JASIURA, Adam, LIPCZYŃSKA, Wiktoria, WARCHOŁ, Konrad, GORZEL, Mateusz, JUSTYŃSKA, Agata, KRAFZIK, Hanna, STĘPIEŃ, Przemysław and KASPRZAK, Hubert. Particulate matter – a cancerous threat to our health? Journal of Education, Health and Sport. 2023;50(1):23-36. eISSN 2391-8306. https://dx.doi.org/10.12775/JEHS.2023.50.01.002
https://apcz.umk.pl/JEHS/article/view/47554
https://zenodo.org/records/10441846

The journal has had 40 points in Ministry of Education and Science of Poland parametric evaluation. Annex to the announcement of the Minister of Education and Science of 03.11.2023 No. 32318. Has a Journal's Unique Identifier: 201159. Scientific disciplines assigned: Health Sciences (Field of medical and health sciences); Medical sciences (Field of medical and health sciences); Cultural and religious studies (Field of humanities); Physical culture sciences (Field of medical and health sciences); Socio-economic geography and spatial management (Field of social sciences); Pedagogy (Field of social sciences); Earth and Environmental Sciences (Field of exact and natural sciences).
Punkty Ministerialne z 2019 - aktualny rok 40 punktów. Załącznik do komunikatu Ministra Edukacji i Nauki z dnia 03.11.2023 Lp. 32318. Posiada Unikatowy Identyfikator Czasopisma: 201159. Przypisane dyscypliny naukowe: Nauki o zdrowiu (Dziedzina nauk medycznych i nauk o zdrowiu); Nauki medyczne (Dziedzina nauk medycznych i nauk o zdrowiu); Nauki o kulturze i religii (Dziedzina nauk humanistycznych); Nauki o kulturze fizycznej (Dziedzina nauk medycznych i nauk o zdrowiu); Geografia społeczno-ekonomiczna i gospodarka przestrzenna (Dziedzina nauk społecznych); Pedagogika (Dziedzina nauk społecznych); Nauki o Ziemi i środowisku (Dziedzina nauk ścisłych i przyrodniczych).

The authors declare that there is no conflict of interests regarding the publication of this paper.
Received: 18.12.2023. Revised: 26.12.2023. Accepted: 27.12.2023. Published: 30.12.2023.

Particulate matter – a cancerous threat to our health?

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Abstract

Introduction: Particulate matter (PM) as a part of outdoor air pollutants are classified as human carcinogens. They are formed majorly as a result of combustion process by industry, power plants and engines. PM can be divided by the size of their particles into $PM_{2.5}$ and PM_{10}, where $PM_{2.5}$ are small enough to penetrate into the alveoli sacs in the lung reaching the bloodstream, whereas PM_{10} affect mostly oral cavity, nose and the throat.

Aim of the study: This study aims to investigate the impact of $PM_{2.5}$ and PM_{10} particle concentrations in the EU NUTS 2 subregions on the death rates due to the most common malignant neoplasms.

Results: There is a positive moderate correlation ($r = 0.421$; $p < 0.001$) between the annual mean concentration of $PM_{2.5}$ and deaths due to malignant tumors. The strongest correlation was observed for malignant neoplasms of larynx, which is a positive correlation with a strong effect ($r = 0.641$; $p < 0.001$); and malignant neoplasm of bladder ($r = 0.523$; $p < 0.001$). For PM_{10}, there is a moderately weak positive correlation ($r = 0,195$; $p = 0.008$) between the annual average concentration of PM_{10} and deaths due to malignant tumors. The strongest correlation was observed for malignant neoplasms of larynx, which is a positive correlation with a strong effect ($r = 0,551$; $p < 0.001$).

Conclusion: The effect of PM impact on the malignant neoplasms is strong to moderate. The most affected neoplasm site are the ones the PMs intake occurs, being in the respiratory

system. However other sites, where PMs can accumulate can be impacted as well. Further studies about the population with the highest risk due to the PMs exposure may be beneficial as other non-air quality-connected predictors may be found.

Key words: air pollution; particulate matter; cancer; mortality.

