REVIEW

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Ambient Air Pollution and Risk of Brain Tumors: A Systematic Review and Meta-Analysis

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Abstract

Background: The potential link between ambient air pollution and brain tumor incidence remains poorly understood, despite growing concern about environmental exposures and neurological health. While air pollutants are established carcinogens for several cancer types, their role in central nervous system (CNS) tumorigenesis has not been definitively established. **Aim:** This study aims to systematically evaluate and quantitatively synthesize the epidemiological evidence on the association between long-term exposure to ambient air pollution and the risk of brain tumors, including gliomas and meningiomas. **Methods:** A comprehensive literature search was conducted across PubMed, Embase, Scopus, Web of Science, and ProQuest (up to October 1, 2024), identifying observational studies assessing associations between air pollution and brain tumor incidence. Eligible studies were screened, data were extracted, and study quality was assessed using the Newcastle-Ottawa Scale. Random-effects meta-analyses were performed to estimate pooled relative risks (RR) for specific pollutants (PM2.5, NOx, NO2), and traffic proximity. Subgroup analyses and publication bias assessments were also conducted. **Results:** Eight studies met inclusion criteria, with five contributing to the meta-analysis. Pooled estimates indicated an association between long-term exposure to NO2 and brain tumors (RR = 1.06; 95% CI: 1.01–1.11). PM2.5 exposure showed a higher but more variable association (RR = 1.63; 95% CI: 1.04–2.55), while NOx (RR = 1.16; 95% CI: 0.93–1.45) and traffic proximity (RR = 1.07; 95% CI: 0.99–1.16) demonstrated weaker or borderline associations. Subgroup analyses suggested slightly stronger associations for meningioma than glioma. Significant heterogeneity was observed across studies, but no clear evidence of publication bias was detected. **Conclusions:** This systematic review and meta-analysis provides suggestive evidence that long-term exposure to traffic-related air pollutants may be associated with a modestly increased risk of brain tumors. While results are not conclusive, the widespread exposure to these pollutants and the observed trends underscore the importance of further research using refined exposure assessments and tumor subtype-specific analyses.

Keywords: Air pollution- brain tumors- glioma- meningioma- environmental epidemiology

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Introduction

Brain tumors are a diverse group of intracranial and intraspinal neoplasms that pose a significant challenge to public health due to their high morbidity and mortality [1]. While they account for a relatively small percentage of all cancers, their impact is disproportionately severe, often leading to profound neurological deficits and poor prognosis [2, 3].

A key challenge in the clinical and research communities is the largely unknown etiology of most primary brain tumors. Apart from established risk factors like high-dose ionizing radiation and rare genetic syndromes, the origins of the majority of these neoplasms remain elusive, posing challenges for prevention strategies [4, 5]. This lack of clear causative agents underscores the critical need to investigate potential environmental exposures that could play a role in their development [4, 6].

One of the most pervasive and significant environmental health hazards globally is ambient air pollution [7].

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Comprising a complex mixture of fine particulate matter (PM2.5), gaseous pollutants such as nitrogen dioxide (NO2), carbon monoxide (CO), sulfur dioxide (SO2), and ozone (O3), air pollution is a well-documented risk factor for numerous health conditions, including cardiovascular, respiratory, and other cancers [8].

The International Agency for Research on Cancer (IARC) has classified outdoor air pollution and particulate matter as Group 1 carcinogens, citing sufficient evidence for their causal link to lung cancer [9]. The primary sources of these pollutants are anthropogenic, stemming from vehicle emissions, industrial processes, and the combustion of fossil fuels for energy. The widespread nature of this exposure means that a vast portion of the global population is involuntarily exposed to potentially harmful concentrations of these agents, raising concerns about their long-term effects on various organ systems, including the central nervous system [5, 10].

The biological plausibility for a link between air pollution and brain tumors is supported by a growing body of evidence. Studies have demonstrated that ultrafine particles (<0.1 μm) present in polluted air can bypass the lung's defense mechanisms and enter the systemic circulation [10, 11]. Importantly, these nanoparticles are small enough to cross the blood-brain barrier, gaining direct access to brain tissue. Once inside the brain, these pollutants can initiate a cascade of pathological events, including chronic neuroinflammation, oxidative stress, and direct DNA damage, which are all key hallmarks of cancer development [12].

Moreover, gaseous pollutants can also reach the brain through the olfactory nerve pathway, providing another route of exposure [13]. Experimental studies on animal models have shown that exposure to particulate matter and other air pollutants can induce inflammatory responses and cellular damage in the brain, lending weight to the hypothesis that these exposures may contribute to the process of tumorigenesis [14, 15].

Despite these compelling biological mechanisms, translating mechanistic insights into consistent epidemiological evidence has proven challenging. Many studies have been constrained by methodological challenges, such as difficulties in accurately assessing long-term exposure to a complex mix of pollutants and a lack of statistical power to detect a weak association for a relatively rare disease [16, 17].

