

**Peer Review File**  
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**Reviewer A**

**Comment 1:** Surprised that only 60 articles were retrieved, considering the broad search terms used. Also, why the authors used the term ‘region [OR] area’?

**Reply:** We agree that our initial search was much too restrictive and had errors in methodology. We have simplified the search and broadened it significantly. We have also added a PRISMA graph to show that we have a total of over 1,000 manuscripts which were part of our review. Although we added only a subset of these to the actual reference list, we feel that your suggestion and our revision allows readers to understand how timely and important this topic is.

**Comment 2:** In the methods: were reviews and meta-analyses included only for cross-reference check? Please clarify.

**Reply:** Yes, this was the purpose of those types of studies. In the manuscript we have now added “Reviews and meta-analyses were included only for cross-reference check.”

**Comment 3:** I think that in the Introduction it should be better clarified that the association of air pollution with chronic respiratory diseases is quite accepted; there is an extensive supporting literature (see for example these reviews: Thurston GD, et al. A joint ERS/ATS policy statement: what constitutes an adverse health effect of air pollution? An analytical framework. *Eur Respir J.* 2017 Jan 11;49(1). And Schraufnagel DE, et al. Air Pollution and Non-Communicable Diseases: A Review by the Forum of International Respiratory Societies' Environmental Committee, Part 1: The damaging effects of air pollution. *Chest.* 2018 Nov 9). Also, it is very focused on US, maybe to add also some references for EU such as ‘De Matteis S, et al. Issue 1 - "Update on adverse respiratory effects of outdoor air pollution". Part 1): Outdoor air pollution and respiratory diseases: A general update and an Italian perspective. *Pulmonology.* 2022 Jul-Aug;28(4):284-296. doi: 10.1016/j.pulmoe.2021.12.008. Epub 2022 Feb 10. PMID: 35153178.’, would give a broader international breath.

**Reply:** Thank you very much for these references. We have included all of them to emphasize the idea that pollution is very much associated with lung disease. We have also included other references because we agree that readers need to see that this association has been recognized widely.

**Comment 4:** The sentence in the review: ‘World Health Organization (WHO) has set firm standards for air quality’ would need a supporting reference. Also, consider adding the related ERS statement (Andersen ZJ, et al. Clean air for healthy lungs - an urgent call to action: European Respiratory Society position on the launch of the WHO 2021 Air Quality Guidelines. *Eur Respir J.* 2021 Dec 2;58(6):2102447. doi: 10.1183/13993003.02447-2021. PMID: 34561297) as an additional comment.

**Reply:** Thank you for this suggestion. We have added an appropriate reference describing these guidelines.

**Comment 5:** In the section on ‘Manufacturing’ the authors should address also the issue of occupational exposures, given it is known from the literature that these factors are important

determinants of respiratory health effects (please see De Matteis S, et al. Lifetime occupational exposures and chronic obstructive pulmonary disease risk in the UK Biobank cohort. *Thorax*. 2022 Jan 26;thoraxjnl-2020-216523. doi: 10.1136/thoraxjnl-2020-216523) and adjustment for it should be performed in air pollution studies (see Doiron D, et al. Air pollution, lung function and COPD: results from the population-based UK Biobank study. *Eur Respir J*. 2019 Jul 25;54(1):1802140. doi: 10.1183/13993003.02140-2018. PMID: 31285306.) So by stopping fossil fuel-based industries, and so reducing sources of air pollution, there would be double health co-benefits in terms of both occupational and environmental respiratory health effects as already shown. (Thurston GD, et al. Maximizing the Public Health Benefits from Climate Action. *Environ Sci Technol*. 2018 Apr 3;52(7):3852-3853. doi: 10.1021/acs.est.8b00859. Epub 2018 Mar 7. PMID: 29512384.). Finally, occupations are important determinant of socio-economic status, that, as correctly stated by the authors, are important factors for air pollution exposure both at home and outside.

**Reply:** Thank you for these thoughtful comments and excellent suggestions! We have added all of these references and have also discussed the risk of occupational exposures.

**Comment 6:** In the section on lung cancer more it should be added, again there are relevant studies outside US, that supported a causal link (Consonni D, et al. Outdoor particulate matter (PM10) exposure and lung cancer risk in the EAGLE study. *PLoS One*. 2018 Sep 14;13(9):e0203539. doi: 10.1371/journal.pone.0203539. PMID: 30216350; PMCID: PMC6157824.). Also, recently it was highlighted the role of air pollution as important mediator of deadly respiratory health trajectories, from asthma to COPD, and lung cancer, and death (De Matteis S. Respiratory effects of air pollution: time to stop this deadly trajectory. *Thorax*. 2023 Mar 27;thorax-2023-220030. doi: 10.1136/thorax-2023-220030. Epub ahead of print. PMID: 36972978.).

**Reply:** Thank you for these suggestions. These are excellent references. We have included them in the reference list and in this section.

**Comment 7:** Why Small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC) are not included in the previous title 'Relationship of air quality with lung cancer'. I would suggest moving it there as they are both types of lung cancer.

**Reply:** Thank you for this comment. You are correct. We have merged these sections as one, since it is describing lung cancer.

## **Reviewer B**

**Comment 1:** The paper tackles an important and up-to-date issue of the harmful effects of air pollution on human health.

**Reply:** Thank you. We agree that this is a timely issue indeed.

**Comment 2:** line 51-52: please describe keywords differently, eg. "respiratory" does really fit the grammar of the rest of the sentence.

**Reply:** Yes, we agree with this thought. We have removed "respiratory" and have simplified the comprehensive literature review. In doing so, we have also broadened our search significantly.

**Comment 3:** line 68: conclusions are too vary. Maybe you could suggest some concrete "mitigation strategies"?

**Reply:** Thank you for this suggestion. In this area we have included "Some of these strategies include more reliance on alternative energy sources, creation of mass transit systems and increased rates of recycling."

**Comment 4:** line 102: only 60 references? I can't really believe that, google scholar gives usually at least >200 or more. Please provide a PRISMA graph. The search terms used are also very narrow and you don't elaborate why these keywords were chosen. Please redo the search more comprehensively.

**Reply:** We agree that this search was much too limited. We have now broadened our search extensively and have included a PRISMA graph. Although the total number of studies is too large to reference each individually in the manuscript, we have allowed readers to see how much literature exists and how important this topic is.

**Comment 5:** line 255: please add a reference to the guidelines. there are also many other sentences that need a reference. (eg. line 304-306, 260, 237-240)

**Reply:** We have added references to each of these areas. Thank you.