Introduction

Outdoor air pollution and particulate matter from outdoor air pollution are classified as carcinogenic to humans (IARC Group 1) by the International Agency for Research on Cancer (IARC) [1]. Outdoor air pollution can be defined as a mixture of multiple pollutants originating from a multitude of both natural and anthropogenic sources, further divided into primary and secondary air pollutants [2].

Primary air pollutants include gaseous pollutants such as sulfur dioxide (SO_2), nitrogen dioxide (NO_2), carbon monoxide (CO), volatile organic compounds (VOCs), and particulate matter (PM), including carbonaceous aerosol particles, such as black soot. They are mainly emitted directly into the environment as a result of the combustion of fossil and biomass fuels [3]–[5]. Secondary air pollutants are formed from primary air pollutants and include gaseous ozone (O_3) and sulfate and nitrate derivatives. Particulate matter can be further distinguished into primary PM, formed in the combustion process by industry, power plants, and engines, and secondary PM, formed in the atmosphere by other primary gaseous pollutants. PM can be fractioned by the size of the particles into PM_{10} and $PM_{2.5}$. The PM_{10} fraction (particles ≤ 10 μm in diameter), consists of the largest inhalable particles, which are mostly not inhaled past the trachea and therefore not reaching the lungs; thereby, they mostly affect the oral cavity, nose, and throat. The $PM_{2.5}$ fraction is known as fine particulate matter (particles ≤ 2.5 μm in diameter), which can be inhaled up to the alveoli sacs in the lungs, reaching the bloodstream [3], [6], [7].

Ambient air pollution exposure has been linked to the incidence and mortality of cardiovascular, respiratory, and cancerous diseases [8]. This connection is strongly based on lung cancer; however, air pollutants can also increase risk in other neoplasm sites such as the bladder [9], kidney [10], and urinary tract [11]–[13], as well as oral, nasopharyngeal [14], cervical [15], and esophageal cancer [16].

In this paper, we aim to search for a relationship between $PM_{2.5}$ and PM_{10} particle concentrations in the EU NUTS2 subregions and the death rates due to the most common malignant neoplasms.

Data

The study used data from public sources available under the Creative Commons 4.0 license. Data on measurements of PM particles comes from the European Environment Agency database. The most recent available period, 2020, was selected. Data on deaths was obtained from the EUROSTAT database created by the European Commission. Standardized coefficients per 1,000 inhabitants were used for the distinguished causes of death in the designated NUTS 2 areas (Causes of death - standardized death rate by NUTS 2 region of residence). The most recent available period, 2020, was selected.

Diagnoses of diseases for hospitalization rates were defined according to ICD-10. The following diseases were distinguished: malignant neoplasms (C00-C97); malignant neoplasms of lip, oral cavity and pharynx (C00-C14); malignant neoplasm of colon, rectum and anus (C18-C21); malignant neoplasm of larynx (C32); malignant neoplasm of trachea, bronchus and lung (C33-C34); malignant neoplasm of bladder (C67).

The study used a territorial division in accordance with Nomenclature of Territorial Units for Statistics (NUTS) based on data provided by EUROSTAT. The data is presented at the NUTS 2 level.

