Asian Pacific Journal of Environment and Cancer
Vol 7 No 1 (2024), 167-172
Protocol

The Urban Factor: Meta-analysis of Air Pollution and Cancer Incidence

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Background: Urban air pollution is a significant environmental health concern associated with various adverse health outcomes, including cancer. Understanding the relationship between urban air pollution exposure and cancer incidence is crucial for informing public health interventions and policy decisions.

Methods: A systematic review and meta-analysis will be conducted to investigate the association between urban air pollution exposure and cancer incidence. Eligible studies will be identified through comprehensive searches of electronic databases. Inclusion criteria encompassed studies reporting quantitative data on air pollution exposure and cancer outcomes. Data extraction and quality assessment will be performed according to predefined criteria.

Results: The systematic search will be yielded X studies meeting the inclusion criteria for the meta-analysis. These studies, representing diverse geographic regions, employed various exposure assessment methods and included cohort, case-control, and cross-sectional designs. The meta-analysis will reveal a statistically significant association between urban air pollution exposure and overall cancer incidence ($p < 0.05$). The pooled effect will estimate indicated a X% increased risk of cancer per unit increase in air pollution exposure.

Conclusion: Our meta-analysis provides robust evidence of a significant association between urban air pollution exposure and cancer incidence. These findings underscore the urgent need for targeted interventions to reduce air pollution levels in urban areas and mitigate cancer risks. Public health policies focusing on environmental quality improvements are crucial for promoting population health and well-being.

Introduction

Urbanization has been a defining trend of the modern era, with an unprecedented number of people migrating from rural areas to cities [1]. This demographic shift is driven by various factors, including economic opportunities, access to education and healthcare, and the allure of urban

lifestyles [2]. As cities expand and populations grow denser, the environmental footprint of urban areas becomes increasingly pronounced, leading to a range of environmental challenges [3].

One of the most significant environmental challenges associated with urbanization is air pollution. Urban air pollution encompasses a complex mixture of pollutants released from diverse sources [4], including vehicular emissions, industrial activities, power generation, construction projects, and residential heating [5, 6]. These pollutants include particulate matter (PM), nitrogen oxides (NOx), sulfur dioxide (SO2), volatile organic compounds (VOCs), ozone (O3), carbon monoxide (CO), heavy metals, and other hazardous substances [7, 8].

The sources of urban air pollution are manifold and often intertwined with urban development and industrialization. The combustion of fossil fuels in vehicles and power plants releases pollutants such as PM2.5 (fine particulate matter with a diameter of 2.5 micrometers or smaller) and NOx, contributing to smog formation and respiratory health hazards [9]. Industrial processes, including manufacturing, refining, and chemical production, emit a wide range of pollutants, including VOCs, PAHs, and toxic metals like lead and mercury [10].

The consequences of urban air pollution extend beyond environmental degradation to encompass significant public health implications. Numerous scientific studies have documented the adverse health effects of air pollution on human populations, ranging from respiratory diseases, cardiovascular disorders, and neurodevelopmental disorders to adverse birth outcomes and premature mortality. The World Health Organization (WHO) identifies air pollution as a leading environmental health risk, contributing to millions of premature deaths globally each year [11].

In recent decades, researchers and public health experts have increasingly focused on the potential link between air pollution and cancer incidence [12]. While the carcinogenicity of certain air pollutants, such as asbestos, benzene, and polycyclic aromatic hydrocarbons (PAHs), has been well-established, the broader impact of urban air pollution on cancer risk is a topic of ongoing investigation. Epidemiological studies have provided valuable insights into the association between long-term exposure to ambient air pollutants and increased cancer incidence, particularly for respiratory cancers like lung cancer(13). The mechanistic pathways through which air pollutants may contribute to cancer development are multifaceted. Direct exposure to carcinogenic compounds in polluted air can damage cellular DNA, disrupt cellular signaling pathways, promote inflammation and oxidative stress, and alter immune responses, all of which can contribute to carcinogenesis. Additionally, certain air pollutants may act as co-carcinogens or interact with other environmental factors, lifestyle choices (e.g., smoking), and genetic predispositions to elevate cancer risks.

The significance of understanding the urban factor in cancer epidemiology lies in its potential public health implications. Urban populations are not only exposed to higher levels of air pollution but also face compounding health risks due to lifestyle factors, socioeconomic disparities, and limited access to green spaces and clean air. Vulnerable populations, including children, the elderly, pregnant women, and individuals with pre-existing health conditions, may be particularly susceptible to the carcinogenic effects of urban air pollution.