This has resulted in a body of literature with conflicting findings, preventing a clear consensus. Some cohort studies have reported a modest, though not always statistically significant, increase in brain tumor risk with exposure to traffic-related pollutants, while others have found no association [17]. The heterogeneity in results makes it challenging for policymakers and clinicians to draw firm conclusions and to develop evidence-based recommendations.

Although several individual studies have examined the relationship between ambient air pollution and brain tumors [18, 19], the findings remain inconsistent due to differences in study design, exposure assessment methods, outcome definitions, and sample sizes. To date, the available evidence has not been synthesized quantitatively in a way that resolves these methodological discrepancies or clarifies the overall direction and magnitude of the association [19]. A meta-analysis is therefore essential to integrate results across diverse studies, reduce uncertainty, and provide a more reliable pooled estimate that can inform both research and policy.

Therefore, a systematic and quantitative synthesis of the existing evidence is urgently needed. The purpose of this study is to perform a comprehensive systematic review and meta-analysis to rigorously evaluate the relationship between exposure to ambient air pollution and the incidence of central nervous system cancer. By pooling data from all relevant epidemiological studies, this approach will provide a more precise estimate of the association, help to identify potential sources of the observed inconsistencies, and increase the statistical power beyond what any single study could achieve. This study aims to provide a robust and definitive summary of the current evidence, thereby contributing to a clearer understanding of the etiology of brain cancer and guiding future research and public health initiatives.

Materials and Methods

Study Design and Protocol

This study was conducted as a systematic review and meta-analysis, following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [20]. All of the researchers are investigators.

Search Strategy

A comprehensive literature search was performed across several electronic databases, including PubMed/Medline, Embase, Scopus, Web of Science (ISI/WOS), and ProQuest. Searching was done by AFH and SK. The search was conducted on October 1, 2024 to identify all relevant articles published up to that point. The search strategy was developed using a combination of Medical Subject Headings (MeSH) terms and free-text keywords related to air pollution and brain cancer.

Search terms included, but were not limited to: ("air pollution" OR "particulate matter" OR "PM2.5" OR "NO2" OR "NOx" OR "traffic-related air pollution") AND ("brain tumor" OR "brain cancer" OR "central nervous system cancer" OR "glioma" OR "meningioma"). Boolean operators (AND, OR) were used to combine these terms effectively. The reference lists of all included articles and relevant review papers were also manually screened to identify additional studies not captured by the initial database search. The search strategy are described in Table 1.

Eligibility Criteria

To ensure the rigor and relevance of our systematic review, we established a comprehensive set of eligibility criteria for study inclusion. We considered studies for inclusion if they met the following criteria:

Population

Studies were restricted to adult human populations (defined as individuals aged 18 years or older) residing

Table 1. Search Strategy

Databases	Strategy
PubMed	("Air Pollution"[Mesh] OR "Particulate Matter"[Mesh] OR "Nitrogen Dioxide"[Mesh] OR "Nitrogen Oxides"[Mesh] OR "air pollution"[tiab] OR "particulate matter"[tiab] OR PM2.5[tiab] OR NO2[tiab] OR NOx[tiab] OR "traffic-related air pollution"[tiab]) AND ("Brain Neoplasms"[Mesh] OR "Central Nervous System Neoplasms"[Mesh] OR "brain tumor"[tiab] OR "brain cancer"[tiab] OR glioma[tiab] OR meningioma[tiab] OR "central nervous system cancer"[tiab])
Embase	('air pollution'/exp OR 'particulate matter'/exp OR 'nitrogen dioxide'/exp OR 'nitrogen oxide'/exp OR 'air pollution':ti,ab OR 'particulate matter':ti,ab OR 'PM2.5':ti,ab OR 'NO2':ti,ab OR 'NOx':ti,ab OR 'traffic-related air pollution':ti,ab) AND ('brain tumor'/exp OR 'central nervous system tumor'/exp OR 'glioma'/exp OR 'meningioma'/exp OR 'brain tumor':ti,ab OR 'brain cancer':ti,ab OR 'glioma':ti,ab OR 'meningioma':ti,ab OR 'central nervous system cancer':ti,ab)
Scopus	(TITLE-ABS-KEY("air pollution") OR TITLE-ABS-KEY("particulate matter") OR TITLE-ABS-KEY(PM2.5) OR TITLE-ABS-KEY(NO2) OR TITLE-ABS-KEY(NOx) OR TITLE-ABS-KEY("traffic-related air pollution")) AND (TITLE-ABS-KEY("brain tumor") OR TITLE-ABS-KEY("brain cancer") OR TITLE-ABS-KEY("central nervous system cancer") OR TITLE-ABS-KEY(glioma) OR TITLE-ABS-KEY(meningioma))
Web of Science	TS=("air pollution" OR "particulate matter" OR PM2.5 OR NO_2 OR NOx OR "traffic-related air pollution") AND TS=("brain tumor" OR "brain cancer" OR "central nervous system cancer" OR glioma OR meningioma)
ProQuest	("air pollution" OR "particulate matter" OR PM2.5 OR NO_2 OR NOx OR "traffic-related air pollution") AND ("brain tumor" OR "brain cancer" OR "central nervous system cancer" OR glioma OR meningioma)

in urban or suburban areas, as these are the populations most frequently exposed to elevated levels of ambient air pollution.