Statistical analysis

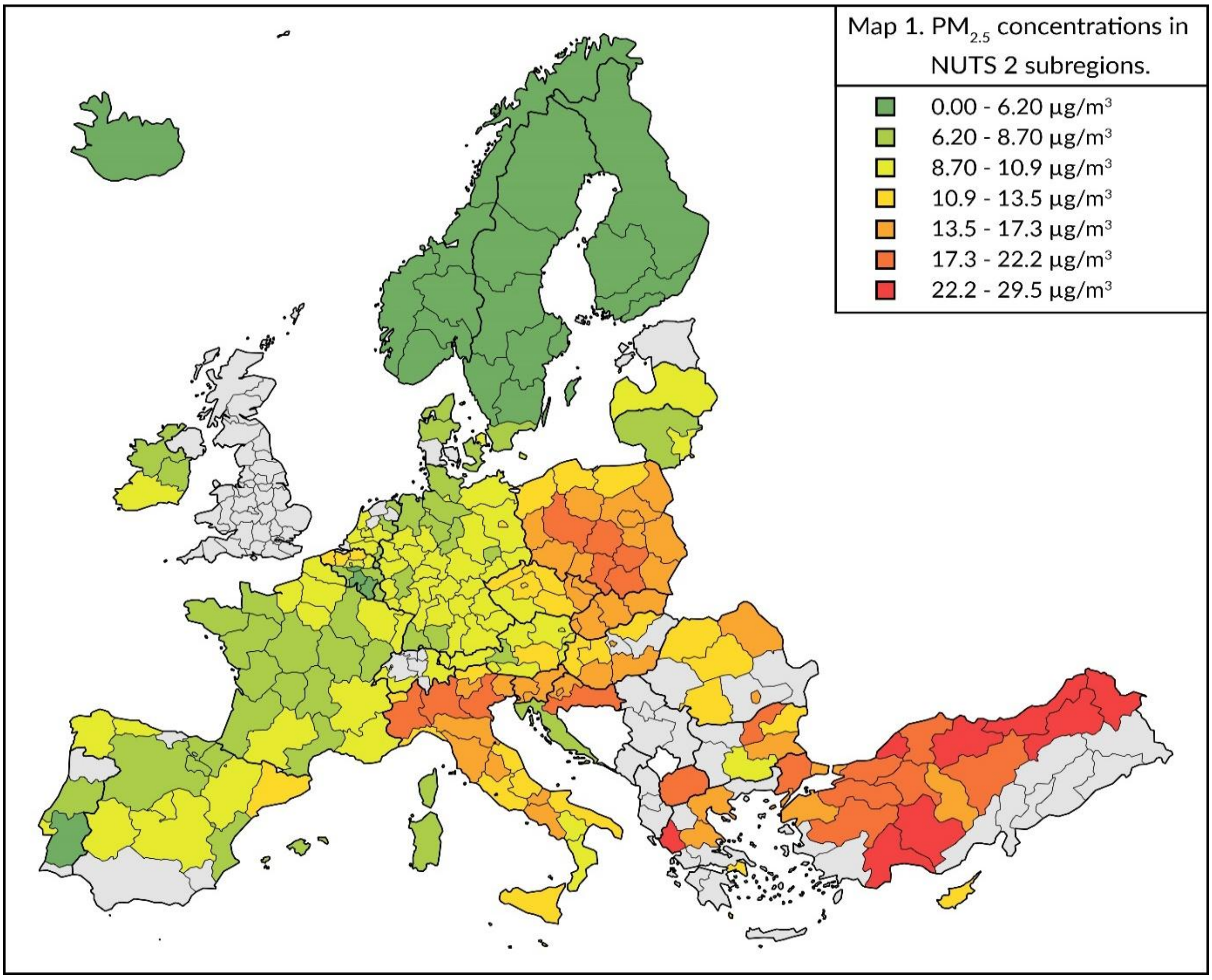
Data from research stations was aggregated for the analyzed NUTS2 areas, calculating the annual average concentration of PM for the subregion. For standardized death rates, the

Shapiro-Wilk test was used to assess the normality of quantitative variables. Correlations were calculated using Pearson's r coefficient. The significance level was set at $\alpha = 0.05$. The analysis was carried out in the TIBCO Statistica 13, QGIS 3.32 and MS Excel environments.

