The mediating role of air pollutants in the association between education and lung function among the elderly, the HAPIEE study



Consuelo Quispe-Haro, Daniel Szabó, Katarzyna Kordas, Nadezda Capkova, Hynek Pikhart, Martin Bobak

PII:	S0048-9697(24)04704-1
DOI:	https://doi.org/10.1016/j.scitotenv.2024.174556
Reference:	STOTEN 174556
To appear in:	Science of the Total Environment
Received date:	5 April 2024
Revised date:	14 June 2024
Accepted date:	4 July 2024

Please cite this article as: C. Quispe-Haro, D. Szabó, K. Kordas, et al., The mediating role of air pollutants in the association between education and lung function among the elderly, the HAPIEE study, *Science of the Total Environment* (2023), https://doi.org/10.1016/j.scitotenv.2024.174556

This is a PDF file of an article that has undergone enhancements after acceptance, such as the addition of a cover page and metadata, and formatting for readability, but it is not yet the definitive version of record. This version will undergo additional copyediting, typesetting and review before it is published in its final form, but we are providing this version to give early visibility of the article. Please note that, during the production process, errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

© 2024 Published by Elsevier B.V.

The mediating role of air pollutants in the association between education and lung function among the elderly, the HAPIEE study.

Consuelo Quispe-Haro^a, Daniel Szabó^a, Katarzyna Kordas^b, Nadezda Capkova^c, Hynek Pikhart^{a,d}, Martin Bobak^{a,d}.

^a RECETOX, Faculty of Science, Masaryk University, Kotlarska 2, Brno, Czech Republic

^b Department of Epidemiology and Environmental Health, University at Buffalo, Buffalo NY, USA

^c National Institute of Public Health, Prague, Czech Republic

^d Research Department of Epidemiology and Public Health, University College London, London, UK

Correspondence to

Professor Hynek Pikhart, Research Department of Epidemiology and Public Health, UCL. London, UK.; h.pikhat@ucl.ac.uk

Abstract

Background: Chronic exposure to air pollutants harms human health, and at a geographical level, concentrations of air pollutants are often associated with socioeconomic disadvantage.

Objectives: The aim of this study was to investigate the effects of educational attainment and air pollution on lung function in older adults, and whether air pollution may mediate the effect of education.

Methods: The study included 6381 individuals (mean age 58.24 \pm 7.14 years) who participated in the Czech HAPPIE (Health, Alcohol, and Psychosocial Factors in Eastern Europe) study. Participants' residential addresses were linked to air pollution data, including mean exposures to PM₁₀ (particulate matter of aerodynamic diameter below 10 µm) and NO₂ (nitrogen dioxide). We used path analysis to link educational attainment and air pollutants to a standardized measure of the Forced Expiratory Volume in the first second (FEV1).

Results: Higher levels of participants' education were associated with lower exposures to PM_{10} and NO_2 . Individuals with tertiary education had higher standardized FEV1 than individuals with primary education (88% vs 95%). Path analysis revealed a direct positive effect of education on FEV1, while about 12% of the relationship between education and lung function was mediated by PM_{10} and NO_2 .

Conclusions: Education (typically completed at young ages) appeared to have a protective effect on lung function later in life, and a small part of this effect was mediated by air pollution.

Keywords:

socioeconomic factors, air pollution, lung function, respiratory health, environmental health

1. Introduction

Studying the associations between outdoor air pollutants and socioeconomic status (SES) is needed as both are important risk factors for numerous health conditions (Glymour et al., 2014; World Health Organization, 2021) including pulmonary outcomes (Orellano et al., 2020; Rocha et al., 2019). Studies in the United States (US) and Europe have reported higher levels of residential exposure to environmental pollutants, particularly PM_{2.5} (particulate matter of aerodynamic diameter below 2.5 µm), PM₁₀ (particulate matter of aerodynamic diameter below 10 µm), and NO₂ (nitrogen dioxide) in people with lower SES (Clark et al., 2014; Hajat et al., 2015; Knobel et al., 2023). However, some European studies found that more deprived groups could be less exposed to air pollutants in urban-rural comparisons, or areas devoted to different economic activities (Fairburn et al., 2019; Padilla et al., 2014; Richardson et al., 2013)

So far, SES's role in the now widely accepted relationship between air pollution and lung function is not fully understood (Hajat et al., 2021). While SES indicators have been proposed to be potential confounders as well as effect modifiers of the association between air pollution and health outcomes (Hajat et al., 2015), it is also possible that air pollution may partly mediate the effects of SES on health (Hajat et al., 2021). Higher educational attainment (as a proxy for SES) may affect the ease (or lack of it) with which individuals choose to live in more (or less) desirable areas (Deluca et al., 2019); these areas might be different in terms of air pollution as well (Wang and Guo, 2023). Furthermore, in as much as educational attainment is related to employment opportunities and income (Glymour et al., 2014), less educated individuals may seek jobs in areas or cities that concentrate polluting industries, thus contributing to higher lifetime air pollution exposures. For example, Padilla et al. (2014) found that the Port of Marseille concentrates poor employees exposed to high levels of NO₂ from steel and petrochemical industries.

SES comprises several dimensions, including income, education, wealth status, and job position; however, education has been among the most widely used in epidemiological research. The vast majority of studies indicate that better-educated individuals fare better concerning health outcomes but also exposure to health risk factors, including air pollution (Cutler and Lleras-Muney, 2010; Donkin, 2014; Hamad et al., 2018). Researchers have investigated the mechanisms underlying the association between education and health, finding evidence for indirect and direct effects. Educational attainment is a powerful predictor of adulthood characteristics, including income and job position, personal control, social support, and health behaviors, which are in turn social determinants of health, indicating an indirect effect on health (Ross and Mirowsky, 2010). Additionally, evidence suggests that individuals with lower SES are more exposed to poorer housing conditions and environmental hazards in their neighborhoods (Evans and Kantrowitz, 2002). Conversely, other researchers argue that education has a more direct impact on health, claiming that it remains a robust predictor of longevity even after controlling for other SES covariates (Baker et al., 2011), and that compulsory schooling laws have shown to be beneficial in reducing mortality, smoking, and obesity (Hamad et al., 2018). Thus, education may influence health both directly and indirectly, serving as a fundamental factor that underlies other SES dimensions.

