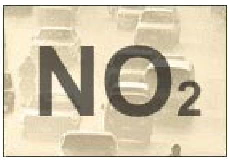
GreenFacts
Facts on Health and the Environment



Scientific Facts on

Air Pollution

Nitrogen Dioxide

Source document:
WHO (2003 - 2004)

Summary & Details:
GreenFacts

Level 2 - Details on Air Pollution

This Digest is a faithful summary of two leading scientific consensus reports produced in 2003 and 2004 by the World Health Organization (WHO):
"Health Aspects of Air Pollution with Particulate Matter, Ozone and Nitrogen Dioxide" and "Answer to follow-up questions from CAFE (2004)"

The full Digest is available at: https://www.greenfacts.org/en/nitrogen-dioxide-no2/

1. What is Nitrogen Dioxide (NO_2)?

Nitrogen dioxide (NO_2) is one of the nitrogen oxides (NO_x), a group of air pollutants produced from combustion processes.

In urban outdoor air, the presence of NO_2 is mainly due to traffic. Nitric oxide (NO), which is emitted by motor vehicles or other combustion processes, combines with oxygen in the atmosphere, producing NO_2. Indoor NO_2 is produced mainly by unvented heaters and gas stoves.

NO_2 and other nitrogen oxides are also precursors for a number of harmful secondary air pollutants such as ozone and particulate matter, and play a role in the formation of acid rain. Exposure to NO_2 may affect health independently of any effects of other pollutants. However, because its presence is closely linked to the formation or presence of other air pollutants, it is difficult to establish the health effects attributable to NO_2 alone.

2. How does Nitrogen Dioxide (NO_2) affect human health?

2.1 Which effects can be expected of long-term exposure to levels of NO_2 observed currently in Europe?

WHO states:

2.1.1 "The epidemiological studies provide some evidence that long-term NO_2 exposure may decrease lung function and increase the risk of respiratory symptoms."

2.1.2 "Methodological limitations constrain identification of harvesting [(the advancement of mortality by only relatively few days)] due to NO_2 itself. The few [available] long-term studies have not shown evidence for association between NO_2 and mortality. Associations have been observed between NO_2 and mortality in daily time-series studies, but on the basis of present evidence these cannot be attributed to NO_2 itself with reasonable certainty."

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2.2 Is NO_2 per se responsible for effects on health?

The evidence for acute effects of NO_2 comes from controlled human exposure studies to NO_2 alone.

For the effects observed in epidemiological studies, a clear answer to the question cannot be given. Effects estimated for NO_2 exposure in epidemiological studies may reflect other, often unmeasured, traffic related pollutants, for which NO_2 is an indicator. Additionally, there are complex interrelationships among the concentrations of NO_2, PM, and ozone in ambient air.

2.3 Are health effects of NO_2 influenced by the presence of other air pollutants?

WHO states: "There have been few controlled human exposure studies on interactions with other chemical pollutants, although several studies show that NO_2 exposure enhances [allergic] responses [of asthmatics] to inhaled pollens. Some epidemiological studies have explored statistical interactions of NO_2 with other pollutants, including particles, but the findings are not readily interpretable."

Source & ©: WHO Europe (2003)

2.4 Which characteristics of individuals may influence how Nitrogen Dioxide affects their health?


See also our Digest on Respiratory Diseases in Children [see https://www.greenfacts.org/en/respiratory-diseases/index.htm]

Are effects of NO_2 dependent upon the subjects' characteristics such as age, gender, underlying disease, smoking status, atopy, education etc?

What are the critical characteristics?

WHO states: "In general, individuals with asthma are expected to be more responsive to short-term exposure to inhaled agents, when compared to individuals without asthma. Controlled human exposure studies of short-term responses of persons with and without asthma to NO_2 have not been carried out. There is limited evidence from epidemiological studies that individuals with asthma show steeper concentration-response relationships. Small-scale human exposure studies have not shown consistent effects of NO_2 exposure on airways reactivity in persons with asthma, even at exposure levels higher than typical ambient concentrations. As for other pollutants, children can reasonably be considered to be at increased risk. There is limited evidence for influence of the other listed factors [such as gender, smoking status, atopy, education, etc.] on the effects of NO_2."