Results

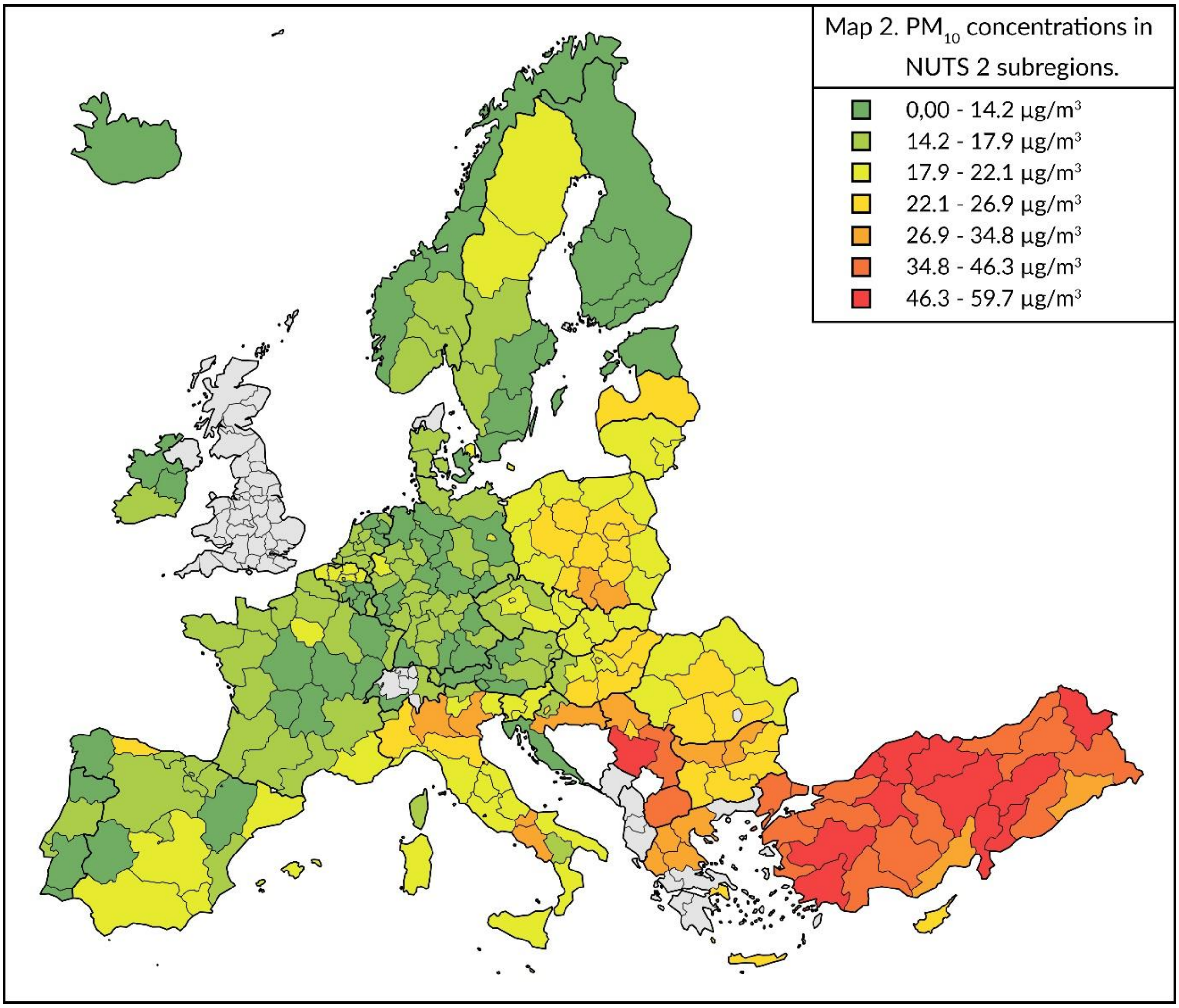
In the analyzed periods, the mean concentration of $PM_{2.5}$ in the studied subregions was 11,3 µg/m3. The lowest average concentrations of $PM_{2.5}$ in the studied subregions were recorded in Island (IS00; 2.886 µg/m^3) and Pohjois - ja Itä-Suomi in Finland (FI1D; 3.464 µg/m^3). Contrarily, the highest were observed in the subregions of Turkey - Erzurum, Erzincan, Bayburt (TRA1; 29.523 µg/m^3), and Konya, Karaman (TR52; 25.461 µg/m^3). The lowest average concentration of $PM_{2.5}$ for the studied countries was recorded in Island (IS; 2.886 µg/m^3), while the highest was in Turkey (TR; 20.792 µg/m^3). The average annual concentrations of $PM_{2.5}$ in the analyzed NUTS2 subregions are presented on Map 1.