To our knowledge, the hypothesis that educational attainment drives pulmonary outcomes partly through air pollution exposure (mediator) has not been previously investigated.

Using individual data from a cohort study of Czech older adults from seven small-mid size cities linked with long-term exposures to outdoor air pollutants we aim to investigate (1) the social (educational) gradient of exposure to PM_{10} and NO_2 and, (2) the association between exposure to air pollutants and lung functions; (3) the

educational gradient in lung function; (4) and the potential mediation effect of air pollution in the association between educational attainment and lung function.

2. Methods

2.1. Population

We used the baseline survey of the Czech Health, Alcohol, and Psychosocial Factors in Eastern Europe (HAPIEE) cohort study conducted from 2002 to 2005. A populationbased urban random sample of older adults was invited to participate in a short physical examination and provide data on health, risk factors, and socioeconomic conditions. Individuals provided their consent to participate. Data were collected by trained personnel. The examination included anthropometric measurements and a spirometry test. A published protocol provides further details (Peasey et al., 2006). A total of 8,835 individuals provided demographic and health data, but only 6,763 individuals underwent the spirometry test. Of them, 27 had missing values on height and 260 had missing geocodes. Additionally, 119 individuals had missing information on smoking behavior and 47 on education. The analytical sample encompassed 6,381 individuals with complete information. Listwise deletion was conducted for missing values as the parameters did not differ from the final sample (Supplement A).

2.2. Lung function

Lung function was assessed by trained personnel and standardized protocol using a Micro-Medical Microplus spirometer. The assessment of lung function was conducted in a sitting position on three to eight occasions. The output includes but is not limited to the Forced Vital Capacity (FVC) and the Forced Expiratory Volume in the first second (FEV1). For this study, the maximum value of FEV1 was chosen according to reproducibility and repeatability criteria (Graham et al., 2019). The predicted values of FEV1 were derived using age and height as primary predictors, stratified by sex, using published equations (Kuster et al., 2008). These predicted values were then compared

to observed values calculating the ratio of each participant's maximum value of FEV1 to their individual predicted value of FEV1. This ratio was multiplied by 100 for easier interpretation as a percentage difference from the expected FEV1. In consequence, 100% standardized FEV1 is considered the optimal reference value.

2.3. Exposure to air pollution

Air pollution (PM_{10} and NO_2) concentrations between 2005 and 2008 were estimated by the Czech Hydrometeorological Institute (CHMI) on a 1 km x 1 km spatial grid. This estimation employed an empirical inverse distance weighting model, combining several data sources and models: (1) CHMI's Gaussian plume SYMOS'97 atmospheric dispersion model, using the national registry of point and line emission sources (*Information System for Air Quality* – ISKO), traffic-related air pollution data from a 2005 national traffic intensity study, meteorological and digital terrain model data; (2) European Eulerian EMEP (50 km x 50 km) model, to estimate the secondary particle and resuspension concentrations for PM_{10} ; and (3) altitude data. The models are developed for urban and rural areas separately and merged into spatial maps based on population density grids (Ostatnická, 2008).

The annual means of PM_{10} and NO_2 in micrograms per cubic meter (μ g/m³) were obtained from 2005 to 2008 and matched to the geocoded addresses of the participants. A missing value was assigned if the geographic address could not be retrieved. The 4-year mean concentrations were calculated and used as an approximation to the long-term exposure to PM_{10} and NO_2 . Given that interpreting the effect size of small unit changes in PM_{10} and NO_2 can be less intuitive, we rescaled both by dividing it by 10. This transformation allows the model coefficients to represent the effect of a 10μ g/m³ change in PM_{10} and NO_2 concentrations, thereby facilitating a clearer understanding of the magnitude of the association of air pollutants and standardized FEV1.

2.4. Socioeconomic status

Participants were asked about their highest level of education achieved. The responses were classified into four categories: (1) primary or incomplete, for those who completed a maximum of 9 years of education; (2) vocational, for those who had four additional years of training in a manual profession; (3) secondary, completed 13 years of education plus a matriculation exam; and (4) tertiary, for individuals with a university degree.

For sensitivity analyses, two additional indicators of SES (deprivation and job as a miner) were used. Three questions were used to assess the level of deprivation: (1) Do you have difficulties in buying food? (2) Do you have difficulties buying clothes? (3) Do you have difficulties paying bills? Answers were formatted on a 4-point Likert scale from 0 (never) to 4 (always). The sum of the three questions ranged from 0 to 12 and were re-categorized as no deprivation (0), low level of deprivation (1-2), and high level of deprivation (3-12). A dummy variable identified whether participants worked as miners (1) or not (0) from free-text occupation descriptions.

2.5. Covariates

Age on the day of the health examination, sex, and smoking behavior were selfreported. Participants were asked if they smoked and had to choose one of the following answers: (1) No, I have never smoked, (2) No, I smoked in the past, but I stopped, (3) Yes, occasionally, less than one cigarette, (4) Yes, regularly, at least one cigarette. These responses were recategorized as follows: (0) never smokers, (1) past and occasional smokers, (2) regular smokers. The body mass index (BMI) was introduced as a continuous variable derived from health examination on weight and height and expressed in kg/m².