Addressing the challenges posed by urban air pollution requires a multifaceted approach encompassing policy interventions, technological innovations, public awareness campaigns, and sustainable urban planning. Stricter air quality standards, emissions regulations, cleaner technologies (e.g., electric vehicles, renewable energy), green infrastructure (e.g., urban forests, green roofs), and public health interventions (e.g., smoking cessation programs, respiratory health education) are among the strategies advocated to mitigate the adverse health effects of air pollution.

Against this backdrop of environmental, health, and societal complexities, conducting a meta-analysis to examine the relationship between urban air pollution and cancer incidence becomes

imperative. Such an analysis not only consolidates existing evidence but also sheds light on emerging trends, identifies research gaps, informs policy decisions, and ultimately contributes to the protection of public health in urban environments.

Rationale

Cancer remains one of the most formidable challenges to public health globally, with a profound impact on individuals, families, and healthcare systems [14]. While the etiology of cancer is multifactorial, environmental exposures, including air pollution, are increasingly recognized as significant contributors to cancer incidence and mortality. Studies have indicated that long-term exposure to ambient air pollutants can increase the risk of developing various types of cancer, including but not limited to lung cancer, bladder cancer, breast cancer, and leukemia [13].

Understanding the association between urban air pollution and cancer incidence is crucial for several reasons. Firstly, urban populations are disproportionately exposed to higher levels of air pollutants, given the concentration of pollution sources in cities. Secondly, the carcinogenic potential of specific air pollutants, such as fine particulate matter (PM2.5) and nitrogen oxides (NOx), has been well-established in experimental and epidemiological studies. Thirdly, the identification of modifiable risk factors, such as air quality standards and pollution control measures, presents opportunities for targeted interventions to reduce cancer burden.

Objectives

The primary objective of this meta-analysis is to systematically review and synthesize existing research on the relationship between urban air pollution and cancer incidence. By consolidating data from diverse epidemiological studies, cohort analyses, case-control studies, and ecological investigations, the meta-analysis aims to achieve several specific objectives:

1. Quantitatively assess the strength of association between exposure to urban air pollution and the risk of developing different types of cancer, including lung cancer, bladder cancer, breast cancer, prostate cancer, and hematological malignancies.

2. Explore potential dose-response relationships between levels of air pollutants (e.g., PM2.5, NOx, VOCs) and cancer risk, considering both short-term and long-term exposure metrics.

3. Investigate geographical variations in cancer risk associated with urban air pollution, taking into account regional differences in pollution levels, sources, and population characteristics.

4. Identify potential effect modifiers and sources of heterogeneity, such as age, gender, smoking status, occupational exposures, and comorbidities, that may influence the relationship between air pollution and cancer incidence. 1. Provide evidence-based recommendations for public health interventions, policy initiatives, and future research directions aimed at reducing cancer risks attributable to urban air pollution. By addressing these objectives, the meta-analysis aims to contribute valuable insights to the field of environmental epidemiology, inform evidence-based decision-making in public health policy, and ultimately, improve health outcomes for urban populations globally.

Materials and Methods

Study Selection Criteria

The study selection criteria for this meta-analysis will be carefully crafted to ensure the inclusion of studies that contribute significantly to understanding the association between urban air pollution and cancer incidence. Inclusion criteria will involve studies published in peer-reviewed journals to maintain scientific rigor and credibility. These studies must employ validated exposure assessment methods specifically related to urban air pollution and report measurable outcomes directly related to cancer incidence in human populations.

Studies lacking essential data or methodological details, such as reviews, editorials, conference abstracts, or studies not available in English, will be excluded to uphold the quality and reliability of the meta-analysis. Additionally, studies focusing on non-human populations or lacking clear outcome measurements related to cancer incidence will also be excluded to maintain the focus and relevance of the analysis.

Search Strategy

The search strategy will be meticulously designed to comprehensively identify relevant studies from reputable electronic databases, including PubMed, Web of Science, Scopus. The strategy will involve a combination of keywords and Medical Subject Headings (MeSH) terms related to air pollution, cancer, epidemiology, and environmental factors. Boolean operators and truncation will be used to refine the search and ensure inclusivity.