Map 1. $PM_{2.5}$ concentarations in NUTS 2 subregions.



In the analyzed periods, the mean concentration of PM_{10} in the studied subregions was 21.12 μg/m^3. The lowest average concentrations of PM_{10} in the studied subregions were recorded in Estonia (EE00; 7.111 μg/m^3) and Região Autónoma dos Açores in Portugal (PT20; 8.851 μg/m^3). Contrarily, the highest were observed in the subregions of Turkey - Gaziantep, Adıyaman, Kilis (TRC1; 59.708 μg/m^3), and Ağrı, Kars, Iğdır, Ardahan (TRA2; 59.272 μg/m^3). The lowest average concentration of PM_{10} for the studied countries was recorded in Estonia (EE; 7.111 μg/m^3), while the highest was in Turkey (TR; 45.125 μg/m^3). The average annual concentrations of PM10 in the analyzed NUTS 2 subregions are presented on Map 2.

Map 2. PM_{10} concentarations in NUTS 2 subregions.



<u>Correlations</u>

There is a positive correlation of moderate effect ($r = 0.421$; $p < 0.001$) between the annual average concentration of $PM_{2.5}$ and deaths due to malignant tumors. In the malignant tumours, the strongest correlation was observed for malignant neoplasms of larynx, which is a positive correlation with a strong effect ($r = 0.641$; $p < 0.001$). Following neoplasm with the greatest relationship with the annual average concentration of $PM_{2.5}$ is malignant neoplasm of bladder, which was shown to have a strong positive correlation ($r = 0.523$; $p < 0.001$). The remaining distinguished neoplasms are positively correlated with the annual average concentration of $PM_{2.5}$ in the studied regions with moderate strength (malignant neoplasms of lip, oral cavity and pharynx, and malignant neoplasm of trachea, bronchus and lung) or weak strength (malignant neoplasm of colon, rectum and anus). Thereby, in regions with a higher annual average concentration of $PM_{2.5}$, there is a higher frequency of deaths due to malignant tumors among the studied residents. The exact results of Pearson's correlation coefficient are presented in Table 1.

Table 1. Correlations between death rates and $PM_{2.5}$ concentration in selected NUTS 2 subregions.

Death rates	**M**	**SD**	**r**	**p**
Malignant neoplasms (C00-C97)	242.24	32.457	**0.421**	**0.000**
Malignant neoplasms of lip, oral cavity and pharynx (C00-C14)	6.037	2.368	**0.413**	**0.000**
Malignant neoplasm of colon, rectum and anus (C18-C21)	21.343	5.204	**0.235**	**0.001**
Malignant neoplasm of larynx (C32)	2.175	1.409	**0.641**	**0.000**
Malignant neoplasm of trachea, bronchus and lung (C33-C34)	47.787	11.131	**0.368**	**0.000**
Malignant neoplasm of bladder (C67)	7.738	2.383	**0.523**	**0.000**

There is a positive correlation of weak effect ($r = 0{,}195$; $p = 0.008$) between the annual average concentration of PM_{10} and deaths due to malignant tumors. In the malignant tumours, the strongest correlation was observed for malignant neoplasms of larynx, which is a positive correlation with a strong effect ($r = 0{,}551$; $p < 0.001$). The next neoplasm with the greatest relationship with the annual average concentration of PM_{10} is malignant neoplasm of bladder, which was shown to have a strong positive correlation ($r = 0{,}449$; $p < 0.001$). The remaining distinguished neoplasms are positively correlated with the annual average concentration of

PM_{10} in the studied regions with a weak strength Hence, in regions with a higher annual average concentration of PM_{10}, there is a higher frequency of deaths due to malignant tumors among the studied residents. The exact results of Pearson's correlation coefficient are presented in Table 1.

Table 2. Correlations between death rates and PM_{10} concentration in selected NUTS2 subregions.

