Environment International 164 (2022) 107262

Contents lists available at ScienceDirect

Environment International

journal homepage: www.elsevier.com/locate/envint

Short communication

Long-term exposure to traffic-related air pollution and selected health outcomes: A systematic review and meta-analysis

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ARTICLE INFO

Handling Editor: Zorana Andersen

Keywords:
Traffic-related air pollution
Birth outcomes
Respiratory outcomes
Cardiometabolic outcomes
Mortality
Systematic review

ABSTRACT

The health effects of traffic-related air pollution (TRAP) continue to be of important public health interest. Following its well-cited 2010 critical review, the Health Effects Institute (HEI) appointed a new expert Panel to systematically evaluate the epidemiological evidence regarding the associations between long-term exposure to TRAP and selected adverse health outcomes. Health outcomes were selected based on evidence of causality for general air pollution (broader than TRAP) cited in authoritative reviews, relevance for public health and policy, and resources available.

The Panel used a systematic approach to search the literature, select studies for inclusion in the review, assess study quality, summarize results, and reach conclusions about the confidence in the evidence. An extensive search was conducted of literature published between January 1980 and July 2019 on selected health outcomes. A new exposure framework was developed to determine whether a study was sufficiently specific to TRAP.

In total, 353 studies were included in the review. Respiratory effects in children (118 studies) and birth outcomes (86 studies) were the most commonly studied outcomes. Fewer studies investigated cardiometabolic effects (57 studies), respiratory effects in adults (50 studies), and mortality (48 studies).

The findings from the systematic review, meta-analyses, and evaluation of the quality of the studies and potential biases provided an overall high or moderate-to-high level of confidence in an association between long-term exposure to TRAP and the adverse health outcomes all-cause, circulatory, ischemic heart disease and lung cancer mortality, asthma onset in children and adults, and acute lower respiratory infections in children. The evidence was considered moderate, low or very low for the other selected outcomes.

In light of the large number of people exposed to TRAP – both in and beyond the near-road environment - the Panel concluded that the overall high or moderate-to-high confidence in the evidence for an association between long-term exposure to TRAP and several adverse health outcomes indicates that exposures to TRAP remain an important public health concern and deserve greater attention from the public and from policymakers.

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https://doi.org/10.1016/j.envint.2022.107262
Received 17 January 2022; Received in revised form 8 April 2022; Accepted 20 April 2022
Available online 25 April 2022
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1. Introduction

Motor vehicles are a significant source of urban air pollution and are important contributors of anthropogenic carbon dioxide and other greenhouse gases. Traffic-related air pollution (TRAP) is a complex mixture of gases and particles resulting from the use of motor vehicles. Motor vehicles emit a variety of pollutants including nitrogen dioxide (NO_2), elemental carbon (EC), ultrafine particles (UFP) and fine particle matter ($PM_{2.5}$). These pollutants can be emitted directly through the vehicle exhaust as tailpipe emissions. They can also be emitted from non-exhaust sources such as evaporative emissions of fuel, the resuspension of dust, the wear of brakes and tires, and the abrasion of road surfaces, which are collectively referred to as non-tailpipe emissions (Harrison et al., 2021; HEI, 2010).

Tailpipe emissions from motor vehicles and ambient concentrations of most monitored traffic-related pollutants have decreased steadily over the last several decades in most high-income countries. This trend is a result of air quality regulations and improvements in vehicular emission control technologies and is likely to continue (Frey, 2018). These positive developments, however, have not been able to compensate fully for the rapid growth and increased vehicular congestion of the motor vehicle fleet due to population growth, urbanization, and economic activity, in addition to the continued presence of older or malfunctioning vehicles on the roads. The introduction of new technologies such as electric vehicles, promises alleviation of some components of TRAP. Adoption has been constrained so far, however, due to the pace and cost of developing battery technology and infrastructure, electricity decarbonization, and fleet turn-over (Khreis et al., 2020). For the foreseeable future, a substantial number of people globally will continue to be exposed to tailpipe and non-tailpipe TRAP, especially in urban settings and locations in proximity to busy roadways, where detectable increases extend to about 500 m.

In 2010, HEI published Special Report 17, *Traffic–Related Air Pollution: A Critical Review of the Literature on Emissions, Exposure, and Health Effects*. This 2010 review, developed by the HEI Panel on the Health Effects of Traffic–Related Air Pollution summarized and synthesized research on emissions, exposure, and health effects from TRAP and drew conclusions about whether the associations between exposure and health outcomes were causal. The 2010 Panel reviewed both toxicological and epidemiological evidence. At that time, the Panel concluded that the evidence was sufficient to support a causal relationship between short and long-term exposure to TRAP and exacerbation of asthma in children. The Panel found suggestive evidence of a causal relationship between exposure to TRAP and other outcomes, including all-cause and cardiovascular mortality, and limited evidence of associations for some other outcomes, such as birth outcomes (HEI, 2010).

