Current knowledge on adverse effects of traffic-related air pollution: have we filled the gap? What more do we need to know?

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Health outcomes associated with traffic-related air pollution

**Birth outcomes:**
- Term low birth weight
- Small for gestational age

**In Children:**
- Asthma onset
- Acute lower respiratory infections
- Asthma ever
- Active asthma

**In Adults:**
- All-cause mortality
- Circulatory mortality
- Ischemic heart disease mortality
- Lung cancer mortality
- Asthma onset
- Respiratory mortality
- Ischemic heart disease events
- Diabetes

Overall confidence in the evidence for an association with long-term exposure to traffic-related air pollution:
- high
- moderate to high
- moderate

Footnote: health outcomes for which the overall confidence in the evidence was low-to-moderate, low or very low are not in the picture.
Overall summary

- The findings have provided an overall high or moderate-to-high level of confidence in an association between long-term exposure to traffic-related air pollution and the adverse health outcomes: all-cause, circulatory and ischemic heart disease mortality, lung cancer mortality, asthma onset in children and adults, and acute lower respiratory infections in children.

- The Panel’s confidence in the evidence was considered moderate, low or very low for the other selected outcomes.

- In light of the large number of people exposed, the results indicate that traffic-related air pollution remain an important public health concern.

- Several future research opportunities emerged from this report.
1. Beyond LUR: improve exposure assessment

**Satellites**: Size and shape of the particles

**Sensors**: personal exposures to gases and particles

**Social media**: Time-activity patterns

**Exposome**: markers of exposure

**Machine learning**: non-linear relations

Apply **Regression Calibration** to address measurement error.
2. Conduct long-term health studies on UFP and non-tailpipe PM

A case for UFP

✓ Exposures to ultrafine and fine particles differ in space and time

✓ Experimental and epidemiological studies suggest independent short-term health effects

✓ Studies on long-term health effects of UFP are limited

A case for non-tailpipe PM components (e.g., Cu, Fe)

✓ No great progress in the last two decades but need to continue to address the issue and search for better evidence
3. The NO\textsubscript{2} dilemma: per se... or not per se

Gain a better understanding of whether the epidemiological associations found for TRAP are due to direct effects of NO\textsubscript{2}, to another component of TRAP, or to the broader mixture of correlated components indicative of TRAP.

Despite:

- Two Integrated Science Assessment (USA EPA 2016; Health Canada 2016)
- One critical assessment, COMEAP 2018 (not all conclusions were unanimous)
- Seven systematic reviews

<table>
<thead>
<tr>
<th>Reference</th>
<th>Number of studies</th>
<th>Summary estimate (95% CI) per 10 ug/m\textsuperscript{3}</th>
</tr>
</thead>
<tbody>
<tr>
<td>HEI traffic review 2022</td>
<td>11</td>
<td>1.041 (1.015-1.068)</td>
</tr>
<tr>
<td>Stieb 2021</td>
<td>39</td>
<td>1.034 (1.018-1.050)</td>
</tr>
<tr>
<td>Stieb 2021*</td>
<td>32*</td>
<td>1.025 (1.012-1.038)</td>
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<tr>
<td>Huang 2021</td>
<td>28</td>
<td>1.032 (1.021-1.043)</td>
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<tr>
<td>Huangfue 2020 (WHO)</td>
<td>24</td>
<td>1.020 (1.005-1.036)</td>
</tr>
<tr>
<td>Atkinson 2018</td>
<td>20</td>
<td>1.020 (1.010-1.030)</td>
</tr>
<tr>
<td>Faustini 2014</td>
<td>12</td>
<td>1.042 (1.019-1.076)</td>
</tr>
<tr>
<td>Hoek 2013</td>
<td>12</td>
<td>1.056 (1.031-1.083)</td>
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</tbody>
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* After excluding studies with probably high or high risk of bias in confounding domain
Long-term NO₂ and mortality: ELAPSE administrative cohorts

Results are robust against adjustments for other pollutants

<table>
<thead>
<tr>
<th>NO₂</th>
<th>Adjusted</th>
<th>Percent increase (95% CI) per 10 ug/m³</th>
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</thead>
<tbody>
<tr>
<td>NO₂</td>
<td>-</td>
<td>4.4% (1.9-6.9%)</td>
</tr>
<tr>
<td>NO₂</td>
<td>PM₂.₅</td>
<td>4.2% (2.0-6.5%)</td>
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<tr>
<td>NO₂</td>
<td>BC</td>
<td>4.1% (0.9-7.3%)</td>
</tr>
<tr>
<td>NO₂</td>
<td>O₃</td>
<td>4.0% (1.2-6.9%)</td>
</tr>
</tbody>
</table>

Stafoggia et al. Lancet Planetary Health (2022)
3. The NO₂ dilemma: need to triangulate evidence capitalizing on experimental studies

- Capacity of NO₂ to induce bronchial hyperresponsiveness and responses to inhaled allergen in patients with asthma

  Particle Depletion Does Not Remediate Acute Effects of Traffic-related Air Pollution and Allergen. A Randomized, Double-Blind Crossover Study. Wooding et al. AJRCCM 2019
  - Controlled chamber exposure experiments in allergen-sensitized individuals
  - Nasal instillation of allergen and diesel exhaust exposure > exhaust particles enhanced both sensitization to neoallergen and the allergen response
  - Filtering out the particles (NO₂ increased) provided no protection

- This strongly implicates NO₂ associated with diesel exhaust as an important adjuvant factor enhancing allergen sensitization (Bosson et al. AJRCCM 2019)
4. Conduct health studies in areas outside North America and Europe