Death rates	M	SD	r	p
Malignant neoplasms (C00-C97)	242.24	32.457	**0.195**	**0.008**
Malignant neoplasms of lip, oral cavity and pharynx (C00-C14)	6.037	2.368	**0.197**	**0.008**
Malignant neoplasm of colon, rectum and anus (C18-C21)	21.343	5.204	**0.146**	**0.049**
Malignant neoplasm of larynx (C32)	2.175	1.409	**0.551**	**0.000**
Malignant neoplasm of trachea, bronchus and lung (C33-C34)	47.787	11.131	**0.157**	**0.035**
Malignant neoplasm of bladder (C67)	7.738	2.383	**0.449**	**0.000**

Linear regression models for $PM_{2.5}$ particles

For the three distinguished neoplasms in the $PM_{2.5}$ study, in which the described correlation coefficients were the highest, linear regression models of death rate were created. The independent variable was the annual average concentration of $PM_{2.5}$ in the analyzed regions.

In the case of malignant neoplasms of lip, oral cavity and pharynx, the average difference between the actual values and the values predicted by the model for the dependent variable was 3.66 (which is 60.62% of the average for the dependent variable). The coefficient of determination ($R^2 = 0.121$), the value of the F statistic (30.748) and its corresponding probability level p ($p < 0.001$) indicate the statistical significance of the model. These values can be interpreted to mean that reducing the annual average concentration of of $PM_{2.5}$ by 1 $\mu g/m^3$ will reduce the frequency of deaths due to malignant neoplasms of lip, oral cavity and pharynx by 0.583 per 1000 residents of the studied regions.

In the case of malignant neoplasms of larynx, the average difference between the actual values and the values predicted by the model for the dependent variable was 3.19. The coefficient of determination (R^2 = 0.38), the value of the F statistic (134.24) and its corresponding probability level p ($p < 0.001$) indicate the statistical significance of the model. These values can be interpreted to mean that reducing the annual average concentration of $PM_{2.5}$ by 1 $\mu g/m^3$ will reduce the frequency of deaths due to malignant neoplasms of larynx by 3.47 per 1000 residents of the studied regions.

In the case of malignant neoplasms of bladder, the average difference between the actual values and the values predicted by the model for the dependent variable was 3.39 (which is 43.8% of the average for the dependent variable). The coefficient of determination (R^2 = 0.244), the value of the F statistic (71.219) and its corresponding probability level p ($p < 0.001$) indicate the statistical significance of the model. These values can be interpreted to mean that reducing the annual average concentration of $PM_{2.5}$ by 1 $\mu g/m^3$ will reduce the frequency of deaths due to malignant neoplasms of bladder by 0.86 per 1000 residents of the studied regions.

Discussion

Particulate matter, especially $PM_{2.5}$ is responsible for 5 million deaths due to cardiovascular, pulmonary, infectious, and cancerous diseases; however, over 7 million people die annually due to exposure to polluted air [17], [18].

The negative influence of air pollution on human health has been noted for many years. Recalling the great London smog of 1952 where air pollution caused the deaths of up to 12,000 people [19]. It could be said that this is when people began to pay more attention to what they breathe. In our work, we focused on PM_{10} and $PM_{2.5}$, as they are largely responsible for systemic dysfunction due to smog.

Our statistical analysis showed a moderate correlation between $PM_{2.5}$ and malignant neoplasms in the studied population; a strong positive correlation between $PM_{2.5}$ and malignant neoplasms of the larynx and bladder. A moderately average correlation came out for malignant cancers of the lips, mouth, esophagus, larynx, bronchus, and lung. Moderately weak correlation for malignant cancers of the colon, rectum.

There is a moderately weak correlation between PM_{10} concentrations and the incidence of malignant neoplasms in the population. The strongest correlation is found in cancers of the larynx and bladder. Other cancers showed a moderately weak correlation. The more significant impact of $PM_{2.5}$ compared to PM_{10} can be explained by the fact that it has the ability to penetrate the alveolar membrane and spread through the bloodstream around the human body [17].

