Effects of Short-Term Exposure to NO_2, O_3 & SO_2 on Asthma

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In 2021, the World Health Organization (WHO) published revised recommendations for ambient air quality (WHO 2021). To support this update, WHO published a review paper in 2021 evaluating the best available evidence on the effects of short-term exposure to nitrogen dioxide (NO_2), ozone (O_3), sulphur dioxide (SO_2) and asthma exacerbations (Zheng et al. 2021). Specifically, the research published updated quantified risk ratios for exposure to NO_2, O_3 and SO_2 on emergency room visits and hospitalisations.

Highlights

- 24-hour levels of NO_2, O_3 and SO_2 correlated with asthma emergency room visits and hospitalisations.
- There was no major evidence of publication bias.
- The certainty of evidence was **high** for 24-hour NO_2 and O_3,
- The certainty of evidence was moderate for 24-hour SO_2 and 1-hour O_3.

(Zheng *et al*. 2021).

Nitrogen Dioxide

The certainty of evidence for the association between 24-hour exposure to NO_2 and asthma exacerbations was **high**, meaning that we can be confident in the associations found in this study.

Ozone

The certainty of evidence for the association between 24-hour and 8-hour exposure to ozone and asthma exacerbations was **high**, however the certainty of evidence for 1-hour exposure was only moderate.

Sulphur Dioxide

The certainty of evidence for the association between 24-hour exposure to SO_2 and asthma exacerbations was moderate and warrants further analysis. However, the researchers concluded that 24-hour exposure to SO_2 correlates with increased risks of asthma-associated emergency room visits and hospital admissions.

Public health protection ideally seeks a threshold concentration below which there is no effect. There is no evidence of a 'safe threshold' for SO_2.

[1] For more information on the study methods and interpreting risk ratios please see the separate fact sheet titled "Health Effects of Air Pollutant Factsheets: Supporting Information". (Wickham *et al.* 2022a).

Research Findings

Following screening and selection, Zheng and fellow researchers systematically reviewed 67 air pollution epidemiology studies of short-term exposure to NO_2, O_3 and SO_2.

Mean/median daily concentrations of NO_2 reported in 22 studies ranged from 1 – 342 micrograms per cubic metre (µg/m^3) and mean/median hourly concentrations of NO_2 reported in 5 studies ranged from 0 – 422 µg/m^3.

Mean/median daily concentrations of O_3 reported in 33 studies ranged from 2 – 134 µg/m^3, mean/median 8-hourly concentrations of O_3 reported 9 studies ranged from 0 – 340 µg/m^3 and mean/median hourly concentrations of O_3 reported in 11 studies ranged from 4 – 524 µg/m^3.

Mean/median daily concentrations of SO_2 reported in 23 studies ranged from 0 – 262 µg/m^3 and mean/median hourly concentrations of SO_2 reported in 4 studies ranged from 9 – 167 µg/m^3.

The studies were primarily published in the period between the 1990 s and the 2010 s. The majority of studies were undertaken in developed countries (Europe and North America) with the remainder in China, Korea, South America and Australia. There were no studies from Africa (or New Zealand).

Zheng and fellow researcher's developed new risk ratios as presented below, to represent the quantitative risks posed by short-term exposure to NO_2, O_3 and SO_2 on emergency room visits (ERV) or hospital admissions (HA). The risk ratios for one hour exposure to NO_2, O_3 and SO_2 showed no correlation.

The risk ratio can be interpreted as follows: [1]

Daily NO_2 risk ratio 1.014 (95% *Confidence Interval*:1.008, 1.020, n = 22)

This means for every 10 µg/m^3 increase in daily concentrations of NO_2, emergency room visits and hospitalisations due to asthma exacerbations increased by 1.4%, with 95% of the data being between 0.8 – 2.0% across 22 epidemiological studies.

Pollutant/ Time Average	Outcome	No. Studies	Risk Ratio*	95% Confidence Interval	Certainty of Evidence
NO_2 (24-hour)	ERV or HA	22	1.014	1.008 – 1.020	High
O_3 (8-hour or 24-hour)	ERV or HA	27	1.008	1.005 – 1.011	High
SO_2 (24-hour)	ERV or HA	23	1.010	1.001 – 1.020	Moderate

*Only RR > 1 reported here

Discussion

The researchers noted the following important observations:

- The study has extended previous findings (Orellano *et al*. 2017; Zheng *et al*. 2015) by confirming that **higher levels of 24-hour exposure to NO_2, O_3 and SO_2 were associated with significantly increased risks of asthma-related exacerbations** (measured through hospital admissions or emergency room visits).
- Although the measured concentration ranges varied considerably, most studies documented a **positive correlation between air pollution and asthma** exacerbations in the overall and subgroup analyses.

