Health effects of long-term exposure to NO_2 and O_3

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In 2021, the World Health Organisation (WHO) published revised recommendations for ambient air quality (WHO 2021). To support this update, WHO published a review paper in 2020 evaluating the best available evidence on the effects of long-term exposure to nitrogen dioxide (NO_2) and ozone (O_3) (Huangfu and Atkinson 2020).

Specifically, the research published updated quantified risk ratios for exposure to NO_2 and all-cause and cause-specific premature mortality (people dying earlier than they otherwise would have). [1]

Highlights

- 46 cohort studies assessed long-term concentrations of NO_2 and O_3 and mortality.
- Meta-analysis of 24 studies found increased risk of death associated with NO_2.
- Weak associations were observed for peak period O_3 and mortality.
- High levels of heterogeneity were observed.
- Certainty in NO_2 associations with mortality was generally low/moderate.

(Huangfu and Atkinson 2020)

Key Facts

This review of cohort studies found positive associations between long-term concentrations of NO_2 and mortality, and limited evidence for O_3 and mortality.

For annual NO_2 and mortality the certainty of evidence was moderate for all-cause mortality, moderate for respiratory mortality, high for chronic obstructive pulmonary disease (COPD), and moderate for acute lower respiratory infection.

For annual O_3 the certainty of the evidence was low for both all-cause and respiratory mortality. For peak O_3 exposures the certainty of evidence was moderate for all-cause mortality and low for respiratory mortality.

[1] The paper also investigated ozone, which is not typically elevated in New Zealand and is only briefly discussed here.

Research Findings

Following screening and selection, Huangfu and Atkinson systematically reviewed 41 air pollution epidemiology studies for NO_2 and 20 studies for O_3. Mean annual concentrations of NO_2 ranged from 17 – 130 micrograms per cubic metre ($\mu g/m^3$).

The studies were published between 1999 and 2018, with the majority of studies from the USA and Europe, and the remainder from Canada, China and Japan. There were no studies from Africa or South America (or New Zealand). It is also important to note that the annual average concentrations of NO_2 in the studies were relatively high (mean annual average NO_2 39 $\mu g/m^3$ reported in 41 studies) compared with typical annual concentrations in New Zealand (national population weighted annual average NO_2 was 7.8 $\mu g/m^3$ in 2016, Kuschel *et al.* 2022).

Huangfu & Atkinson developed new risk ratios as presented below, to represent the quantitative risks posed by long-term exposure to NO_2.

Pollutant Exposure	Mortality type	No. Studies	Risk Ratio	95% Confidence Interval	Certainty of Evidence
Annual NO_2	All-cause	24	1.02	1.01 – 1.04	Moderate
	Respiratory	15	1.03	1.01 – 1.05	Moderate
	COPD	9	1.03	1.01 – 1.04	High
	ALRI	5	1.06	1.02 – 1.10	Moderate
Peak O_3	All-cause	12	1.01	1.00 – 1.02	Moderate

COPD – chronic obstructive pulmonary disease, ALRI = acute lower respiratory infection

The risk ratio can be interpreted as follows:

Annual NO_2 risk ratio 1.02 (95% *Confidence Interval*:1.01, 1.04, n = 24)[2]

This means for every 10 $\mu g/m^3$ increase in annual concentrations of NO_2, deaths in the wider population due to all causes increased by 2%, with 95% of the data being between 1 – 4% in 24 epidemiological studies.

[2] 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*. 2022).

Discussion

The researchers noted the following important observations:

- The **risk ratios for all-cause mortality are broadly comparable to previous reviews** (per 10 µg/m^3);
    - 1.04 (1.02, 1.06) n = 12 Faustini *et al*. 2014
    - 1.06 (1.04, 1.08) n = 11 Hoek *et al*. 2013
    - 1.02 (1.01, 1.03) n = 23 Atkinson *et al*. 2018
- The review identified **very high levels of heterogeneity for all causes of death except COPD**. *Heterogeneity* is an indicator of the extent to which variations between study estimates is too great to be explained by chance.
- The evidence base continues to be **dominated by studies from North America and Europe**. The researchers noted the limitations in terms of geographical spread and, for some outcomes, the small number of independent cohorts. They considered this precluded any meaningful meta-regression to explore the causes of heterogeneity.
- Only a small number of studies investigated the shape of the concentration-response relationship. These generally found **little evidence to reject the assumption of linearity across the concentration range**.

Conclusions

Associations for NO_2 and mortality were positive and risk ratios were developed for all cause, respiratory, chronic obstructive pulmonary disease and acute lower respiratory infection mortality.

Certainty in the associations with mortality was rated moderate for each exposure outcome pair, except for NO_2 and COPD mortality where the certainty of evidence was judged as high.

The researchers considered the substantial heterogeneity for most outcomes in the review requires explanation. The shortcomings in the existing literature base makes determining the precise nature (magnitude and linearity) of the associations challenging.

WHO Long-Term NO_2 and O_3 Guidelines

The long-term WHO 2021 air quality guideline (AQG) levels are defined as the lowest exposure level of an air pollutant above which WHO is confident that there is an increase in adverse health effects (WHO 2021).

Ozone has a peak season AQG and no annual AQG. Peak season for ozone is the average of daily maximum 8-hour mean O_3 concentration in the six consecutive months with the highest six-month running-average O_3 concentration (usually summer).

Pollutant / Time Average	Guideline (µg/m^3)
NO_2	
Annual	15
O_3	
Annual	-
Peak Season	50

References

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