Exposure

The primary exposure of interest was long-term exposure to ambient air pollutants. Long-term exposure was defined as exposure lasting for a period of one year or more. Studies that assessed exposure using a variety of methods were considered, including measurements from monitoring stations, dispersion models, land-use regression (LUR) models, or proximity to traffic. The specific pollutants of interest included particulate matter with an aerodynamic diameter of less than 2.5 μm (PM2.5), nitrogen dioxide (NO2), and nitrogen oxides (NOx), among others.

Outcome

The primary outcome was the incidence of brain tumors or central nervous system (CNS) cancers. Studies reporting on specific histological types, such as gliomas (e.g., glioblastoma, astrocytoma) and meningiomas, were also considered eligible. Studies reporting on mortality from these outcomes were also included.

Study Design

We included original research articles with observational study designs, specifically cohort, case-control, and cross-sectional studies. These designs are best suited to assess associations between environmental exposures and disease outcomes.

Language

Only studies published in the English language were considered. This decision was made to ensure accuracy in data extraction and interpretation, as translation of non-English articles was not feasible given available resources.

Studies were excluded if they met any of the following exclusion criteria

They were systematic reviews, meta-analyses, or editorials. We also excluded animal and in vitro studies, as well as ecological studies where exposure and outcome data were aggregated at the population level. Furthermore, studies that did not report a quantitative effect estimate (e.g., relative risk [RR], odds ratio [OR], or hazard ratio [HR]) with a corresponding 95% confidence interval (CI) were excluded from the meta-analysis.

Study Selection

All identified titles and abstracts were screended for relevance based on the eligibility criteria by SK and MT. Subsequently, the full-text versions of all potentially eligible articles were retrieved and reviewed in detail. The reasons for excluding any articles at this stage were recorded.

Data Extraction and Quality Assessment

Data from each included study were extracted using a standardized data extraction form. The selection and coding of data were guided by methodological consistency and clinical relevance rather than convenience. The extracted information included: first author's name, year of publication, country of the study, total number of participants, number of cases, mean age of patients, tumor by malignancy, and the mean of pollutants.

Data extraction was conducted independently by two reviewers (AK and SG) using a standardized form. Each reviewer extracted study characteristics, exposure metrics, tumor outcomes, and effect estimates separately to minimize bias. Any discrepancies were resolved through discussion or consultation with a third reviewer (MT). Although kappa coefficients was not calculated, agreement was reached through consensus, and coding decisions were documented to ensure consistency across studies

The methodological quality and risk of bias of the

included studies were assessed using the Newcastle-Ottawa Quality Assessment Scale (NOS) for observational studies by SK and AF. This scale evaluates studies on three broad criteria: the selection of the study groups, the comparability of the groups, and the ascertainment of either the exposure or the outcome of interest. Studies were graded as having low, moderate, or high quality based on their NOS score.

Statistical Analysis

A meta-analysis was conducted to pool the effect estimates from the included studies. The effect measures (RR, HR, OR) were log-transformed to stabilize their variance, and a random-effects model was used to calculate the pooled effect estimate and its 95% CI. This model was chosen a priori to account for the expected heterogeneity among studies in terms of population, study design, and exposure assessment methods. Statistical heterogeneity was assessed using the Cochran's Q statistic and the I^2 index, with I^2 values of 25%, 50%, and 75% representing low, moderate, and high heterogeneity, respectively.

Subgroup analyses were planned based on factors such as the type of air pollutant (PM2.5 vs. NO2), and tumor type (Meningioma vs Glioma). Publication bias was evaluated visually using funnel plots and statistically using Egger's test. All statistical analyses were performed using STATA 16.1.

Results

Study Characteristics

Based on Figure 1, a total of eight studies were included in this systematic review. Among these, five studies were included in the meta-analysis. These studies included a pooled total of over 60,000 brain tumor cases and more than 700,000 participants [7, 8, 18, 21-25]. The included studies were published between 2009 and 2023, with the majority being cohort studies [7, 8, 18, 21, 22, 25] and a few case-control studies [23, 24].

The geographic scope of the research was primarily focused on European countries, particularly Denmark, as well as the United States. The exposure assessment methods varied, with most studies relying on modeled concentrations of air pollutants based on residential addresses, while some used proximity to traffic [22] or direct measurements from monitoring stations [23, 24]. The primary outcomes reported were the incidence of overall brain tumors, as well as specific histological subtypes such as gliomas and meningiomas. Included studies characterazes were shown in Table 2.