Turner et al. in their study tried to substantiate the correlation of bladder cancer incidence with $PM_{2.5}$ and NO_2 concentrations in the Spanish population. They attempted to divide the study population by age group, sex, region, education, cigarette smoking status, and pack-years, but showed no significant differences between the groups. They also created a model for each air pollutant separately but did not obtain significant results [9]. They did not obtain conclusive results, probably due to the lack of data regarding patients' previous exposure to selected air pollutants, and indicate the requirement to repeat the study on a larger group of subjects. In contrast, Zare Sakhvidi et al. in their review on the effect of air pollution on bladder, kidney and ureteral cancer found a significant association between bladder cancer and air pollution, which only in a few papers considered in their review reached statistical significance. Most unfortunately, it indicated a link between air pollution and bladder cancer without statistical significance, which also opens a window to create further analyses to prove the connection [11].

Josyula et al. in their meta-analysis showed the correlation of household air pollution (which includes $PM_{2.5}$ and PM_{10}) with cancers of the oral cavity, nasopharynx, pharynx and larynx. However, they point out the relevance of the type of fuel used to power the home, as each type of fuel contains different carcinogens. In their work, they showed a trend of a higher incidence of laryngeal cancer in coal-burners, while wood-burners had a higher incidence of oral cancer. However, this requires further analysis due to the small number of studies specifying the type of fuel [16].

It would be worthwhile to consider the significance of reducing at least some air pollution. In our statistical analysis, we prove that reducing PM concentrations by even 1 $\mu g/m^3$ is capable of reducing cancer mortality. In our view, any action to reduce air pollution, even on a small scale, has global significance for the well-being of the population and each individual.

The main association of pollutants in PM relates to lung cancer as, for example, in the study by Liu et al. where they prove the effect of $PM_{2.5}$ on the increase in lung cancer incidence [20]. Their work took into account the increase in $PM_{2.5}$ pollution levels over 29 years in Asian countries and showed a high correlation with an increase in lung cancer incidence. The risk of other cancers is also increasing, however, it is not supported by such strong evidence.

There is a need for more epidemiological studies that target non-lung cancers, taking into account survival and incidence in regions where exposure to PM particles is greatest and their potential impact on incidence. It may be possible to implement some kind of preventive program aimed at reducing air pollution, or if that is not possible, at the people who are most affected by it, so this would require further delving into the group of the population that is most at risk of cancer incidence and death from PM exposures.

Conclusions

Air pollution is a major health problem worldwide. Although the negative effects of PM exposure have been confirmed majorly for neoplasms of lung, it is an important risk factor for morbidity and mortality from other malignant neoplasms as well. More epidemiological studies are needed that target non-lung cancers in terms of incidence and survival in regions, where PM exposure is the highest. It may be beneficial to implement some kind of preventive programs aimed not only at reducing air pollution, but also, if that is not feasible in certain subregions, at the people who are most exposed. This would require deeper research into the subpopulation that is most at risk of being adversely affected by PM exposure, and other non-air quality predictors.

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Supplementary Materials

The following supporting information can be downloaded at:

https://drive.google.com/drive/folders/1xdLcpYfFvcdL0m7CszV3svJrBrK6bTko?usp=sharin
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Map 1. $PM_{2.5}$ concentarations in NUTS 2 subregions.

Map 2. PM_{10} concentarations in NUTS 2 subregions.

Table 1. Correlations between death rates and $PM_{2.5}$ concentration in selected NUTS 2 subregions.

Table 2. Correlations between death rates and PM_{10} concentration in selected NUTS2 subregions.

Author Contributions

Conceptualization, A.J.; writing—original draft preparation, A.J., W.L., K.W. M.G., P.S., H.K.; writing—review and editing A.J., K.W.; project administration, A.J.

All authors have read and agreed to the published version of the manuscript.

Funding

This research received no external funding.

Institutional Review Board Statement

Not applicable.

Informed Consent Statement

Not applicable.

Data Availability Statement

Publicly available datasets were analyzed in this study. PM particles comes from the European Environment Agency database. Data on deaths was obtained from the EUROSTAT database created by the European Commission.

Acknowledgments

Not applicable

Conflicts of Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.