Systematic review of selected health effects of long-term exposure to traffic-related air pollution

Hanna Boogaard, HEI

HEI Annual Conference, June 2022
The New HEI Traffic Review has been published!

Join the webinar for a deep(er) dive into the evidence regarding traffic-related air pollution and the selected health outcomes on July 13, from 11 AM to 1 PM EDT

https://www.healtheffects.org/meeting/new-hei-review-webinar-health-effects-traffic-related-air-pollution
A Panel was convened to review the traffic and health literature up to 2008.

Detailed chapters on emissions, exposure, toxicology and epidemiology.

At that time, evidence was considered sufficient to support a causal relationship between traffic-related air pollution and exacerbation of asthma in children. Suggestive and/or limited evidence for other health outcomes.

https://www.healtheffects.org/
New Review of the Traffic and Health Literature

Strong interest in an update of the review:

- Substantial new research published
- Regulations and vehicular technology have advanced
- Interest in non-tailpipe emissions and traffic noise is increasing

HEI appointed a new panel to systematically review epidemiologic studies in 2018.

The full chain of events linking TRAP to health effects. Source: Center for Advancing Research in Transportation Emissions, Energy and Health (CARTEEH), available from: https://www.carteeh.org/
HEI Panel on the Health Effects of Long-term Exposure to Traffic-Related Air Pollution

Co-chairs:
Francesco Forastiere, Imperial College London
Frederick Lurmann, Sonoma Technology

Members:
Richard Atkinson, University of London
Jeffrey Brook, University of Toronto; HEI Research Committee
Howard Chang, Emory University
Gerard Hoek, Utrecht University
Barbara Hoffmann, University of Düsseldorf; HEI Research Committee
Sharon Sagiv, University of California
Evi Samoli, University of Athens; HEI Research Committee
Audrey Smargiassi, University of Montreal
Adam Szpiro, University of Washington
Danielle Vienneau, Swiss Tropical and Public Health Institute
Jennifer Weuve, Boston University

Consultants to the Panel:
Julia Fussell, Imperial College London
Frank Kelly, Imperial College London
Tim Nawrot, University of Hasselt
Gregory Wellenius, Boston University; HEI Research Committee

Contractor: Meltem Kutlar Joss and Ron Kappeler, Swiss Tropical and Public Health Institute

HEI: Hanna Boogaard, Dan Crouse, Dan Greenbaum, Robert O’Keefe, Martha Ondras, Allison Patton, Ellen Mantus, Rashid Shaikh, Eleanne van Vliet, Annemoon van Erp
The Special Report was subjected to detailed Peer Review

**Chair:**
Bert Brunekreef, *Professor Emeritus, Utrecht University*

**Peer Reviewers Full Report:**
Haneen Khreis, *University of Cambridge*
Michael Jerrett, *University of California – LA; HEI Review Commitee*
Susan Norris, *Oregon Health & Science University*
Annette Peters, *Helmholtz Zentrum München*
Neil Pearce, *London School of Hygiene and Tropical Medicine; HEI Research Commitee*
Marie Pedersen, *University of Copenhagen*
David Savitz, *Brown University; Chair HEI Research Commitee*
Jay Turner, *Washington University in St. Louis*

**Peer reviewers Specific Chapters:**
Chad Bailey, *United States Environmental Protection Agency*
David Carslaw, *University of York*
Flemming Cassee, *National Institute for Public Health and the Environment, Netherlands*
David Foster, *University of Wisconsin–Madison*
Mark Frampton, *Professor Emeritus, University of Rochester Medical Center*
Monica Guxens, *Barcelona Institute for Global Health*
Michael Kleeman, *University of California–Davis*
Nick Molden, *Emissions Analytics, UK*
Marc Weisskopf, *Harvard T.H. Chan School of Public Health*

*And edited by HEI’s Publication Department*
A Systematic Review

✓ Use methods largely based on standards set by Cochrane Collaboration, World Health Organization, and the National Institute of Environmental Health Sciences

✓ Summarize epidemiological results quantitatively, where possible

✓ Include an evaluation of the risk of bias in individual studies

✓ Reach conclusions about the confidence in the quality of the body of evidence and with assessing the level of confidence in the presence of an association.