Geographical location of the studies in the HEI systematic review

The effects of sociodemographic, travel behavior, living conditions, and health status on personal PM2.5 exposure in Beijing. Liang et al, BMC Public Health 2019
5. Conduct additional research on outcomes for which there are suggestions of an association with TRAP, but for which the evidence is still limited

- Critical windows of exposure in birth outcome studies, and for asthma onset in children
- TRAP and COVID-19 incidence, hospitalization and mortality, especially after vaccination and new variants
- Additional long-term TRAP studies are needed for:
  - COPD and ALRI in adults
  - Cardiometabolic outcomes
  - COPD, stroke, and ALRI mortality
6. Consider spatially correlated factors like **poverty**, **traffic noise**, and factors related to the built environment, such as presence of **green space**

Asthma and poverty in NYC, Caplin et al. 2019

Conceptual framework of the relationship between hypertension and urban and transport planning, traffic ...Mannucci &Ancona, EHJ, 2021
7. Evaluate the fuller range of potential impacts of transportation and (new) mobility on public health

This includes the opportunities for physical activity and active transport to mitigate the adverse health effects of TRAP

8. Evaluate the mechanisms behind the association of TRAP with the selected outcomes by studying markers and subclinical outcomes

“Meet-in-the-middle” approach (Chadeau-Hyam et al. 2011)

Meet-in-the middle approach consists of measuring intermediate biomarkers (often with an agnostic omic investigation) and relating them

(a) Retrospectively to measurements of external exposure and
(b) Prospectively to a health outcome (disease, or ageing, or other outcomes).

If the same set of markers is robustly associated with both ends of the exposure-to-disease continuum, this is a validation of a causal hypothesis according to the pathway perturbation paradigm. See Vineis et al. 2020.

Oxidative stress and the cardiovascular effects of air pollution (Miller et al. 2020)
9. Improve the methodological aspects related to the synthesis of the scientific evidence and its overall evaluation

- **Causal relationship**: the consistency and coherence of evidence integrated across scientific disciplines and related health outcomes are sufficient to rule out chance, confounding, and other biases with reasonable confidence.

- **Likely to be a causal relationship**: there are studies where results are not explained by chance, confounding, or other biases, but uncertainties remain in the evidence overall. For example, the influence of other pollutants is difficult to address, or evidence among scientific disciplines may be limited or inconsistent.

- **Suggestive of, but not sufficient to infer, a causal relationship**: evidence is generally supportive but not entirely consistent or overall is limited. Chance, confounding, and other biases cannot be ruled out.

- **Inadequate to infer a causal relationship**: there is insufficient quantity, quality, consistency, or statistical power of results from studies.

- **Not likely to be a causal relationship**: several adequate studies, examining the full range of human exposure concentrations and potential at-risk populations and lifestages, consistently show no effect.

**Environmental health and clinical medicine are two different disciplines**

- **Clinical medicine**
- **Environmental health**
Tension between two approaches

Grades of Recommendation Assessment, Development and Evaluation

GRADE: an emerging consensus on rating quality of evidence and strength of recommendations

Guidelines are inconsistent in how they rate the quality of evidence and the strength of recommendations. This article explores the advantages of the GRADE system, which is increasingly being adopted by organisations worldwide.

www.gradeworkinggroup.org
2008 BMJ series
2011 JCE series

The most famous shape in football: the triangle
Use of two approaches: narrative and modified OHAT

Separate assessments for confidence in the quality of the body of evidence (modified OHAT) and in the presence of an association (narrative) (high, moderate, low, and very low)

For each exposure-outcome pair by study design

For each exposure-outcome pair

For each health outcome

Overall confidence
9. Improve methods in evidence synthesis

The assessment of the evidence should be based on Bradford Hill criteria:

1. Strength (effect size)
2. Consistency (reproducibility)
3. Temporality
4. Biological gradient (dose-response relationship)
5. Biological Plausibility
6. Coherence between epidemiological and laboratory findings

Triangulation is important and is very difficult in a GRADE-type framework
Some lessons learned regarding evidence synthesis of observational studies in environmental health

- To maximize what can be learned from observational studies in environmental health, a “narrative” approach is needed to complement the mechanistic up-and-downgrading of certain factors in evaluating the quality of a body of evidence.

- Observational studies can offer high confidence evidence in environmental health, where randomized controlled trials are generally not feasible.

- All relevant studies should be included in evidence synthesis, beyond the subset of evidence included in meta-analyses.

- Consistency of associations across study designs, populations, and exposure assessment methods provides additional confidence in the results.

- We call for identifying and quantifying possible key biases, their most likely direction, and their potential impacts on the results. (see Savitz, 2019 in Am J Epidemiol)
Conclusions: research opportunities

1. Improve exposure assessment to TRAP using novel methodologies
2. Additional epidemiological studies on an array of traffic pollutants including UFP and non-tailpipe PM indicators
3. Evaluate direct effects of NO$_2$, or to another component of TRAP, or to the broader mixture of correlated components indicative of TRAP
4. More health studies in areas outside North America and Europe
5. Conduct additional research on outcomes for which there are suggestions of an association with TRAP, but for which the evidence is still limited
6. Evaluate the role of spatially correlated factors that may either confound and/or modify the health effects of TRAP, most notably poverty, traffic noise, and factors related to the built environment, such as presence of green space.
7. Evaluate the fuller range of potential impacts of transportation and (new) mobility on public health
8. Evaluate the mechanisms behind the association of TRAP with the selected outcomes by studying biomarkers and subclinical outcomes (lung function, blood pressure, atherosclerosis, structure and function of the brain, ....)
9. Improve methods in systematic reviews and evidence synthesis
Thanks to the HEI Panel, Consultants, Contractors, external reviewers and HEI staff

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