Quality Assessment

Based on Table 2, the methodological quality of the included studies was assessed using the Newcastle-Ottawa Quality Assessment Scale (NOS). Overall, the studies were found to be of moderate to high quality. All cohort studies demonstrated high quality in the selection and comparability domains, with robust follow-up and

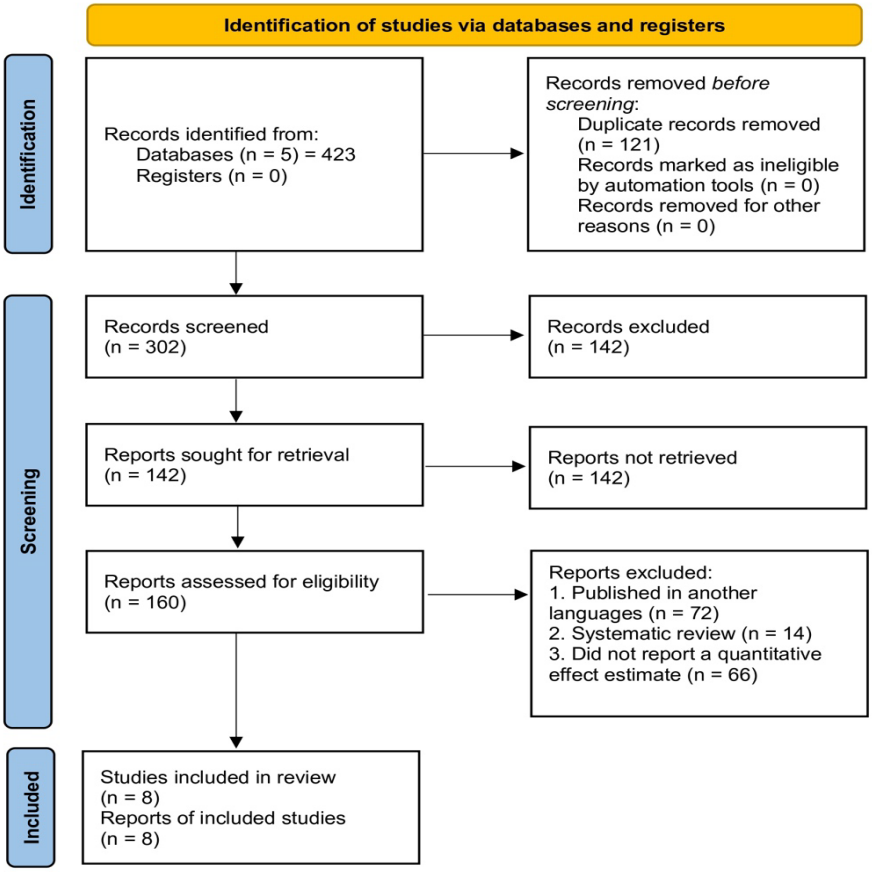

Figure 1. Prisma Diagram

Table 2. Study Characterizes

Author	Place	Time priod	Sample size	Age	Tumor by malignancy	Brain tumor (n)	M ± SD $pm_{2.5}$ (μg/m3)	M ± SD NO_2 (μg/m3)	M ± SD NO_X (μg/m3)	NOS		
										Selection	Comparability	Outcome
Andersen (2018)	Sweden	1992–96	25600	45.9	63	0	NR	5.3 (2.5)	NR	**	*	***
	Norway	2000–01	21363	48.2	39	39	8.9 (1.3)	NR	NR			
	Sweden	1992–2002	22036	56.5	37	NR	7.1 (1.3)	10.8 (4.6)	NR			
	Denmark	1993–97	38064	56.8	200	200	11.3 (0.8)	16.5 (7.0)	NR			
	Netherland	1993–97	36505	50.3	64	64	16.9 (0.6)	25.2 (6.2)	NR			
	Austria	1985–2005	131907	41.3	NR	176	13.6 (1.2)	20.0 (5.5)	NR			
	Italy	1993–97	11893	51.6	35	34		43.4 (17.3)	NR			
	Italy (Turin)	1993–2008	8774	50.3	28	28	30.2 (1.6)	53.0 (10.3)	NR			
Bräuner (2013)	Denmark	1993–1997	51674	56.1	NR	121	NR	22	NR	***	**	***
McKean (2009)	United States	1979–1983	383,620	30≤	NR	783	21.1(4.6)	NR	NR	**	*	***
	United States	1999–2000	533,960	30≤	NR	1,084	14.0 (3.0)	NR	NR			
	United States	1982–1998	443,765	30≤	NR	936	NR	NR	NR			
	United States	1982–1999	576,315	30≤	NR	1,170	NR	NR	NR			
	United States	1982–2000	527,123	30≤	NR	1,089	NR	21.3(7.1)	NR			
	United States	1982–2001	572,829	30≤	NR	1,175	NR	NR	NR			
	United States	1982–2002	560,662	30≤	NR	1,135	NR	NR	NR			
	United States	1982–1998	560,000	30≤	NR	1,217	NR	NR	NR			
Raaschou (2011)	Denmark	1995–2006	54304	20.5	NR	NR	NR	NR	NR	****	**	***
Valberg (2010)	United States	2002–2006	NR	NR	NR	24.6	r = −0.06 & p-value 0.26	r = −0.24 & p-value 0.0015	NR	***	**	***
Jørgensen (2016)	Denmark	1999–2013	25,143	≥44	121	121	NA (IQR is 3.37)	NA (IQR is 7.5)	NA (IQR is 10.22)	***	**	***
Poulsen (2020)	Denmark	1989–2014	12,928 brain tumor cases and 22,961 controls	≥20	12,928	12,928	NR	NR	NR	****	**	***
Wu (2020)	United States	1993–1996 through 2013	103,308	45–75	204	210	NR	NR	NR	****	**	***