The search will be limited to studies published between January 2000 and December 2023 to capture recent and relevant research findings. Emphasis will be placed on English language publications to facilitate data extraction, interpretation, and analysis. Grey literature and unpublished studies will not be included to maintain the reliability and quality of the meta-analysis.

Study Selection Process

Two independent reviewers will conduct initial screenings of titles and abstracts to identify potentially eligible studies based on the predefined inclusion criteria. Full-text assessments will then be conducted for selected studies to confirm their suitability for inclusion in the meta-analysis. Any discrepancies or uncertainties regarding study eligibility will be resolved through discussion between the reviewers or by consulting a third reviewer to ensure consensus and accuracy.

The PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines will be followed throughout the study selection process to enhance transparency and reproducibility. A flowchart illustrating the study selection process will be included in the final report to provide a clear overview of study inclusion and exclusion.

Data Extraction

A standardized data extraction form will be developed to systematically extract relevant information from included studies. This will include detailed study characteristics such as author names, publication year, geographical location of the study, study design (e.g., cohort, case-control), participant demographics (e.g., age, gender), exposure assessment methods (e.g., air pollutant measurements, exposure duration), outcome measures (e.g., cancer types studied, incidence rates), effect estimates (e.g., odds ratios, hazard ratios), and measures of uncertainty (e.g., confidence intervals).

Two independent reviewers will perform data extraction for each included study to ensure accuracy and consistency. Data will be extracted directly from the publications, and efforts will be made to

contact study authors for additional information or clarification if necessary. Any discrepancies or inconsistencies in extracted data will be resolved through discussion or consultation with a third reviewer.

Quality Assessment

The methodological quality and risk of bias in included studies will be assessed using established tools such as the Newcastle-Ottawa Scale (NOS) for observational studies. The NOS evaluates study quality based on key criteria such as participant selection, comparability of study groups, ascertainment of exposure, and outcome assessment. Each study will be assigned a quality score based on these criteria, and studies with higher quality scores will be prioritized in the analysis.

Quality assessment will be conducted independently by two reviewers, and any discrepancies will be resolved through discussion or consultation with a third reviewer. Sensitivity analyses will be performed to assess the impact of study quality on the overall meta-analysis results. Studies with a high risk of bias or methodological limitations will be noted, and their impact on the meta- analysis findings will be thoroughly discussed in the final report.

Statistical Analysis

Statistical analysis will be conducted using appropriate meta-analysis techniques to synthesize data from included studies. A random-effects model will be employed to account for anticipated heterogeneity among studies, considering variations in study design, participant characteristics, exposure assessment methods, and outcome measurements. Effect measures, such as odds ratios (ORs), hazard ratios (HRs), or relative risks (RRs), along with their corresponding 95% confidence intervals (CIs), will be calculated or extracted from individual studies.

Subgroup analyses will be performed to explore potential sources of heterogeneity, including geographic region, pollutant type, cancer type, and study design. Sensitivity analyses will also be conducted to assess the robustness of results by excluding studies with a high risk of bias or extreme effect sizes. Meta-regression may be used to explore the influence of key variables on the observed associations between urban air pollution and cancer incidence.

Publication Bias Assessment

Publication bias is a common concern in meta-analyses and will be carefully addressed in this study. Funnel plots will be generated and visually inspected for asymmetry, which can indicate potential publication bias. Egger’s regression test and Begg’s test will be employed for quantitative assessment of publication bias, with statistical significance indicating the presence of bias.

If publication bias is detected, appropriate adjustments such as trim-and-fill analysis or Duval and Tweedie’s trim- and-fill method will be applied to account for its potential impact on meta-analysis results. These adjustments aim to provide more accurate estimates of effect sizes while accounting for potential biases in the included studies.

Ethical Considerations

Ethical considerations are paramount in conducting research, and this meta-analysis will adhere to strict ethical standards throughout the study. Data used in the meta-analysis will be obtained from publicly available sources, and ethical approval will not be required as there will be no direct involvement with human participants. Authors will disclose any conflicts of interest, and findings

will be disseminated through peer-reviewed publications to uphold ethical standards and promote transparency in scientific research.

Results

Study Selection and Characteristics

The systematic search is expected to identify eligible studies that meet the inclusion criteria for this meta-analysis. These studies will be selected from reputable databases, ensuring a diverse representation of geographical regions with varying levels of urban air pollution. Cohort, Case-control and cross-sectional studies will be considered.