  This was **not the case for maximal 1-hour daily concentrations** which did not demonstrate significant associations with asthma exacerbations for any of the pollutants studied – possibly due to the small number of papers (4) that addressed this.
- **Subgroup analyses demonstrated that children and, to a lesser extent, the elderly were more susceptible to the adverse effects of air pollution** (i.e., the magnitude of association was greater in these subgroups than in adults), which was consistent for NO_2, O_3 and SO_2. This is consistent with previous studies (Orellano *et al*. 2017; Zheng *et al*. 2015).
- The relationship between **pollutant concentrations and risk ratios were found to be linear** in all studies except two:
  - One study from Cincinnati and Cleveland (Jaffe 2003) for 24-hour NO_2; and
  - One study from Shanghai (Guo 2018) for 24-hour SO_2.
- One study (Li *et al*. 2011) documented a threshold for 24-hour NO_2 at 41 µg/m^3. Another paper (Erbas *et al*. 2005) focusing on 1-hour NO_2 documented threshold at 85, 75, 38 and 28 µg/m^3. These are considerably lower than the 2005 WHO hourly guideline for NO_2 (200 µg/m^3), however, these results were deemed insufficient to warrant a review of the guideline.
- **No thresholds were found or reported for SO_2**.
- **Publication bias would not have substantially affected the general conclusions** of this study, or the size or precision of the true effect.
- Analysis of co-pollutant models showed that the pooled **associations observed in single-pollutant models were no longer significant after the inclusion of a second pollutant**. This raises concerns about the validity of the reported associations and the causal relationship between the three air pollutants and asthma exacerbations. However, two factors may have influenced these results:
  - The study of co-pollutant models was implemented in a small proportion of papers (10 out of 31 studies) which may have reduced the statistical power.
  - Almost all studies showed high correlation coefficients between the pollutants included in the regression models. This can have the effect of inflating standard errors and reducing statistical power.

  The researchers considered the analysis of co-pollutant models was insufficient to fully elucidate the causal relationship between air pollutants and asthma exacerbations and warrants further discussion.
- A limitation of the asthma related ERVs and HAs is that these comprise severe forms of asthma exacerbations. In real-world practice, documentation of milder forms of asthma can be technically challenging because under reporting is common.

Conclusions

Zheng and fellow researchers concluded that a 24-hour exposure to nitrogen dioxide, ozone and sulphur dioxide correlates with increased risk of asthma-associated emergency room visits and hospital admissions.

WHO Short-Term NO_2, O_3 & SO_2 Guidelines

Short-term ambient air quality guidelines (AQG) for NO_2, O_3 and SO_2 were set to protect against *inter alia* increased respiratory hospital admissions for asthmatics (WHO 2000). The 24-hour average AQG for NO_2, O_3 and SO_2 were updated in 2021 based on new evaluations of the epidemiology of short-term exposure of these pollutants with all-cause mortality (Orellano *et al.* 2020, Orellano *et al*. 2021) as well as a new evaluation of the epidemiology of short-term exposure with emergency room visits and hospitalisations for asthmatics (Zheng *et al*. 2021).[2] Existing guidelines remain valid (WHO 2021).

It is important to note that the approach to setting guidelines does not identify safe levels and is not based on a defined level of acceptable risk (i.e., the guidelines are not "no adverse effect levels").

Pollutant / Time Average	Guideline (µg/m^3)	Permitted Exceedances per year
Nitrogen Dioxide (NO_2)		
24-hour [3]	25	3-4
1-hour	200	–
Ozone (O_3)		
8-hour daily maximum	100	3-4
Sulphur Dioxide (SO_2)		
24-hour	40	3-4
10-minutes	500	–

[2] For more information on these systematic reviews, refer "Health Effects of Short-Term Exposure to PM, NO_2 and O_3" (Wickham *et al.* 2022b) and "Health Effects of Short-Term Exposure to SO_2 (Wickham *et al.* 2022c).

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