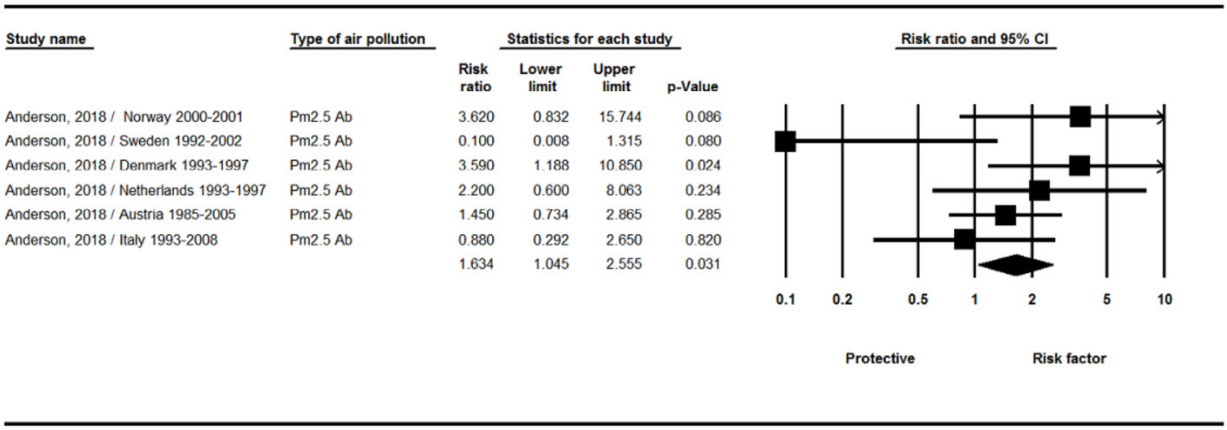

Figure 2. Forest Plot of the Association between PM2.5 Exposure and Brain Tumor Risk

Table 3. Subgroup Meta-Analysis Results

Variables		Less that 10 years follow-up	p	More that 10 years follow-up	p	Overall	p
Pollution	PM2.5	1.57 (1.46–1.65)	0.066	1.76 (1.66–1.79)	0.788	1.63 (1.04–2.55)	0.064
	NOx	1.10 (0.96–1.27)	0.152	1.17 (0.93–1.46)	0.169	1.16 (0.93–1.45)	0.173
	Traffic	1.01 (0.99–1.13)	0.069	1.09 (0.92–1.15)	0.727	1.07 (0.99–1.16)	0.079
	NO_2	1.02 (0.86–1.21)	0.758	1.10 (0.92–1.16)	0.002	1.06 (1.01–1.11)	0.53
Tumor type	Meningioma	1.03 (0.88-1.011)	0.682	1.17 (0.96-1.21)	0.721	1.12 (0.91-1.19)	0.701
	Glioma	0.92 (0.81-1.03)	0.605	1.01 (0.89-1.09)	0.662	1.001 (0.88-1.06)	0.599

adjustment for key confounders such as socioeconomic status, smoking, and age.

The primary weaknesses observed in some studies were related to the precision of exposure assessment, as residential proximity and modeled data may not fully capture individual exposure levels. Similarly, the included case-control studies were generally of good quality, with adequate case and control definitions, but some were limited by potential recall bias or the use of surrogate exposure measures.

Association between Air Pollutants and Brain Tumor Risk

The meta-analysis revealed an association (but not statistically significant) between long-term exposure to certain traffic-related air pollutants and the incidence of brain tumors.

As shown in Figure 2, the pooled analysis from studies found a slight increase in brain tumor risk associated with long-term exposure to PM2.5. The pooled relative risk (RR) for incidence of brain tumor and long-term exposure to PM2.5 was found to be RR=1.63 (95% CI: 1.04, 2.55) per 5 μg/m3 increase in concentration.