Source & ©: WHO Europe (2003)

2.5 Is there a threshold below which nobody's health is affected by NO_2?

WHO states: "The evidence is not adequate to establish a threshold for either short or long-term [NO_2] exposure. While a number of epidemiological studies have described concentration-response relationships between ambient NO_2 and a range of health outcomes, there is no evidence for a threshold for NO_2."

Source & ©: WHO Europe (2003)

See also: General Issues and Recommendations on Air Pollutants:

- Question 5.3 on uncertainties in defining thresholds
- Question 7.1 recommendations regarding the concept of thresholds

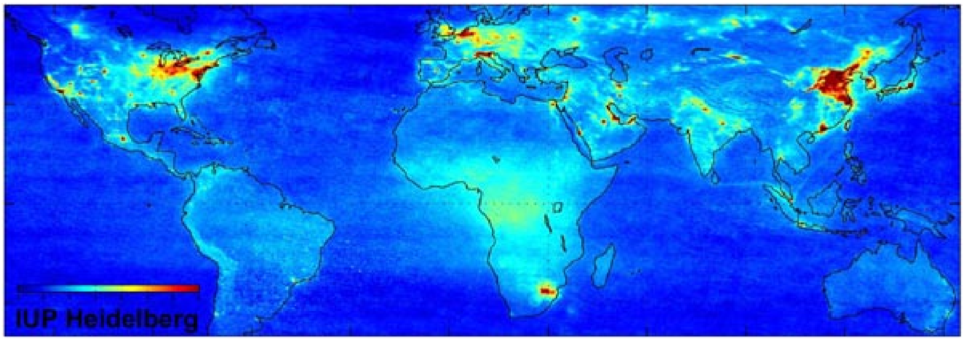
3. How are we exposed to Nitrogen Dioxide (NO_2)?

3.1 Which are the critical sources of NO_2 responsible for health effects?

WHO states: "In most urban environments in Europe, the principal source of NO_2 is NO_x from motor vehicles of all types and energy production in some places [e.g., power plants, domestic heating]."

Source & ©: WHO Europe (2003)

The map below illustrates regions where traffic and fuel combustion contribute to NO_2 air pollution. It shows the mean ground level nitrogen dioxide (NO_2) concentration between January 2003 and June 2004, as measured by Satelite.



Source: European Space Agency www.esa.int/esaCP/ [see http://www.esa.int/esaCP/SEm340NKPZD_index_1.html] Credits: University of Heidelberg

3.2 What is the relationship between ambient levels and personal exposure to NO_2?

Can the differences influence the results of studies?

WHO states: "In any particular setting the answer will depend on the relative contributions of outdoor and indoor sources and on personal activity patterns. A direct relationship between personal exposure and outdoor concentrations is found in the absence of exposure to indoor sources such as unvented cooking or heating appliances using gas, and tobacco smoking. However, since outdoor NO_2 is subject to wide variations caused by differences in proximity to road traffic and local weather conditions, the relationship of personal exposure to measurements made at outdoor monitoring stations is variable. Results of epidemiological studies relying on outdoor NO_2 concentrations may be difficult to interpret if account is not taken of exposure to indoor sources."

See also our summaries on:

Indoor Air Pollution [see https://copublications.greenfacts.org/en/indoor-air-pollution/index.htm]

Active & passive smoking [see https://www.greenfacts.org/en/tobacco/index.htm]

3.3 What is the health relevance and importance of short-term exposure to high peak levels or exposure in hot spots for NO_2?

Adverse health effects have been documented after short-term exposure to peaks, as well as after long-term exposure to relatively low concentrations of NO_2. Experimental studies indicate that short-term exposure to high concentrations of NO_2 increases responsiveness to allergens. NO_2 exposure over time has also been linked to mortality and disease progression. A direct comparison of the health relevance of short term and long-term exposures has not been reported for NO_2.

Some studies have documented that subjects living close to busy roads experience more short- term and long-term effects of air pollution than subjects living further away. In urban areas, up to 10% of the population may be living at such "hot spots". The public health burden of such exposures is therefore significant. Unequal distribution of health risks over the population also raises concerns of environmental justice and equity.

