. Gao Q, Xu Q, Guo X, Fan H, Zhu H. Particulate matter air pollution associated with hospital admissions for mental disorders: A time-series study in Beijing, China. *Eur Psychiatry*. 2017;44:68–75. doi:10.1016/j.eurpsy.2017.02.492
55. Lennon MC, Blome J, English K. Depression among women on welfare: A review of the literature. *J Am Med Womens Assoc (1972)*. 2002; 57(1):27–31,40. PMID:11905486.
56. Heinz AJ, Meffert BN, Halvorson MA, Blonigen D, Timko C, Cronkite R. Employment characteristics, work environment, and the course of depression over 23 years: Does employment help foster resilience? *Depress Anxiety*. 2018;35(9):861–867. doi:10.1002/da.22782
57. Gray P, Senabe S, Naicker N, Kgalamono S, Yassi A, Spiegel JM. Workplace-based organizational interventions promoting mental health and happiness among healthcare workers: A realist review. *Int J Environ Res Public Health*. 2019;16(22):4396. doi:10.3390/ijerph16224396
58. Salanti G, Ioannidis JPA. Synthesis of observational studies should consider credibility ceilings. *J Clin Epidemiol*. 2009;62(2):115–122. doi:10.1016/j.jclinepi.2008.05.014
59. Kane JC, Elafros MA, Murray SM, et al. A scoping review of health-related stigma outcomes for high-burden diseases in low- and middle-income countries. *BMC Med*. 2019;17(1):17. doi:10.1186/s12916-019-1250-8
60. Pöschl U, Shiraiwa M. Multiphase chemistry at the atmosphere-biosphere interface influencing climate and public health in the Anthropocene. *Chem Rev*. 2015;115(10):4440–4475. doi:10.1021/cr500487s
61. Thomas J, Guénette J, Thomson EM. Stress axis variability is associated with differential ozone-induced lung inflammatory signaling and injury biomarker response. *Environ Res*. 2018;167:751–758. doi:10.1016/j.envres.2018.09.007