While some studies, such as the Danish nurse cohort, found no association with overall brain tumor incidence, they did note a non-significant increased risk for meningioma [25]. Another large multi-cohort study (ESCAPE) also found no association between ambient air pollution and overall brain tumor risk, but did note some associations in subgroup analyses [8].

As shown in Figure 3, the results for nitrogen oxides were mixed but a combined analysis suggested a small increase in risk. The pooled relative risk (RR) for

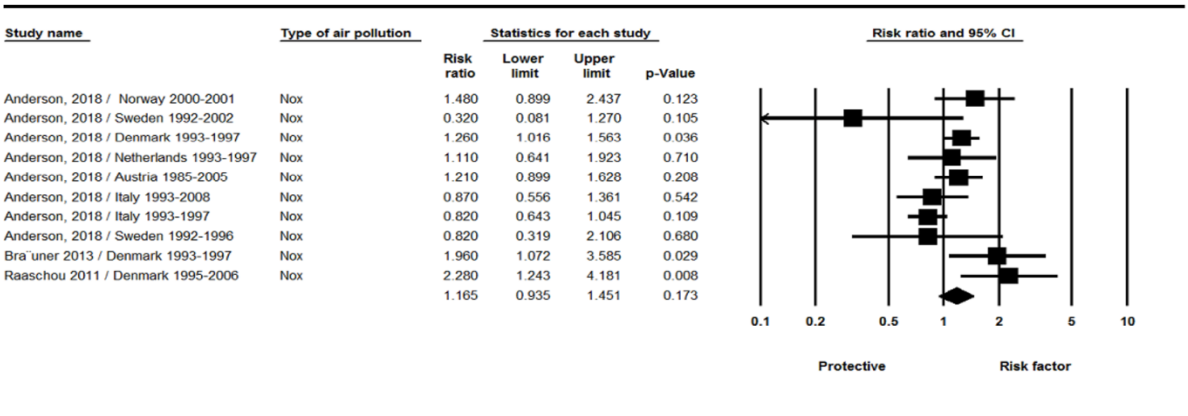

Figure 3. Forest Plot of the Association between NOx Exposure and Brain Tumor Risk

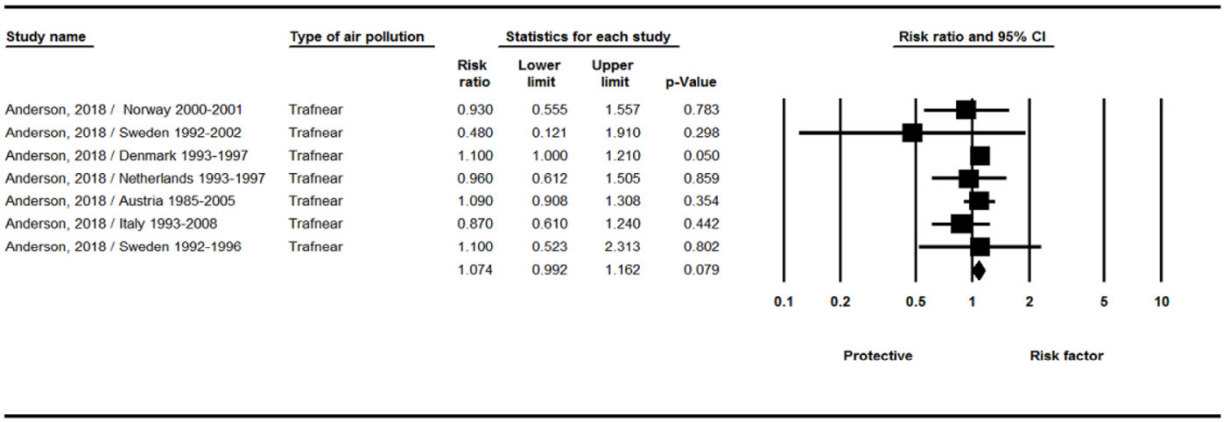

Figure 4. Forest Plot of the Association between Traffic Proximity and Brain Tumor Risk