2.6. Statistical Analysis

First, using linear regression, we estimated the association between the level of education and four-year average PM₁₀ and NO₂ levels. Multiple linear regressions were used to test the strength of the associations between education and the standardized FEV1 when controlled for covariates in successive models: model 0 was adjusted for age and sex; model 1 additionally adjusted for body mass index (BMI) and smoking status; model 2 was further adjusted for outdoor air pollutants – PM₁₀ and NO₂. The strength of the association between air pollutants and standardized FEV1 was tested using a similar method but model 2 was adjusted for education instead. During the post hoc sensitivity analysis, we included additional indicators of SES (deprivation and job as a miner) to model 2, and to take into account different sources of exposure the results were separated by city category, i.e. presence of mining industry.

Finally, we used structural equation modeling (SEM) builder to perform a mediation analysis. The software output provided the coefficients of the hypothesized paths. We would refer to full mediation if the total direct effect is zero and to partial mediation if it is non-zero. The total direct effect is the coefficient of the path from education to the standardized FEV1. Two indirect effects were calculated: one through PM_{10} and one through NO_2 . To calculate the indirect effect through PM_{10} , we multiply the coefficient of education on PM_{10} by the coefficient of PM_{10} on standardized FEV1. Identical computation was done with the coefficients through NO_2 . Both indirect effects were summed up to obtain the total indirect effect. To find the percentage mediated we divided the total indirect effect by the sum of total indirect and total direct effects. The model was adjusted for age, sex, smoking, and BMI. The analyses are based on individuals with complete information using Stata v 16.1, at 95% confidence intervals, and bootstrapping on 5000 resamples for SEM.

3. Results

The analytical sample included 6,381 individuals, of which 54% were females (**Table 1**). The mean age was 58.24 ± 7.14 years. In the period 2005-2008, participants were

exposed to a mean of $33.68 \pm 8.26\mu g/m^3$ of PM_{10} , and $20.57 \pm 9.26\mu g/m^3$ of NO_2 . Currently, the limit for annual exposure to PM_{10} is 15 $\mu g/m^3$ and for NO_2 is 10 $\mu g/m^3$ (World Health Organization, 2021). The mean of standardized FEV1 was 91.91 \pm 17.06. Features disaggregated by the level of education showed that tertiary education was more common among males compared to females, higher levels of PM_{10} were observed among individuals with lower education levels, and mining cities—Havirov and Karvina—had a higher proportion of individuals with low levels of education.

3.1. Education and air pollution

In age and sex adjusted linear regression analyses, PM_{10} exposure was strongly associated with education; specifically, persons with tertiary education had significantly lower exposures than those with primary or incomplete education, although the difference was small in absolute terms, about $4\mu g/m^3$ (**Figure 1**, left panel). A similar relationship was observed between NO₂ and education: people at the highest level of education had lower exposure to NO₂ (**Figure 1**, right panel).

3.2. Determinants of lung function

The simultaneous associations of PM_{10} and NO_2 with the standardized FEV1 adjusted for multiple risk factors in ordered steps are presented in **Table 2**. When adjusted for age and sex (model 0), a 10μ g/m³ increase in PM_{10} was associated with 1.78% (95% CI: -2.33 to -1.23) lower FEV1, while a 10μ g/m³ increase in NO_2 was not significantly related to FEV1 (0.29, 95% CI: -0.20 to 0.78). The introduction of BMI and smoking (model 1) and then education (model 2) explained part of the association between PM_{10} and FEV1. No changes in the association between NO_2 and standardized FEV1 were observed with the addition of covariates.

After adjusting for multiple factors in successive linear regressions, a strong educational gradient was observed as individuals with higher levels of education had better lung function than those in an immediately inferior category (**Table 3**). In model

0, the regression coefficients showed that people with tertiary education had seven percentage points higher standardized FEV1 than people with primary or incomplete education. When BMI and smoking were included (model 1) in the regression analysis, the differences between the effect of the highest and the lowest education categories on FEV1 became smaller. However, there remained almost a five-point gap in standardized FEV1 between the lowest and highest education groups. Model 2, with air pollutants added, reduced the educational gradient by only an extra 0.51 points in standardized FEV1 compared to model 1.

In sensitivity analyses, first, we tested for interactions between sex and level of education and found non-significant differences (Supplement B). Then, given the differences in educational attainment between Havirov and Karvina, cities historically devoted to the mining industry, compared to other cities (Supplement C), a separate analysis by city category of model 2 was considered (Supplement D). Finally, we tested the strength of the associations when other SES indicators were included. Table 4 presents the regression coefficients for the association of educational attainment, deprivation, job as a miner, and air pollutants with standardized FEV1. Education had a strong positive association with standardized FEV1 in both groups of cities. In Havirov and Karvina, people with tertiary education had almost six percentage points higher standardized FEV1 than people with primary or incomplete education. PM10 had a stronger negative effect in the historically mining cities of Havirov and Karvina: a $10\mu g/m^3$ increase in PM₁₀ reduced the standardized FEV1 by five points, while in the non-mining cities, the reduction was not statistically significant. NO₂ showed no significant associations with standardized FEV1. Additionally, in Havirov and Karvina people with the highest level of deprivation showed a 2.49% reduction in standardized FEV1 and miners lost 2.99% in standardized FEV1 (Table 4). Deprivation was not associated with lower lung function in non-mining cities.

Mediation analysis

Table 5 and **Figure 3** display the effects of the proposed paths. All paths show statistically significant associations, except for the path from NO₂ to standardized FEV1. Higher educational attainment was associated with less exposure to PM_{10} and less exposure to NO_2 . PM_{10} was negatively associated with the standardized FEV1, which means that higher levels of air pollution led to poorer lung function. The increase in $10\mu g/m^3$ of PM_{10} was associated with reduced standardized FEV1 by 1.32%.

The coefficients from education were multiplied by the coefficients toward standardized FEV1 to obtain the indirect effects specific to each mediator (**Table 6**). We found significant indirect effects through PM_{10} (b=0.20, CI 95%: 0.11 to 0.29) but not for NO_2 (b=-0.03, -0.06 to 0.01). The total indirect effect through PM_{10} and NO_2 accounts for 12% of the total effect.