Since the 2010 HEI review, regulations and vehicular technology have advanced significantly, exposure assessment has been enhanced, and many additional studies investigating the health effects of exposure to TRAP have been published. Therefore, HEI formed a new Panel, consisting of 13 experts in epidemiology, exposure assessment, and statistics at institutions in North America and Europe, to conduct a new review. This review is the largest systematic effort to date to evaluate the epidemiological evidence regarding the associations between long-term exposure to TRAP and selected adverse health outcomes. The report will be published later this year (HEI, 2022). Here, we summarize the main findings of the review.

2. Objective

The objective of this review was to systematically evaluate the epidemiological evidence regarding the associations between long-term exposure to ambient TRAP and selected adverse health outcomes. Results were quantitatively combined to evaluate the strength of the evidence, where appropriate. The Panel was charged with drawing 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.

3. General methods

The Panel used a systematic approach to search the literature, select studies for inclusion in the review, assess study quality, summarize results, and reach conclusions about the confidence in the body of evidence, based largely on standards set by Cochrane, World Health Organization, and the National Institute of Environmental Health Sciences. To this end, a review protocol was published in 2019 (HEI, 2019) and registered in Prospero.

Health outcomes were selected by the Panel based on evidence of causality (causal or likely causal) according to the latest determination for *general* air pollution (broader than TRAP) from available authoritative integrated science assessments (e.g., Health Canada, 2016; IARC, 2016; U.S. EPA, 2016, 2019), and other considerations such as relevance for public health and policy, and resources available. The selected health outcomes were clinical outcomes (rather than preclinical) and included birth outcomes (e.g., term low birth weight: <2,500 g for infants born at term > 37 weeks of gestation), respiratory outcomes (e.g., asthma onset), cardiometabolic outcomes (e.g., ischemic heart disease and diabetes) and all-cause and cause-specific (e.g., circulatory, respiratory) mortality. The Panel acknowledged the limitations in the selection of health outcomes.

A PECOS (Population, Exposure, Comparator, Outcome and Study) question was developed and inclusion and exclusion criteria were listed for each PECOS domain in relation to the selected health effects of long–term exposure to TRAP (months to years). The focus of the review was on health effects observed in the general population. Cohort, case-control, cross-sectional, and intervention studies using individual-level data were included.

An extensive search was conducted of literature published between January 1980 and July 2019. Studies were checked for eligibility for inclusion by two reviewers. Data from all included studies were extracted and evaluated extensively, including key information for meta-analysis. Effect estimates from single pollutant models were selected for the meta-analysis. Results from multi-pollutant models were de-emphasized as we were not interested in the associations of single pollutants *independent* of other pollutants. Instead, we considered the associations of single pollutants to represent the associations of the TRAP mixture. We performed random-effects meta-analysis when at least three estimates were available for a specific exposure-outcome pair. The Panel decided to use the pollutant concentration increments from the ESCAPE study to reflect a realistic range of exposure contrasts in most studies (Beelen et al., 2014, 2015). The following increments were used: 10 $\mu g/m^3$ for NO_2, 1 $\mu g/m^3$ for EC, and 5 $\mu g/m^3$ for $PM_{2.5}$. The increments used are in the same range as other reviews (e.g., Chen and Hoek, 2020; Huangfu and Atkinson, 2021; Khreis et al., 2017).

We assessed risk of bias for all exposure-outcome associations that were included in the meta–analyses, using a modified version of the tool developed for the risk of bias assessment in the WHO Air Quality Guidelines review (WHO, 2020, 2021).

Where possible, the Panel performed additional analyses to assess consistency of the association, for example, across geographic region, within time period, by level of risk of bias, and with more extensive adjustment for individual-level lifestyle factors (i.e., smoking). An adapted GRADE (Grading of Recommendations Assessment, Development and Evaluation) assessment of the confidence in the quality of the body of evidence was made using the Office of Health Assessment and Translation (OHAT) method as a guide (OHAT, 2019). Because the OHAT assessment was heavily geared towards the studies entering a meta-analysis, and it focused on the quality of the body of evidence and less on the presence of an association, the Panel deemed it necessary to accompany the OHAT assessment with a broader approach. Hence, we developed a narrative assessment to evaluate the level of confidence in

the presence of an association, considering the meta-analyzed studies as well as all other studies not included in the meta-analysis. Subsequently, we combined the findings from the narrative assessment and the modified OHAT assessment into an overall confidence assessment, with the two approaches considered complementary.