4. Should current NO_2 guidelines be reconsidered?

4.1 Have positive impacts on public health of reductions of emissions and/or ambient concentrations of NO_2 been shown?

WHO states: "It has not been possible to study impacts of reduction in NO_x emissions or NO_2 concentrations in the ambient air because there have been no good examples of such reductions."

Source & ©: WHO Europe (2003)

4.2 What averaging period (time pattern) is most relevant from the point of view of protecting human health?

Would additional protection be provided by setting standards for more than one averaging period for NO_2?

WHO states: "With regard to protection against acute health effects, either the peak-hour average or 24hr (daily) average NO_2 concentrations can be used as a measure of direct short-term exposure, since they are highly correlated in urban areas.

Having a longer-term guideline value is also supported by the evidence on possible direct effects of NO_2, and on its indirect consequences through the formation of secondary pollutants."

Source & ©: WHO Europe (2003)

4.3 Is there new scientific evidence to justify reconsideration of the current WHO Guidelines for NO_2?

The current WHO guideline values for NO_2 are:

- a 1-hour level of 200 µg/m^3 and
- an annual average of 40 µg/m^3.

There is evidence from toxicological studies that long-term exposure to NO_2 at concentrations higher than current ambient concentrations has adverse effects. However, at current ambient air concentrations in Europe, uncertainty remains over the significance of NO_2 as a pollutant with a direct impact on human health. Moreover, there is still no firm basis for selecting a particular concentration as a long-term guideline for NO_2. The former group that proposed the 40 µg/m^3 annual guideline value selected that value from a prior WHO review.

In recent epidemiological studies on the effects of mainly traffic generated air pollution, NO_2 has been associated with adverse health effects even when the annual average NO_2 concentration is within a range that includes 40 µg/m^3. No alternative guideline could be established from these studies, therefore it was recommended that the WHO annual specific guideline value of 40 µg/m^3 should be retained or lowered.

No recent human exposure study supports the need to change the 1-hour guideline value.

5. What are the uncertainties regarding this study?

5.1 Uncertainties of the WHO answers, guidelines, and risk assessments

How could these influence the conclusions for policy-makers?

Uncertainties linked to gaps in knowledge exist and will continue to exist in the future. The expert group which wrote the reference documents for this Digest was aware of these uncertainties, and tried to take them into account – to the best of their knowledge – when drawing their conclusions.

Uncertainties were addressed in a systematic way, following the recommendations of a WHO guideline document. It was not feasible to quantify the uncertainties linked to all answers within this study.

It was stressed that, in accordance with the precautionary principle, uncertainties should not be taken as a cause for not acting, if the potential risks are high and measures to reduce the risks are available at a reasonable cost.

Examples of uncertainties related to this study are:

- Potential **publication bias**. For example, studies that have found no association between a pollutant and a particular effect may not have been published (see question 5.2).
- **Diverging evidence**. For example, data suggesting either the existence or non-existence of a threshold for ozone (see question 5.3).
- Uncertainties regarding the **contribution of different sources** of particulate matter to health effects (see question 5.4).
- Uncertainty related to the use of different **models** (see question 5.5).

- Uncertainties regarding **regional differences** in the effects of air pollution (see question 5.6).

5.2 Consideration of publication bias in the review

WHO states: "Publication bias occurs when the publication process is influenced by the size of the effect or direction of results. The bias is usually towards statistical significant and larger effects. It can be detected and adjusted for using statistical techniques. Bias may also occur when literature is selectively ascertained and cited.

This review used a systematic approach to identify all short-term exposure studies, but it did not formally investigate publication bias. The reviewers were aware that evidence of publication bias has been identified in meta-analyses of single city time series studies, but when estimates were corrected for this bias, significant positive associations remained. Furthermore, the multi-city time series studies, which have published results from all participating cities and are free from publication bias, have reported significant positive associations.

Because of the size and experience of the review group and referees, it is unlikely that any important published long-term study has been missed. Formal assessment of a possible publication bias has not been undertaken. Every effort was made to systematically ascertain long-term exposure studies."