4. Discussion

In this Czech population-based urban study, most of our findings were consistent with the existing literature. First, exposure to higher levels of PM_{10} was associated with worse lung function (Doiron et al., 2019), and we confirmed educational gradients in exposure to air pollutants and lung function. Given these observations, we explored the potential mediation effect of air pollution between educational attainment and lung function. We found a partial mediation: around 12% of the total effect of educational attainment on lung function can be attributed to exposure to air pollution. This finding supports our hypothesis that the level of education could influence the degree of air pollution people are exposed to. Nevertheless, 88% of the effect of educational attainment on lung function remained unexplained by air pollutants.

The educational gradient observed for air pollutants, for FEV1, and the partial mediation detected suggest that the level of attained education may at least partly determine exposure to outdoor air pollution later in life. The highest level of education is generally completed by early adulthood, thus other characteristics of SES could

better explain the association with air pollution exposure and lung function in late adulthood. However, in this sample of Czech individuals, education was a stronger socioeconomic predictor of long-term health outcomes. Furthermore, we have already described the association between social mobility and lung function elsewhere (Quispe-Haro et al., 2022). Given the cross-sectional design and lack of additional information, we were neither able to quantify the residential relocations during the life course of HAPPIE study participants, nor to test whether being born in a polluted or deprived area could lead to lower levels of attained education in our sample. Others have explored the associations between the migration of talented individuals, exposure to air pollutants, and socioeconomic conditions (Germani et al., 2021; Wang and Guo, 2023). The reasons for voluntary or involuntary migration are complex and diverse. Individuals with any level of education migrate and consider not only housing quality and job opportunities but also family ties, costs, and familiarity (Deluca et al., 2019); hence longitudinal data is needed to analyze to what extent people consider the level of air pollution in the residential area and the posterior health consequences when relocating.

Epidemiologists have focused on the effect modification by SES in the relationship between air pollution and pulmonary outcomes. A systematic review found weak evidence of effect modification of SES when evaluating the association between air pollution and asthma exacerbation in children (Rodriguez-Villamizar et al., 2016). For low-income adults, stronger harmful effects of air pollution on FEV1 and FVC were reported, when controlled by the level of education (Doiron et al., 2019). Barker et al. (2011) argue that the causal role of education on health has been questioned in part due to the lack of sophisticated statistical approaches to "control for wealth and other dimensions of socioeconomic status". In our sample, the educational gradient remained strong after stratifying the analysis between mining and non-mining cities and adding other SES indicators alongside education, such as working as a miner and level

of economic deprivation. In additional analyses, we rejected other probable mechanisms involved, including the interaction between education and sex explored in other studies (Forastiere et al., 2007; Hajat et al., 2021).

As proposed by Hajat et al. (2021), economic constraints could force people of lower SES to live near roads or industrial areas where housing prices are affordable. However, in Europe geographic heterogeneity of social conditions and air pollution have been described (Padilla et al., 2014; Stroh et al., 2005), suggesting that the environmental inequalities found might be specific for the studied area. In our data, low-educated individuals were exposed to higher levels of both PM₁₀ and NO₂. However, these results are inconsistent with previous ecological observations of the distribution of air pollutants in the Czech Republic (Branis and Linhartova, 2012), where higher levels of NO₂ were associated with a higher proportion of citizens with university education. This may be explained, firstly, by the sample consisting solely of individuals living in urban areas and the vicinity of major road networks, generally predicting transport accessibility and mobility, that can be associated with higher SES scores, especially when compared to peripheral areas. Additionally, the discrepancy can be attributed to the spatial resolution used, which was 1x1 km, potentially leading to less precise estimates. Compared to PM₁₀, NO₂ has different distance-decay gradients, a predominant association with line sources (traffic-related air pollution), and thus higher variance within the grid cells associated more with area/volume sources with less spatial variability (McAdam et al., 2011). Thus, unlike PM_{10} , the NO₂ levels may instead indicate the urban economic centrality. Inaccuracies in the computation of air pollution exposure can lead to exposure misclassification (Lu, 2023). Consequently, if more precise estimates of air pollution were used, the proportion mediated by air pollutants (12%), though significant, might be slightly different. This is primarily because the effect size was driven by PM_{10} rather than NO₂. We speculate that a more spatially precise measurement of NO₂ could help improve our models.

Most evidence on the association of SES, air pollution exposure, and health outcomes comes from Western countries where income or job position could be more appropriate to describe their social standing. Western countries with high educational attainment have a limited variation in schooling which could explain the limited capacity of education to capture the health effects (Baker et al., 2011). On the contrary, the educational attainment in the Czech Republic might be a better indicator of the social hierarchy. Previous analyses of the HAPIEE study have demonstrated that education is the strongest socioeconomic predictor of health outcomes (Vandenheede et al., 2014),

This study had several limitations that must be acknowledged. Firstly, a single indicator of SES was used in our mediation analysis, but other aspects of SES could independently predict health outcomes, such as control over one's own life and job, income, and the self-perception of position in the social hierarchy (Marmot, 2004; Theodossiou and Zangelidis, 2009). Moreover, the study did not account for the influence of time spent outdoors and commuting (Makri and Stilianakis, 2008), or the contribution of indoor air pollution on total exposure to air pollutants, which could have potential implications for the results. The cross-sectional nature of the data does not allow us to assess temporality, although – at least in relation to education – reverse causality is unlikely. Nevertheless, a long-term follow-up study would provide more robust evidence.

Air pollution levels have improved in Western Europe in general as well as in the Czech Republic since the early 2000 (Shen et al., 2022), hence it is probable that participants' lifetime exposure to outdoor pollution was substantially higher, therefore we could underestimate the contribution of air pollutants. The lack of consideration for residential mobility further adds to the study's limitations. We assumed that the level of education would affect adults in terms of job opportunities and mobility, however, these speculations should be supported by evidence that will consider the conscious or

unconscious decisions of people in terms of career, income, family, housing and environmental expectations, and opportunities.