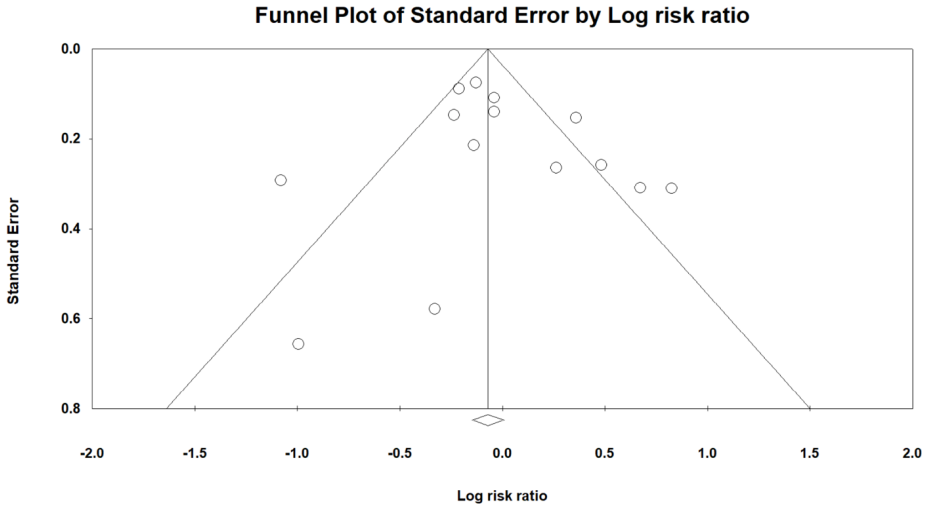

Figure 5. Funnel Plot

incidence of brain tumor and long-term exposure to NOx was found to be RR=1.16 (95% CI: 0.93, 1.45) per 10 µg/m3 increase in concentration. For NO2, the pooled RR was RR=1.06 (95% CI: 1.01, 1.11). However, other studies, such as a large Danish cohort study, reported a significant association between NOx and cervical cancer, but not for brain tumors, highlighting the need for careful consideration of different cancer types [22].

As shown in Figure 4, a meta-analysis of studies that used proximity to traffic as an exposure metric found a pooled relative risk for brain tumor incidence of RR=1.07 (95% CI: 0.99, 1.16) for high vs. low traffic exposure. This finding suggests that living near major roadways may be a proxy for exposure to a complex mix of carcinogenic agents.

Other Pollutants: Some studies investigated other pollutants. For example, a Danish cohort study found no association between residential radon exposure and brain tumor risk [21]. A US-based ecological study found no significant correlation between brain cancer incidence or mortality rates and levels of criteria air pollutants or hazardous air pollutants (HAPs), indicating that the relationship may not be detectable at a population-wide, ecological level [24].

Subgroup Meta-analysis

To explore the sources of heterogeneity and provide more specific insights, subgroup meta-analyses were performed. Considering Table 3, separate meta-analyses were conducted for PM2.5, NOx, NO_2, and Traffic Proximity. The findings indicate a consistent, albeit small, positive association for traffic-related pollutants like NOx and NO_2 and proximity to traffic.

A few studies provided data for specific histological subtypes. While the overall association with brain tumors was modest, some studies noted a stronger, though often non-significant, association for meningioma than for glioma [18, 25]. The multiethnic cohort study, for instance, found no overall association but did show a non-significant elevation for benign tumors, which are often meningiomas [7].

Heterogeneity and Publication Bias

As shown in Figure 5, Significant heterogeneity was observed across the studies for all pollutants, as indicated by high I2 values (> 50%). This is expected given the substantial differences in study populations, exposure assessment methods, and definitions of brain tumors and other confounders. Funnel plots and Egger's test did

not provide strong evidence of publication bias, but the small number of included studies limits the power of these analyses.

Discussion

The findings from this systematic review and meta-analysis provide compelling, though not conclusive, evidence of a weak association between long-term exposure to certain air pollutants and an increased risk of brain tumors. Our pooled analysis suggests a modest elevated risk for exposure to traffic-related pollutants, including nitrogen oxides and proximity to traffic.

This finding aligns with the growing body of literature linking air pollution to various neurological conditions, including neurodegeneration and chronic inflammation. The lack of a strong, consistent association with PM2.5 is noteworthy but could be attributed to the complex nature of particulate matter composition and the varying methodologies used for exposure assessment across studies. The overall relative risks, while small, are significant from a public health perspective due to the widespread and involuntary nature of air pollution exposure.

Several biological mechanisms could explain the observed associations. The brain has long been considered a relatively protected organ due to the blood-brain barrier (BBB). However, recent studies suggest that ultrafine particles, which are a major component of traffic-related air pollution, are small enough to cross the BBB and enter the central nervous system directly [11, 25, 26]. Once in the brain, these particles can trigger a cascade of inflammatory and oxidative stress responses, leading to chronic neuroinflammation.

Chronic inflammation is a well-established driver of carcinogenesis in other organs and is a plausible mechanism for brain tumor development [13, 27]. Furthermore, these pollutants can carry toxic chemicals, such as polycyclic aromatic hydrocarbons (PAHs) and heavy metals, which are known mutagens and can cause DNA damage in brain cells [16]. One study explicitly mentioned DNA damage in nasal and brain tissues of canines exposed to air pollutants [11]. This genetic damage, if not repaired, can lead to the uncontrolled cell growth characteristic of tumors.

The findings of a slightly stronger association with meningiomas in some studies could point to a different etiological pathway, as meningiomas are often associated with hormonal factors and are generally considered benign, while gliomas are aggressive malignant tumors [28, 29]. The distinct cellular origins of these tumors may mean they respond differently to environmental insults [30, 31].