4. Exposure assessment framework

Assessing exposure to TRAP is challenging because TRAP is a complex mixture of particulate matter and gaseous pollutants and exhibits high spatial and temporal variability. The Panel developed a new exposure framework to define, as transparently as possible, exposure characterization approach(es) most likely to specifically assess TRAP as opposed to air pollution exposure more generally. Studies meeting the framework's criteria were considered TRAP-specific and thus eligible for inclusion in the current review. The exposure assessment framework included three strategies to determine whether a study was sufficiently TRAP-specific, namely the selection of traffic-related air pollutants, the exposure assessment method, and the spatial resolution. None of the pollutants considered are uniquely traffic-specific and therefore these additional criteria were needed.

Broadly, emissions from motorized traffic may affect air quality at the local, neighborhood, urban and regional scale. The Panel judged, however, that epidemiological studies that focused on exposure contrasts at the local and neighborhood scale offered the greatest potential in determining associations with outcomes that are most confidently derived from TRAP emissions.

In brief, the Panel included studies that evaluated exposure to NO_2, EC (including related metrics such as black carbon, black smoke and PM absorbance), carbon monoxide (CO), UFP, and other pollutants and indirect traffic measures (distance and density), as well as $PM_{2.5}$ and PM_{10} (particles smaller than 2.5 and 10 μm, respectively). For studies that evaluated exposure to $PM_{2.5}$ and PM_{10}, but not to other pollutants, even more stringent requirements for inclusion were needed regarding exposure assessment and study setting to indicate that the exposure contrasts were likely due to variation in traffic emissions. For example, the Panel excluded PM studies where the exposure assessment was solely derived from monitoring data. The Panel also excluded nationwide studies on any pollutant where the primary exposure contrast was due to between-cities variations, rather than within-cities.

5. Main findings of the systematic review

In total, 353 studies were included in this review. Respiratory effects in children (118 studies, 33%) and birth outcomes (86 studies, 24%) were the most common outcomes studied. Fewer studies investigated cardiometabolic effects (57 studies, 16%), respiratory effects in adults (50 studies, 14%), and mortality (48 studies, 13%). The studies were conducted in populations residing in a wide range of countries, though the majority were done in Europe (163 studies, 46%), and North America (130 studies, 37%). Studies in Asia (predominantly China) emerged more recently (41 studies, 12%). More TRAP studies in low- and middle-income countries are needed. Most meta-analyses by outcome pertained to NO_2, followed by EC and $PM_{2.5}$. Few studies were identified for some pollutants, in particular non-tailpipe PM indicators and UFP, and such studies were identified as a future research need.

The results of the meta-analyses of associations between long-term exposure to the most commonly studied TRAP exposure indicators (NO_2, EC and $PM_{2.5}$) and selected health outcomes are displayed in Table 1. We use the term relative risk to describe effect estimates, as it is easier to communicate, even if in some of the included studies it would be technically more correct to refer to an odds ratio, or hazard ratio.

Following are important considerations while reviewing the results: 1) Although the results are presented by pollutant, the individual pollutants are considered indicators of the TRAP mixture. 2) Effect estimates cannot be compared directly across traffic-related pollutants since selected increments do not necessarily represent the same contrast in exposure. 3) Studies included in a meta-analysis represent only about half of all studies considered, such as when multiple studies conducted in the same population, <3 studies were available for a particular exposure-outcome pair, or definitions of indirect traffic measures varied across studies. Thus, the Panel did not pursue meta-analyses of indirect traffic measures. Despite not being included in the meta-analyses, the remaining studies added important information to the overall assessment.

For each health outcome, Fig. 1 and Table 1 also provide the overall level of confidence in an association with long-term exposure to TRAP, based on a combination of the narrative assessment and the modified OHAT assessment (see above). Detailed descriptions of the overall confidence assessment are listed in Table 2. Below, we describe the main findings for each broad health outcome category.

5.1. Birth outcomes

The summary estimates showed that $PM_{2.5}$ exposure over the entire pregnancy is most clearly associated with measures of fetal growth restriction. The summary relative risk was 1.11 (95% CI: 1.03; 1.20) for term low birth weight and 1.09 (1.04; 1.14) for small for gestational age (birth weight below the 10th percentile for a gestational age and sex according to national growth curves, for example), and a mean difference in term birth weight of −17.3 (–33.2; −1.5) grams per 5 μg/m^3. The $PM_{2.5}$ associations are supported by consistent associations with PM_{10} as well. Associations for preterm birth were largely null, though a few studies of traffic-PM and indirect traffic measures (distance and density measures) supported an association. Associations for the other meta-analyzed traffic-related air pollutants, including NO_2, NO_X, and EC, with all four birth outcomes were mostly null, with the exception of an association of NO_X with term low birth weight. Studies that were not included in the meta-analyses broadly agreed with the summary estimates for the various pollutants.