To address these issues and enhance future research, incorporating critical concepts such as the social exposome perspective, life course analysis, and differential vulnerability would be valuable (Gudi-Mindermann et al., 2023). Additionally, considering time spent in various activities that influence exposure outside residence can provide more comprehensive insights into the intricate interactions between air pollutants, health effects, and socioeconomic factors. By acknowledging and rectifying these limitations, future studies can contribute significantly to the understanding and management of this crucial public health issue.

5. Conclusion

Individuals with lower educational attainment (representing lower SES) are likely to be exposed to worse air quality. We found evidence of a partial mediation effect of air pollution in the association of education and lung function. Higher levels of education showed both a protective direct effect on lung function and a protective effect on exposure to air pollutants. Higher spatial resolution of NO₂ concentration data could help to capture the effects on lung function. Insights from other fields should be incorporated to understand better the relationship between an individual's socioeconomic circumstances, mobility patterns, environmental exposures, and health.

Acknowledgment

Authors thank the Research Infrastructure RECETOX (number LM2023069) and project CETOCOEN EXCELLENCE (number CZ.02.1.01/0.0/0.0/17_043/0009632) financed by the Czech Ministry of Education, Youth and Sports for supportive background. This work was supported by the European Union's Horizon 2020 Research and Innovation Programme under grant agreement number 857560

(CETOCOEN Excellence) and 857487 (R-Exposome Chair). This publication reflects only the author's view, and the European Commission is not responsible for any use that may be made of the information it contains. KK was supported by the 2023-24 Czech Fullbright Commission Distinguished Scholar Award.

Funding

The authors have disclosed the receipt of the following financial support for the research, authorship and/or publication of this article: the HAPIEE study was funded by the Wellcome Trust (grant WT064947 and WT081081), the US National Institute of Aging (grant R01 AG23522) and the MacArthur Foundation. This work was financially supported by the project Systemic Risk Institute (LX22NPO5101, NPO - EXCELES) funded by the European Union - Next Generation EU.

Ethics approval

This study involves human participants and was approved by the University College London, UK and by the local ethics committee in every participating centre. Participants gave informed consent to participate in the study before taking part. The study protocols were approved by ethical committees at University College London, UK, and at each participating centre.

References:

- Baker, D.P., Leon, J., Smith Greenaway, E.G., Collins, J., Movit, M., 2011. The education effect on population health: A reassessment. Popul Dev Rev 37, 307–332. https://doi.org/10.1111/j.1728-4457.2011.00412.x
- Branis, M., Linhartova, M., 2012. Association between unemployment, income, education level, population size and air pollution in Czech cities: Evidence for environmental inequality? A pilot national scale analysis. Health Place 18, 1110–1114. https://doi.org/10.1016/j.healthplace.2012.04.011
- Clark, L.P., Millet, D.B., Marshall, J.D., 2014. National patterns in environmental injustice and inequality: Outdoor NO2 air pollution in the United States. PLoS One 9. https://doi.org/10.1371/journal.pone.0094431

- Cutler, D.M., Lleras-Muney, A., 2010. Understanding differences in health behaviors by education. J Health Econ 29, 1–28. https://doi.org/10.1016/j.jhealeco.2009.10.003
- Deluca, S., Wood, H., Rosenblatt, P., 2019. Why Poor People Move (and Where They Go): Residential Mobility, Selection and Stratification. City Community 18, 556–593. https://doi.org/10.1111/cico.12386
- Doiron, D., de Hoogh, K., Probst-Hensch, N., Fortier, I., Cai, Y., de Matteis, S., Hansell, A.L., 2019. Air pollution, lung function and COPD: Results from the population-based UK Biobank study. European Respiratory Journal 54. https://doi.org/10.1183/13993003.02140-2018
- Donkin, A.J.M., 2014. Social Gradient, in: Cockerham, W.C., Dingwall, R., Quah, S. (Eds.), The Wiley Blackwell Encyclopedia of Health, Illness, Behavior, and Society. John Wiley & Sons, Chichester, pp. 2172–2178. https://doi.org/10.1002/9781118410868.wbehibs530
- Evans, G.W., Kantrowitz, E., 2002. Socioeconomic status and health: The potential role of environmental risk exposure. Annu Rev Public Health. https://doi.org/10.1146/annurev.publhealth.23.112001.112349
- Fairburn, J., Schüle, S.A., Dreger, S., Hilz, L.K., Bolte, G., 2019. Social inequalities in exposure to ambient air pollution: A systematic review in the WHO European region. Int J Environ Res Public Health 16. https://doi.org/10.3390/ijerph16173127
- Forastiere, F., Stafoggia, M., Tasco, C., Picciotto, S., Agabiti, N., Cesaroni, G., Perucci, C.A., 2007. Socioeconomic status, particulate air pollution, and daily mortality: Differential exposure or differential susceptibility. Am J Ind Med 50, 208–216. https://doi.org/10.1002/ajim.20368
- Germani, A.R., Scaramozzino, P., Castaldo, A., Talamo, G., 2021. Does air pollution influence internal migration? An empirical investigation on Italian provinces. Environ Sci Policy 120, 11–20. https://doi.org/10.1016/j.envsci.2021.02.005
- Glymour, M., Avendano, M., Kawachi, I., 2014. Socioeconomic Status and Health, in: Brakman,
 L., Kawachi, I., Glymour, M. (Eds.), Social Epidemiology. Oxford University Press, New
 York, pp. 17–62.
- Graham, B.L., Steenbruggen, I., Barjaktarevic, I.Z., Cooper, B.G., Hall, G.L., Hallstrand, T.S., Kaminsky, D.A., McCarthy, K., McCormack, M.C., Miller, M.R., Oropez, C.E., Rosenfeld, M., Stanojevic, S., Swanney, M.P., Thompson, B.R., 2019. Standardization of Spirometry 2019 Update. An Official American Thoracic Society and European Respiratory Society Technical Statement. https://doi.org/10.1164/rccm.201908-1590ST 200, E70–E88. https://doi.org/10.1164/RCCM.201908-1590ST
- Gudi-Mindermann, H., White, M., Roczen, J., Riedel, N., Dreger, S., Bolte, G., 2023. Integrating the social environment with an equity perspective into the exposome paradigm: A new conceptual framework of the Social Exposome. Environ Res 233, 116485. https://doi.org/10.1016/j.envres.2023.116485
- Hajat, A., Hsia, C., O'Neill, M.S., 2015. Socioeconomic Disparities and Air Pollution Exposure: a Global Review. Curr Environ Health Rep. https://doi.org/10.1007/s40572-015-0069-5