* https://www.healthyeffects.org/announcements/panel-publishes-protocol-review-traffic-related-air-pollution
** https://www.crd.york.ac.uk/PROSPERO/display_record.php?RecordID=150642

The review protocol was published in July 2019 on the HEI website* and registered with Prospero**
Important Methodological Features of the Traffic Review

Conducted largest effort of this type to date.

- Evaluates the epidemiologic literature only.
- Focuses on a selected set of health outcomes chosen *a priori*, including mortality, cardiovascular and respiratory morbidity and birth outcomes.

Applies a new exposure framework.

- Considers only long-term exposure to traffic-related air pollution.
- Considers exposure contrasts in near-roadway and neighborhood environments.

Assesses confidence in the evidence for an association.

- 2 complementary methods with ratings of very low, low, moderate, or high for traffic-related air pollution mixture, not individual pollutants.
Exposure Framework

Exposure assessment of TRAP is challenging because it is a complex mixture and is characterized by high spatial and temporal variability.

- Still no pollutant specific for traffic sources
- TRAP impacts at different scales

Three strategies were developed to select ‘traffic-related’ studies, namely the selection of traffic-related pollutants, the exposure assessment method and its spatial resolution.

Source: Fuzzi et al. 2015.

Source: Karner et al. 2010.
Confidence Assessments

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
Methods for Confidence in the Quality of the Body of Evidence (Modified OHAT* – or GRADE**-type approach)

<table>
<thead>
<tr>
<th>Initial Confidence by Key Features of Study Design</th>
<th>Factors Decreasing Confidence</th>
<th>Factors Increasing Confidence</th>
<th>Confidence in the Body of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>High (++++) 4 Features</td>
<td>Risk of Bias</td>
<td>Large Magnitude of Effect</td>
<td>High (++++)</td>
</tr>
<tr>
<td>Moderate (+++) 3 Features</td>
<td>Unexplained Inconsistency</td>
<td>Dose Response</td>
<td>Moderate (+++)</td>
</tr>
<tr>
<td>Low (+) 2 Features</td>
<td>Indirectness</td>
<td>Residual Confounding</td>
<td>Low (+)</td>
</tr>
<tr>
<td>Very Low (+) ≤1 Features</td>
<td>Imprecision</td>
<td>Consistency</td>
<td>Very Low (+)</td>
</tr>
<tr>
<td></td>
<td>Publication Bias</td>
<td>Other</td>
<td></td>
</tr>
</tbody>
</table>

- Risk of Bias
- Unexplained Inconsistency
- Indirectness
- Imprecision
- Publication Bias
- Large Magnitude of Effect
- Dose Response
- Residual Confounding
  - Studies report an effect and residual confounding is toward null
  - Studies report no effect and residual confounding is away from null
- Consistency
  - Across animal models or species
  - Across dissimilar populations
  - Across study design types
- Other
  - e.g., particularly rare outcomes

*Initial rating based on study design features

Upgrade or downgrade based on certain factors

The Panel did not apply the methods in a “mechanistic” way

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Addition of a Broader “Narrative” Approach to Maximize What can be Learned from Observational Studies

✓ GRADE-type assessments focus on the quality of the body of evidence rather than the presence of an association.
✓ Those assessments are heavily geared towards studies entering a meta-analysis.
✓ Hence, the Panel deemed it necessary to accompany the GRADE-type assessment with a broader “narrative” assessment.
Number of studies identified

Systematic review on the health effects of long-term exposure to traffic-related air pollution

# studies:

13,660

1,106

353

161

69

January 1980 - July 2019

Title/abstract screening

Key words in abstracts of peer-reviewed articles

Apply criteria for study design, exposure, and selected health outcomes

Studies included in review

Studies included in systematic review

Studies included in meta-analysis

Studies included in separate literature reviews
Literature Search Results

353 studies included

<table>
<thead>
<tr>
<th>Health outcome Category</th>
<th>Total number of studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth outcomes</td>
<td>86</td>
</tr>
<tr>
<td>Respiratory outcomes - children</td>
<td>118</td>
</tr>
<tr>
<td>Respiratory outcomes - adults</td>
<td>50</td>
</tr>
<tr>
<td>Cardiometabolic outcomes</td>
<td>57</td>
</tr>
<tr>
<td>Mortality</td>
<td>48</td>
</tr>
</tbody>
</table>
Geographical Location of the Studies