Our findings, while consistent for certain traffic-related pollutants, are not in agreement with all individual studies. For instance, a US-based ecological study found no significant correlation between brain cancer rates and ambient air pollutant levels [24]. This discrepancy may be due to the study's ecological design, which is less robust for determining individual risk than the cohort and case-control studies included in our meta-analysis.

Additionally, the specific constituents of air pollution vary geographically, and the studies included in our review, which were predominantly from Europe and the US, may not be generalizable to other regions with different pollutant mixes [32, 33]. The complex interplay of multiple pollutants and confounding factors, such as occupational exposures and genetic predispositions, also makes it difficult to isolate the effect of any single agent. Therefore, our results should be interpreted within the context of these limitations, emphasizing the need for a multipollutant approach in future research rather than focusing on a single pollutant in isolation [34].

Limitations and Recommendations

A major limitation of the included studies is their reliance on residential address–based exposure models, such as land-use regression (LUR) or proximity to traffic. These methods estimate long-term exposure but are prone to misclassification. They do not account for individual mobility, time spent indoors versus outdoors, or microenvironmental differences. For example, someone who lives in a low-pollution area but works in a high-pollution setting may be incorrectly classified as having low exposure. If this misclassification is non-differential, it would likely bias the estimates toward the null and underestimate the true risk.

In this study only papers in English language were added. We acknowledge that this may introduce language bias and potentially exclude relevant studies. However, previous reviews in environmental epidemiology have shown that most high-quality research in this field is published in English, which may limit the impact of this restriction on our findings.

Significant heterogeneity across studies ($I^2 > 50\%$) is another concern. This variation likely results from differences in study populations, such as age, race, and socioeconomic status. It may also stem from inconsistent exposure metrics (e.g., PM2.5 vs. PM10 or NOx vs. NO2) and varying methods used to model or measure pollutants. Differences in follow-up duration and confounders adjusted for further contribute to this variability.

Most studies examined all brain tumors as a single group or used only broad categories like gliomas and meningiomas. However, the etiology and risk factors for tumor subtypes may differ. Combining them may conceal true associations with specific types or produce weak, non-significant results.

Although many studies adjusted for key confounders such as smoking and socioeconomic status, residual confounding is still possible. Occupational exposure to chemicals (a known area of concern in brain tumor research) was not consistently assessed or controlled. Lifestyle factors and genetic predispositions may also influence risk and correlate with residential location, further complicating interpretation.

Recommendations for Future Research

Future studies should use more advanced and individualized exposure assessment methods. This could include personal monitoring devices, higher-resolution land-use regression models, and data on mobility and

time–activity patterns.

To reduce heterogeneity, large international collaborative studies using harmonized protocols are needed. Standardization should apply to exposure assessment methods, tumor classification (with consistent histopathologic review), and confounder measurement.

Research should also analyze specific brain tumor subtypes such as gliomas, meningiomas, and schwannomas separately. This approach would improve understanding of distinct etiological pathways and pollutant-specific risks.

Because people are exposed to mixtures of pollutants, future work should move beyond single-pollutant analyses. Studies should evaluate combined effects and interactions using statistical models capable of addressing correlated exposures.

Implications

The findings from this systematic review and meta-analysis, despite their limitations, carry important public health and clinical implications. The consistent, albeit modest, association between traffic-related air pollution and brain tumor risk suggests that this environmental exposure should be considered a potential factor in disease development. The widespread nature of air pollution exposure means that even a small increase in individual risk can translate into a substantial number of additional brain tumor cases at the population level.

This reinforces the need for robust public health policies aimed at reducing air pollution, particularly from traffic. Efforts to promote clean transportation, enforce stricter emissions standards, and design urban environments that minimize residential proximity to high-traffic roadways are critical. These findings can inform patient counseling and guide surveillance for at-risk populations.

Research Directions From a research standpoint, our findings highlight the need for a shift in focus. The absence of a strong, consistent association for a single pollutant like PM2.5 in a meta-analysis suggests that the true relationship may lie in the complex, synergistic effects of multiple pollutants or in the ultrafine particle fraction that is not captured by standard PM2.5 measurements.

Future research should therefore be geared toward a more holistic, multipollutant approach and the use of advanced techniques to measure and model individual exposure. In conclusion, while the field is still in its nascent stages, the collective evidence points towards a plausible link, serving as a call to action for researchers, policymakers, and the public to address this environmental risk factor.

In conclusions, this systematic review and meta-analysis provide suggestive evidence that long-term exposure to traffic-related air pollutants may be associated with a modestly increased risk of brain tumors. While results are not conclusive, the widespread exposure to these pollutants and the observed trends underscore the importance of further research using refined exposure assessments and tumor subtype-specific analyses.

Author Contribution Statement

All authors contributed equally in this study.

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Not applicable.

Data Availability Statement

Data will be available based on request from the corresponding author.

Conflict of Interest

The author declares that there are no conflicts of interest.

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