- Hajat, A., Maclehose, R.F., Rosofsky, A., Walker, K.D., Clougherty, J.E., 2021. Confounding by socioeconomic status in epidemiological studies of air pollution and health: Challenges and opportunities. Environ Health Perspect 129. https://doi.org/10.1289/EHP7980
- Hamad, R., Elser, H., Tran, D.C., Rehkopf, D.H., Goodman, S.N., 2018. How and why studies disagree about the effects of education on health: A systematic review and meta-analysis of studies of compulsory schooling laws. Soc Sci Med. https://doi.org/10.1016/j.socscimed.2018.07.016
- Knobel, P., Hwang, I., Castro, E., Sheffield, P., Holaday, L., Shi, L., Amini, H., Schwartz, J., Yitshak Sade, M., 2023. Socioeconomic and racial disparities in source-apportioned PM2.5 levels across urban areas in the contiguous US, 2010. Atmos Environ 303. https://doi.org/10.1016/j.atmosenv.2023.119753
- Kuster, S.P., Kuster, D., Schindler, C., Rochat, M.K., Braun, J., Held, L., Brändli, O., 2008.
 Reference equations for lung function screening of healthy never-smoking adults aged 18–80 years. European Respiratory Journal 31, 860–868.
 https://doi.org/10.1183/09031936.00091407
- Lu, Y., 2023. Assessing air pollution exposure misclassification using high-resolution PM2.5 concentration model and human mobility data. Air Qual Atmos Health 16, 2225–2238. https://doi.org/10.1007/s11869-023-01404-2
- Makri, A., Stilianakis, N.I., 2008. Vulnerability to air pollution health effects. Int J Hyg Environ Health 211, 326–336. https://doi.org/10.1016/j.ijheh.2007.06.005
- Marmot, M., 2004. Status syndrome. Significance 1, 150–154. https://doi.org/10.1111/j.1740-9713.2004.00058.x
- McAdam, K., Steer, P., Perrotta, K., 2011. Using continuous sampling to examine the distribution of traffic related air pollution in proximity to a major road. Atmos Environ 45, 2080–2086. https://doi.org/10.1016/j.atmosenv.2011.01.050
- Orellano, P., Reynoso, J., Quaranta, N., Bardach, A., Ciapponi, A., 2020. Short-term exposure to particulate matter (PM10 and PM2.5), nitrogen dioxide (NO2), and ozone (O3) and allcause and cause-specific mortality: Systematic review and meta-analysis. Environ Int 142. https://doi.org/10.1016/j.envint.2020.105876
- Ostatnická, J., 2008. ZNEČIŠTĚNÍ OVZDUŠÍ NA ÚZEMÍ ČESKÉ REPUBLIKY V ROCE 2008 [WWW Document]. Český hydrometeorologický ústav - Úsek ochrany čistoty ovzduší. URL https://www.chmi.cz/files/portal/docs/uoco/isko/grafroc/groc/gr08cz/kap22.html (accessed 3.5.24).
- Padilla, C.M., Kihal-Talantikite, W., Vieira, V.M., Rossello, P., Nir, G. Le, Zmirou-Navier, D., Deguen, S., 2014. Air quality and social deprivation in four French metropolitan areas-A localized spatio-temporal environmental inequality analysis. Environ Res 134, 315–324. https://doi.org/10.1016/j.envres.2014.07.017
- Peasey, A., Bobak, M., Kubinova, R., Malyutina, S., Pajak, A., Tamosiunas, A., Pikhart, H., Nicholson, A., Marmot, M., 2006. Determinants of cardiovascular disease and other noncommunicable diseases in Central and Eastern Europe: Rationale and design of the HAPIEE study. BMC Public Health 6, 1–10. https://doi.org/10.1186/1471-2458-6-255/TABLES/2