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5.3 Consistency of epidemiological and toxicological evidence in defining thresholds

5.3.1 WHO states:

"Multiple factors determine whether a threshold is seen [for effects due to exposure to air pollutants] and the level at which it can occur. Exposure-response curves depend on the age and gender of the subjects, their health status, their level of exercise (ventilation) and, especially the health effect selected. For highly uniform population groups, with a specific exposure pattern, a full range of concentrations, and a specific health outcome, one could identify a specific threshold. However, when there are different exposure-response curves for different groups, thresholds are harder to discern in population studies, and may ultimately disappear. Therefore, the evidence coming from the epidemiological and toxicological studies is not contradictory."

5.3.2 Ozone: "Chamber studies [(controlled exposure studies)] may show thresholds for mean effects of ozone on lung function and airway inflammation but a few individuals show these responses below these levels. As mentioned previously, a particular threshold in a particular experimental situation does not necessarily contradict a finding of effects below these levels in other situations. The time-series results often have insufficient data to distinguish between a linear and non-linear model with confidence. In addition, the statistical analyses applied to investigate thresholds in datasets on particles have not been applied to the same extent to datasets on ozone. There remain uncertainties in interpreting the shape of exposure-response relationships in epidemiological studies due to different patterns of confounding by other pollutants and correlations with personal exposure across the range of ozone concentrations. Although there is evidence that associations exist below the current [ozone] guideline value, our confidence in the existence of associations with health outcomes decreases as concentrations decrease. The answer and rationale [in question 2.3] refer to acute effects of ozone, as this is most important for health impact assessment of the effects of ozone."

5.3.3 Particulate matter: "Most epidemiological studies on large populations have been unable to identify a threshold concentration below which ambient PM has no effect on mortality and morbidity. It is likely that within any large human population, there is a wide range in susceptibility so that some subjects are at risk even at the low end of current concentrations"

Source & ©: WHO Europe (2004)

5.4 Contribution of different sources to PM-related health effects

WHO states: "Only a few epidemiological studies have addressed source contributions specifically. These studies have suggested that combustion sources are particularly important.

Toxicology, because of its simpler models and potential to tightly control exposures, provides an opportunity to determine the relative toxic potency of components of the PM mix, in contrast to epidemiology. Such toxicology studies have highlighted the primary, combustion-derived particles having a high toxic potency. These are often rich in transition metals and organics [organic compounds and matter], in addition to their relatively high surface area. By contrast, several other components of the PM mix are lower in toxic potency, e.g. ammonium salts, chlorides, sulphates, nitrates and wind- blown crustal dust such as silicate clays.

Despite these differences among constituents under laboratory conditions, it is currently not possible to precisely quantify the contributions from different sources and different PM components to health effects from exposure to ambient PM."

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5.5 Impact of methods of analysis used in epidemiological studies

WHO states: "This answer addresses matters relating to uncertainties in methods of analysis used. Epidemiological studies use statistical models of various types, including Poisson and logistic regression. The estimates of effect provided by air pollution studies are generally accompanied by confidence intervals. These convey the precision of the estimate or statistical uncertainty that arises because the analyses are subject to a degree of random error. To a varying degree, the results of these analyses are sensitive to the details of the model and the specification of confounding and interacting factors. Extensive sensitivity analyses have shown that associations between air pollution and health remain irrespective of the methods of analyses used."

Source & ©: WHO Europe (2004)

5.6 Possible regional characteristics modifying the effects of air pollution

WHO states: "Potentially this could be a very influential issue since the characteristics of populations, environments and pollution (including particle concentration, size distribution and composition) vary throughout Europe. However, at this stage there is not sufficient evidence to advocate different guidelines for particles or other priority pollutants in different parts of Europe.

Several studies on short and long-term effects of particulate matter have consistently reported an association between pollution levels and mortality; however, there are differences in the size of the estimated effects of PM according to geographical region or according to the levels of other variables (potential effect modifiers). For example, it has been reported that the short-term effects of PM_{10} are greater where long term average NO2 concentration is higher, when the proportion of the elderly is larger and in warmer climates. Modification by socioeconomic factors, such as the level of education, has also been reported. Plausible explanations for some of these observations have been proposed.