<table>
<thead>
<tr>
<th>Region</th>
<th>Total number of studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Europe</td>
<td>163</td>
</tr>
<tr>
<td>North America</td>
<td>130</td>
</tr>
<tr>
<td>Asia</td>
<td>41</td>
</tr>
<tr>
<td>Other regions</td>
<td>19</td>
</tr>
</tbody>
</table>
Number of Studies by Outcome and Pollutant
### Meta-analysis NO$_2$ – All cause mortality

<table>
<thead>
<tr>
<th>Study</th>
<th>Study Name</th>
<th>Relative Risk</th>
<th>RR</th>
<th>95% -CI</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beelen et al. 2008</td>
<td>NLCS-AIR</td>
<td>1.03</td>
<td>1.03 [1.00; 1.05]</td>
<td>9.8%</td>
<td></td>
</tr>
<tr>
<td>Carey et al. 2013</td>
<td>English National Cohort</td>
<td>1.02</td>
<td>1.02 [1.00; 1.04]</td>
<td>10.8%</td>
<td></td>
</tr>
<tr>
<td>Cesaroni et al. 2013</td>
<td>Rome Longitudinal</td>
<td>1.03</td>
<td>1.03 [1.02; 1.04]</td>
<td>12.2%</td>
<td></td>
</tr>
<tr>
<td>Yorifuji et al. 2013</td>
<td>Shizuoka Elderly</td>
<td>1.12</td>
<td>1.12 [1.07; 1.18]</td>
<td>6.1%</td>
<td></td>
</tr>
<tr>
<td>Beelen et al. 2014</td>
<td>ESCAPE</td>
<td>1.01</td>
<td>1.01 [0.99; 1.03]</td>
<td>10.6%</td>
<td></td>
</tr>
<tr>
<td>Crouse et al. 2015</td>
<td>1991 CanCHEC</td>
<td>1.05</td>
<td>1.05 [1.04; 1.07]</td>
<td>11.3%</td>
<td></td>
</tr>
<tr>
<td>Nieuwenhuijsen et al. 2018</td>
<td>Barcelona Mega Cohort</td>
<td>1.02</td>
<td>1.02 [1.00; 1.04]</td>
<td>10.6%</td>
<td></td>
</tr>
<tr>
<td>Yang et al. 2018</td>
<td>Hong Kong Elderly</td>
<td>1.00</td>
<td>1.00 [0.99; 1.01]</td>
<td>11.7%</td>
<td></td>
</tr>
<tr>
<td>Dirgawati et al. 2019</td>
<td>HIMS</td>
<td>1.06</td>
<td>1.06 [1.00; 1.13]</td>
<td>4.8%</td>
<td></td>
</tr>
<tr>
<td>Hanigan et al. 2019</td>
<td>45 and Up Study</td>
<td>1.06</td>
<td>1.06 [0.97; 1.16]</td>
<td>2.9%</td>
<td></td>
</tr>
<tr>
<td>Hvidfeldt et al. 2019</td>
<td>DDCH</td>
<td>1.07</td>
<td>1.07 [1.04; 1.10]</td>
<td>9.3%</td>
<td></td>
</tr>
</tbody>
</table>

Random effects model
- Prediction interval
- Heterogeneity: $I^2 = 83\%$, $\tau^2 = 0.0006$, $p < 0.01$
Meta-analysis of associations between traffic-related air pollutants and all-cause mortality

Effect estimates cannot be directly compared across the different traffic-related pollutants because the selected increments do not necessarily represent the same contrast in exposure. The individual pollutants are considered as indicators of the TRAP mixture.
The following increments were used: 10 µg/m³ for NO₂, 1 µg/m³ for EC, and 5 µg/m³ for PM₂.₅.