- Quispe-Haro, C., Pajak, A., Tamosiunas, A., Capkova, N., Bobak, M., Pikhart, H., 2022.
 Socioeconomic position over the life course and impaired lung function of older adults in Central and Eastern Europe: The HAPIEE study. J Epidemiol Community Health (1978) 77, 49–55. https://doi.org/10.1136/jech-2022-219348
- Richardson, E.A., Pearce, J., Tunstall, H., Mitchell, R., Shortt, N.K., 2013. Particulate air pollution and health inequalities: A Europe-wide ecological analysis. Int J Health Geogr 12. https://doi.org/10.1186/1476-072X-12-34
- Rocha, V., Soares, S., Stringhini, S., Fraga, S., 2019. Socioeconomic circumstances and respiratory function from childhood to early adulthood: A systematic review and metaanalysis. BMJ Open 9. https://doi.org/10.1136/bmjopen-2018-027528
- Rodriguez-Villamizar, L.A., Berney, C., Villa-Roel, C., Ospina, M.B., Osornio-Vargas, Alvaro and Rowe, B.H., 2016. The role of socioeconomic position as an effect-modifier of the association between outdoor air pollution and children's asthma exacerbations: an equity-focused systematic review. Rev Environ Health 31, 297–309.
- Ross, C., Mirowsky, J., 2010. Why Education Is the Key to Socioeconomic Differentials in Health, in: Bird, C., Conrad, P., Fremont, A., Timmermans, S. (Eds.), Handbook of Medical Sociology. Vanderbilt University Press, Nashville, pp. 33–51.
- Shen, Y., de Hoogh, K., Schmitz, O., Clinton, N., Tuxen-Bettman, K., Brandt, J., Christensen, J.H., Frohn, L.M., Geels, C., Karssenberg, D., Vermeulen, R., Hoek, G., 2022. Europe-wide air pollution modeling from 2000 to 2019 using geographically weighted regression. Environ Int 168, 107485. https://doi.org/10.1016/J.ENVINT.2022.107485
- Stroh, E., Oudin, A., Gustafsson, S., Pilesjö, P., Harrie, L., Strömberg, U., Jakobsson, K., 2005. Are associations between socio-economic characteristics and exposure to air pollution a question of study area size? An example from Scania, Sweden. Int J Health Geogr 4. https://doi.org/10.1186/1476-072X-4-30
- Theodossiou, I., Zangelidis, A., 2009. The social gradient in health: The effect of absolute income and subjective social status assessment on the individual's health in Europe. Econ Hum Biol 7, 229–237. https://doi.org/10.1016/j.ehb.2009.05.001
- Vandenheede, H., Vikhireva, O., Pikhart, H., Kubinova, R., Malyutina, S., Pajak, A., Tamosiunas, A., Peasey, A., Simonova, G., Topor-Madry, R., Marmot, M., Bobak, M., 2014.
 Socioeconomic inequalities in all-cause mortality in the Czech Republic, Russia, Poland and Lithuania in the 2000s: findings from the HAPIEE Study. J Epidemiol Community Health (1978) 68, 297–303. https://doi.org/10.1136/jech-2013-203057
- Wang, H., Guo, F., 2023. City-level socioeconomic divergence, air pollution differentials and internal migration in China: Migrants vs talent migrants. Cities 133. https://doi.org/10.1016/j.cities.2022.104116
 - World Health Organization, 2021. WHO global air quality guidelines. Particulate matter (PM2.5 and PM10), ozone, nitrogen dioxide, sulfur dioxide and carbon monoxide. Geneva.

Fig. 1. Linear regression coefficients of categories of attained education for exposure to PM_{10} and NO_2 . Coefficients and confidence intervals are adjusted for age and sex.



Figure 1. Linear regression coefficients of categories of attained education for exposure to PM_{10} and NO_2 . Coefficients and confidence intervals are adjusted for age and sex.

Solution

Figure 2. Mediation effects of PM_{10} and NO_2 in relationship between education and standardized FEVI(%). *Statistically significant coefficients. Model adjusted for age, sex, BMI, and smoking behavior. Model fit: X2(9) = 177.337, p<0.001, CFI=0.775, RMSEA = 0.054, 90% CI RMSEA [0.047, 0.061].



Figure 2. Mediation effects of PM₁₀ and NO₂ in relationship between education and standardized FEV1(%). *Statistically significant coefficients. Model adjusted for age, sex, BMI, and smoking behavior. Model fit: $\chi 2(9) = 177.337$, p<0.001, CFI = 0.775, RMSEA = 0.054, 90% CI RMSEA [0.047, 0.061].

Solution

	Total	Primary or	Vocational	Secondary	Tertiary	
		incomplete				
Age, mean (SD),	58.24	(7) 70 07			57.86	
years	(7.14)	60.07 (7)	58.15 (7)	57.87 (7)	(7)	
Sex, n (%)						
Male	2917				504 (40)	
	(46)	157 (6)	1292 (44)	944 (32)	524 (18)	
Female	3464		4000 (04)	4.400 (44)	0.40 (4.0)	
	(54)	615 (18)	1083 (31)	1420 (41)	346 (10)	
Smoking status, n (%))		0			
Never	2848	367 (13)	957 (34)	1073 (38)	151 (16)	
	(45)	307 (13)	937 (34)	1073 (30)	431 (10)	
Past and occasional	2067		770 (00)		077 (40)	
	(32)	209 (10)	779 (38)	802 (39)	277 (13)	
Regular	1466	106 (12)	620 (44)	190 (22)	142 (10)	
	(23)	190 (13)	059 (44)	409 (00)	142 (10)	
Education	5					
Primary or	772					
incomplete	(12)					
Vocational	2375					
	(37)					
Secondary	2364					
	(37)					
Tertiary	870					
	(14)					
BMI, mean (SD),	28.23	29.60 (5)	28.74 (5)	27.68 (4)	27.13	

Table 1. Participants' characteristics by level of educational attainment (n=6381)

Journal Pre-proof					
kg/m²	(4.55)				(4)
Air pollutants, mean (SD), µg/m³				
DM from 2005 00	33.68	20.40.(40)	34.54 (9)	32.49 (7)	32.16
PM ₁₀ Irom 2005-08	(8.26)	36.40 (10)			(7)
	20.57				19.42
NO ₂ from 2005-08	(9.26)	22.15 (9)	20.67 (9)	20.36 (9)	(10)
^a Standardized FEV1,					
mean (SD), % of	91.91	88.46 (19)	90.87 (17)	92.87 (17)	95.20
predicted value	(17.06)			<u> </u>	(16)
			~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~		
Cities, n (%)					
Havirov	785	138 (18)	357 (45)	214 (27)	76 (10)
	(12)			( )	( )
Hradec	732	50 (7)	235 (32)	315 (13)	132 (18)
	(11)	50 (7)	200 (02)	515 (45)	132 (10)
Jihlava	657	70 (40)	004 (40)	044 (07)	74 (44)
	(10)	78 (12)	264 (40)	244 (37)	71 (11)
Karvina	478 (7)	116 (24)	230 (48)	107 (23)	25 (5)
Kromeriz	1271				/
	(20)	118 (9)	434 (34)	492 (49)	227 (18)
Liberec	876				142
	(14)	70 (8)	287 (33)	377 (43)	(16)
Usti nad Labem	1582				
	(25)	202 (13)	568 (36)	615 (39)	197 (12)
^a Optimal value of stand	^a Optimal value of standardized FEV1=100%				