Effect modification, for example by the age distribution in a population and by climate should, if possible, be taken into account in sensitivity analysis of health impact assessments or risk assessments.

Possible effect modifiers of other criteria pollutants have not been investigated to any extent so far."

Source & ©: WHO Europe (2004)

6. Are certain population groups particularly vulnerable?

Are there specific population groups that should be brought into special attention?

WHO states: "A number of groups within the population have potentially increased vulnerability to the effects of exposure to air pollutants.

These groups comprise:

- those who are innately more susceptible to the effects of exposure to air pollutants than others,
- those who become more susceptible for example as a result of environmental or social factors or personal behaviour and
- those who are exposed to unusually large amounts of air pollutants.

Members of the last group are vulnerable by virtue of exposure rather than as a result of personal susceptibility.

Groups with innate susceptibility include those with genetic predisposition that render them unusually sensitive, for example, to the broncho-constrictor effects of ozone or liable to produce an unusually marked inflammatory response on exposure to allergens. Very young children and unborn babies are also particularly sensitive to some pollutants.

Groups which develop increased sensitivity include the aged, those with cardio-respiratory disease or diabetes, those who are exposed to other toxic materials that add to or interact with air pollutants and those who are socioeconomically deprived. When compared with healthy people, those with respiratory disorders (such as asthma or chronic bronchitis) may react more strongly to a given exposure both as a result of increased responsiveness to a specific dose and/or as a result of a larger internal dose of some pollutants than in normal individuals exposed to the same concentration of pollutants. Increased particle deposition and retention has been demonstrated in the airways of subjects suffering from obstructive lung diseases.

Lastly, those exposed to unusually large amounts of air pollutants perhaps as a result of living near a main road or spending long hours outdoors, may be vulnerable as result of their high exposure".

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7. General Conclusions

7.1 Recommendations

Clean air policies aim to develop strategies to reduce the risk of adverse consequences of ambient air pollution for human health and for the environment as a whole. In the case of air pollutants, the concept of thresholds may no longer be useful in setting standards to protect public health. This is because certain population groups are very susceptible and are affected even at low levels, and because we are now able to detect even rare cases. Therefore, the application of the policy principle of providing an adequate margin of safety in order to eliminate adverse effects even for the most susceptible groups may not be realistic.

Risk reduction strategies are nevertheless effective in promoting public health. To develop such strategies, both qualitative and quantitative knowledge about the most relevant effects is required.

Therefore, for ozone and particulate matter, a meta-analysis of available data was recommended. This analysis should evaluate the relative risk increase (risk coefficients) related to ozone and to specific fractions of particulate matter for different health effects (endpoints).

It was also recommended:

- to update the concentration-response table for ozone in the current WHO Air quality guidelines,
- to identify which risk coefficients should be used in order to estimate long term mortality in relation to PM exposure, and
- to carry out a more comprehensive monitoring programme for PM-related health effects (not only relying on $PM_{2.5}$) in different European cities.

7.2 What other aspects of air pollution are important to address in the development of air pollution policy in Europe?

Other substances and pollutants posing risk to health which are currently not adequately addressed in the development of air pollution policy in Europe include:

- Carbon monoxide (CO) and sulphur dioxide (SO_2), with new evidence of links to severe health effects.
- Persistent organic pollutants (POP) such as PAH.
- Heavy metals, in particular lead and some transition metals. Lead is of concern since there are new studies suggesting effects at low concentrations.

- The carcinogenic volatile organic compounds 1.3-butadiene and benzene.
- Nitrogen trichloride, since there is evidence of health effects from this substance from epidemiological studies.

Few experts suggested assessing the health effects from diesel versus gasoline exhaust fumes.

An important issue that remains unresolved concerns the combined effects on health of urban air pollution mix.

7.3 Concluding remarks

- The body of evidence has grown stronger over the past few years regarding the health effects of air pollution at levels currently common in Europe.
- There is sufficient evidence to strongly recommend further policy action to reduce levels of particulate matter (PM), nitrogen dioxide (NO_2), and ozone (O_3) in air. This would lead to considerable health benefits.
- Further targeted research and subsequent systematic evaluation is needed to reduce the existing uncertainty.