Meta-analysis of associations between traffic-related air pollutants and selected mortality outcomes*

<table>
<thead>
<tr>
<th>Pollutants</th>
<th>NO₂</th>
<th>EC</th>
<th>PM₂.₅</th>
</tr>
</thead>
</table>

The following increments were used: 10 µg/m³ for NO₂, 1 µg/m³ for EC, and 5 µg/m³ for PM₂.₅.

*Outcomes selected where the confidence in the evidence for an association with TRAP was judged high (all-cause, circulatory and ischemic HD; moderate to high (lung cancer), or moderate (respiratory).
**Birth outcomes**

<table>
<thead>
<tr>
<th>Pollutant</th>
<th>N</th>
<th>RR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Term low birth weight</td>
<td>12</td>
<td>1.01</td>
</tr>
<tr>
<td>5</td>
<td>1.01</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>1.11</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>1.02</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>1.09</td>
<td></td>
</tr>
</tbody>
</table>

**Respiratory outcomes**

<table>
<thead>
<tr>
<th>Pollutant</th>
<th>N</th>
<th>RR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asthma onset in children</td>
<td>12</td>
<td>1.05</td>
</tr>
<tr>
<td>5</td>
<td>1.11</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>1.09</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>1.30</td>
<td></td>
</tr>
<tr>
<td>21</td>
<td>1.09</td>
<td></td>
</tr>
<tr>
<td>Asthma ever in children</td>
<td>3</td>
<td>1.30</td>
</tr>
<tr>
<td>3</td>
<td>1.29</td>
<td></td>
</tr>
<tr>
<td>Active asthma in children</td>
<td>12</td>
<td>1.12</td>
</tr>
<tr>
<td>3</td>
<td>1.25</td>
<td></td>
</tr>
<tr>
<td>Asthma onset in adults</td>
<td>7</td>
<td>1.10</td>
</tr>
</tbody>
</table>

**Cardiometabolic outcomes**

<table>
<thead>
<tr>
<th>Pollutant</th>
<th>N</th>
<th>RR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ischemic heart disease events</td>
<td>5</td>
<td>0.99</td>
</tr>
<tr>
<td>5</td>
<td>1.01</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>1.09</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>1.04</td>
<td></td>
</tr>
<tr>
<td>Diabetes incidence</td>
<td>3</td>
<td>1.16</td>
</tr>
<tr>
<td>4</td>
<td>1.05</td>
<td></td>
</tr>
</tbody>
</table>

**Pollutants**
- **NO2**
- **EC**
- **PM2.5**

The following increments were used:
- 10 µg/m³ for NO₂
- 1 µg/m³ for EC
- 5 µg/m³ for PM₂.₅

RR = point estimate (significant in **bold**)

N = number of studies in meta-analysis

*Outcomes selected where the confidence in the evidence for an association with TRAP was judged moderate to high (asthma onset, acute lower respiratory infections), or moderate (remainder)

1.00 = no association
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

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

- This review has 3 times more studies than the 2010 report, though a direct comparison is difficult because of the difference in scope.

- Only half of the total number of identified studies entered a meta-analysis.

- The most common reason for a lower confidence judgement was “imprecision”, most often for cardiometabolic outcomes.

- The most common reason for a higher confidence judgement was evidence for a “monotonic exposure-response relationship”.

- Most of the studies were rated as low to moderate “risk of bias” for all but the “confounder” domain, for which about one third of the meta-analyzed studies were rated as high “risk of bias”.

- Several future research opportunities emerged from this report.
Several Future Research Opportunities

- Evaluate the mechanisms behind the association of TRAP with the selected outcomes by studying biomarkers and subclinical outcomes (e.g., lung function, blood pressure, atherosclerosis, structure and function of the brain,...)

- Evaluate the role of spatially correlated factors that may either confound and/or modify the health effects of TRAP, most notably socioeconomic status, traffic noise, and factors related to the built environment, such as presence of green space

- Evaluate the fuller range of potential impacts of transportation and (new) mobility on public health.

- Improve methods in systematic reviews and evidence synthesis of observational studies in environmental health

And many more...
Overall Conclusions

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 findings indicate that traffic-related air pollution remain an important public health concern and deserve greater attention from the public and from policymakers.