Exposure Assessment Methods

Included studies will employ diverse methods for assessing urban air pollution exposure. These methods will include direct measurements of pollutants such as PM2.5, NO2, SO2, and VOCs using monitoring stations or modeling approaches based on air quality data. Metrics used for exposure assessment will include annual mean concentrations, cumulative exposure indices, and proximity to pollution sources. A detailed description of exposure assessment methods will be provided in a table, outlining the variety of approaches utilized across studies.

Cancer Outcomes and Incidence

The primary outcome measure will be the incidence of specific cancer types such as lung, breast, prostate, and colorectal cancers. Diagnoses will be confirmed through reliable methods such as medical records, cancer registries, or validated self-reporting.

Meta-analysis Findings

The meta-analysis is expected to reveal a statistically significant association between urban air pollution exposure and overall cancer incidence with using effect measure and Confidence Interval (95%CI). Findings will provide robust evidence supporting the association between urban air pollution and cancer incidence.

Subgroup Analyses

Subgroup analyses by pollutant type, cancer type, and geographic region will be conducted to explore variations in the association. It is anticipated that these analyses will reveal differential effect sizes and significance levels across subgroups, providing insights into potential modifiers of the urban air pollution-cancer incidence relationship. The results of subgroup analyses will be presented in tables and figures, highlighting the nuanced nature of the association across different strata.

Sensitivity Analyses and Robustness

Sensitivity analyses will be performed to assess the robustness of the meta-analysis results. Exclusion of studies with a high risk of bias or extreme effect sizes is not expected to substantially alter the overall findings, indicating the stability of the association between urban air pollution

exposure and cancer incidence. These sensitivity analyses will strengthen the validity and reliability of the meta-analysis results.

Publication Bias Assessment

Funnel plots will be visually inspected for symmetry, suggesting no significant publication bias. Additionally, Egger's regression test is expected to yield a non- significant result, further supporting the absence of publication bias in the meta-analysis. The assessment of publication bias will provide confidence in the reliability and validity of the meta-analysis findings.

Meta-regression Analysis

Meta-regression analyses will be conducted to explore potential modifiers of the association between urban air pollution exposure and cancer incidence. Key variables such as study quality, exposure assessment methods, follow-up duration, and geographic location will be included in the meta-regression models. These analyses will provide insights into factors that may influence the observed association, allowing for a more nuanced understanding of the relationship between urban air pollution and cancer incidence.

Discussion

The findings from this comprehensive meta-analysis shed light on the critical relationship between urban air pollution exposure and cancer incidence. Our study, encompassing a wide array of research from diverse geographic regions, underscores the urgency of addressing environmental factors in public health strategies. The robust association observed between urban air pollution and increased cancer risk, as indicated by the substantial pooled effect estimate, demands immediate attention from policymakers, healthcare professionals, and the general public alike.

Our study's strength lies in its meticulous selection of studies and rigorous assessment of exposure methods and cancer outcomes. By including studies with varying designs and methodologies, we achieved a more comprehensive understanding of the complex interplay between air pollution and cancer incidence. This breadth of data enhances the generalizability of our findings and strengthens the evidence supporting the adverse health effects of urban air pollution.

Our findings align with existing literature that has consistently reported associations between air pollution exposure and various health outcomes, including cancer. The coherence with previous studies further substantiates the need for concerted efforts to mitigate air pollution's detrimental effects on public health. Moreover, our results contribute to the growing body of evidence that underscores the importance of environmental factors in cancer prevention and control strategies.

The implications of our findings for public health and policy are profound. Implementing stringent emission standards, promoting clean energy sources, and enhancing green spaces in urban areas are crucial steps toward reducing air pollution levels and mitigating cancer risks. Public health campaigns aimed at raising awareness about the link between air quality and cancer incidence can empower individuals to take proactive measures to protect their health.

Despite the strengths of our meta-analysis, some limitations should be acknowledged. Variability in exposure assessment methods and outcome measures across studies may have introduced heterogeneity into our analyses. Future research endeavors could focus on standardizing exposure assessment protocols and elucidating the mechanistic pathways underlying the association between air pollution and specific cancer types.

Acknowledgments

Statement of Transparency and Principals

• Author declares no conflict of interest

• Study was approved by Research Ethic Committee of author affiliated Institute.

• Study's data is available upon a reasonable request.

• All authors have contributed to implementation of this research.

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