		Model 0	Model 1	Model 2
		b ^a (95% CI)	b ^a (95% CI)	b ^a (95% CI)
PM ₁₀ per	10	-1.78 (-2.33 to -	-1.53 (-2.07 to -0.99)	-1.33 (-1.87 to -0.78)
µg/m³		1.23)		
NO ₂ per	10	0.29 (-0.20 to 0.78)	0.35 (-0.12 to 0.83)	0.36 (-0.12 to 0.84)
µg/m³			X	
AIC		54227.07	53909.11	53884.48
BIC		54260.88	53963.21	53958.85
LR test			χ ² (3) =323.95,	$\chi^{2}(3) = 30.64,$
			p<0.001	p<0.001

**Table 2.** Linear regression coefficients for the association of  $PM_{10}$  and  $NO_2$  with standardized FEV1(%) among Czech adults participating in the HAPPIE study.

Model 0: adjusted for age and sex.

Model 1: as model 0 additionally adjusted for BMI and smoking status.

Model 2: as model 1 additionally adjusted for education.

^ab coefficient of -1 means that standardized FEV1 reduces by one percentage point per

 $10 \ \mu g/m^3$  increase in air pollutant concentration.

		Model 0	Model 1	Model 2
		b ^a (95% CI)	b ^a (95% CI)	b ^a (95% CI)
Primary	or	0	0	0
incomplete				
Vocational		3.00 (1.59 to	2.41 (1.03 to 3.79)	2.17 (0.78 to 3.55)
		4.41)		
Secondary		4.61 (3.22 to	3.19 (1.82 to 4.57)	2.71 (1.33 to 4.09)
		6.00)		
Tertiary		7.43 (5.76 to	5.16 (3.49 to 6.82)	4.65 (2.97 to 6.32)
		9.11)	Ø	
AIC		54184.68	53903.66	53884.47
BIC		54225.24	53964.51	53958.84
LR test			χ ² (3) =287.01,	χ ² (2) =23.19,
			p<0.001	p<0.001

**Table 3.** Linear association of educational attainment with standardized FEV1(%) among Czech adults participating in the HAPPIE study.

Model 0: adjusted for age and sex.

Model 1: as model 0 additionally adjusted for BMI and smoking status.

Model 2: as model 1 additionally adjusted for PM₁₀ and NO₂.

^ab coefficient of -1 means that standardized FEV1 reduces by one percentage point per

category of education compared to individuals with primary or incomplete education

**Table 4:** Multivariable linear association coefficients of variables included in model 2 plus otherSES indicators (deprivation and job as miner) on Standardized FEV1. n=6187

	Mining cities		Non-mining cities	
	(Havirov and Karvina)		(Hradec, Jihlava,	Kromeriz, Liberec, Usti
			nad Labem)	
	b	95% CI	b	95% CI
Education				
Primary	or			
incomplete	Ref.		Ref.	
Vocational	2.88	0.23 to 5.53	1.40	-0.30 to 3.11
Secondary	4.48	1.60 to 7.35	1.81	0.13 to 3.48
Tertiary	5.65	1.54 to 9.76	3.69	1.72 to 5.65
Air pollutants				
^a PM ₁₀ per 10 μg/m ³	-4.98	-8.83 to -1.14	-1.16	-2.60 to 0.28
^a NO₂ per 10 µg/m ³	1.08	-0.70 to 2.85	-0.28	-0.23 to 0.79
Deprivation	2			
No deprivation	Ref.		Ref.	
Low deprivation	-1.84	-4.17 to 0.49	-0.80	-1.93 to 0.33
High deprivation	-2.49	-4.73 to -0.24	-1.11	-2.27 to 0.06
Miner, yes	-2.99	-5.90 to -0.08		

^aAverage concentration of air pollutants from 2005 to 2008 expressed in  $\mu$ g/m³. b coefficient of -1 means that standardized FEV1 reduces by one percentage point per 10  $\mu$ g/m³ increase in air pollutant concentration.

**Table 5.** Mediation effects of  $PM_{10}$  and  $NO_2$  in the relationship between educational attainment and standardized FEV1(%) among Czech adults participating in the HAPPIE study.

Exposure	Outcome	b	Standard error	95% CI
	Standardized FEV1(%)	1.34	0.250	0.85 to 1.83
Education	ΡΜ ₁₀ , μg/m ³	-0.15	0.011	-0.18 to -0.13
	NO ₂ , μg/m ³	-0.07	0.013	-0.10 to -0.05
PM ₁₀ per 10 µg/m ³		-1.32	0.283	-1.87 to -0.76
NO ₂ per 10 µg/m ³	Standardized FEV1(%)	0.34	0.246	-0.14 to 0.83
Model adjusted for age, sex, BML and smoking behavior				

Quind Real

	b	Standard error	95% Confidence interval
Total indirect effect	0.18	0.043	0.09 to 0.26
ΡΜ ₁₀ , μg/m ³	0.20	0.046	0.11 to 0.29
NO₂, μg/m³	-0.03	0.019	-0.06 to 0.01

**Table 6.** Bootstrapped indirect effects coefficients in the mediation analysis between education and standardized FEV1(%).

## **Declaration of interests**

⊠The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

## Graphical abstract

#### Mediation effects of PM₁₀ and NO₂ between education and lung function.



# Highlights

- We investigated lung function in older adults from seven Czech cities.
- We noticed an educational gradient in lung function and exposure to air pollutants.
- PM₁₀ and NO₂ partly mediated the association between education and lung function.
- Educational attainment had direct and indirect association with lung function.