The majority of studies of TRAP and birth outcomes were conducted in North America and Europe. Most used a cohort study design and registry data and therefore lacked potentially important confounder information on lifestyle factors, such as maternal smoking during pregnancy and pre-pregnancy body mass index. As a result, those studies were rated high risk of bias for potential confounding, which reduced confidence in the body of evidence, particularly for term birth weight and preterm birth (births < 37 weeks of gestation).

The Panel concluded that there was an overall moderate level of confidence in the evidence for an association between exposure to TRAP and term low birth weight (categorical outcome) and small for gestational age, and low confidence for term birth weight (continuous outcome) and preterm birth.

5.2. Respiratory outcomes

The summary estimates for NO_2 per 10 μg/m^3 were 1.05 (95% CI: 0.99; 1.12) for asthma onset in children and 1.10 (95% CI:1.01; 1.21) for asthma onset in adults, and 1.09 (95% CI: 1.03; 1.16) for acute lower respiratory infections in children. For these outcomes, positive associations were also reported for other traffic-related air pollutants, either in meta-analyses or in single large studies. Most were cohort studies that were conducted in different populations and had low or moderate risk of bias.

The Panel concluded that the overall level of confidence in the evidence for an association of exposure to TRAP with asthma onset in both children and adults and with acute lower respiratory infections in children was considered moderate-to-high. Studies examining exposure to NO_2 made the greatest contribution to this evaluation. The overall level of confidence in the evidence was moderate for prevalence of asthma ever and active asthma in children. Asthma ever refers to lifetime asthma prevalence and active asthma refers to prevalence of asthma in

Table 1
Overall confidence assessment and meta-analytical summary estimates of associations between long-term exposure to the most common traffic-related air pollutants (NO_2, EC, $PM_{2.5}$) and health outcomes. (NOTE: the individual pollutants are considered indicators of TRAP).

Health outcome				NO_2 per 10 μg/m^3		EC per 1 μg/m^3		$PM_{2.5}$ per 5 μg/m^3	
			Overall confidence assessment	N	Relative risk	N	Relative risk	N	Relative risk
Birth outcomes		Term low birth weight	Moderate	12	1.01 (0.99;1.03)	5	1.01 (0.99;1.04)	7	1.11 (1.03;1.20)
		Term birth weight	Low	8	−3.2 (−11.0;4.6)[3]	4	−2.6 (-6.1;0.9)[3]	6	−17.3 (–33.2;-1.5)[3]
		Small for gestational age	Moderate	11	1.00 (0.98;1.02)	3	1.02 (0.92;1.14)	4	1.09 (1.04;1.14)
		Preterm birth	Low	14	1.00 (0.96;1.04)	5	1.02 (0.97;1.07)	4	0.99 (0.90;1.09)
Respiratory outcomes	Children	Asthma onset[1]	Moderate-to- high	12	1.05 (0.99;1.12)	5	1.11 (0.94;1.31)	5	1.33 (0.90;1.98)
		Asthma ever[2]	Moderate	21	1.09 (1.01;1.18)	3	1.30 (0.56;3.04)	3	1.29 (0.58;2.87)
		Active asthma[2]	Moderate	12	1.12 (1.02;1.23)	3	1.25 (0.98;1.59)	<3	NA
		Acute lower respiratory infections[1]	Moderate-to-high	11	1.09 (1.03;1.16)	4	1.30 (0.78;2.18)	<3	NA
	Adults	Asthma onset[1]	Moderate-to- high	7	1.10 (1.01;1.21)	<3	NA	<3	NA
		Acute lower respiratory infections[1]	Very low-to-low	3	1.07 (0.71; 1.61)	<3	NA	<3	NA
		Chronic obstructive pulmonary disease[1]	Low	7	1.03 (0.94;1.13)	<3	NA	4	0.91 (0.62;1.36)
Cardiometabolic outcomes		Ischemic heart disease events[1]	Moderate	5	0.99 (0.94;1.05)	5	1.01 (0.99;1.03)	4	1.09 (0.86;1.39)
		Coronary events[1]	Low	7	1.03 (0.95;1.11)	<3	NA	<3	NA
		Stroke events[1]	Low-to-moderate	7	0.98 (0.92;1.05)	6	1.03 (0.98;1.09)	4	1.08 (0.89;1.32)
		Diabetes[1]	Moderate	7	1.04 (0.96;1.13)	3	1.16 (0.57;2.36)	4	1.05 (0.96;1.15)
		Diabetes[2]		7	1.09 (1.02;1.17)	<3	NA	3	1.08 (0.70;1.67)
Mortality		All–cause	High	11	1.04 (1.01;1.06)	11	1.02 (1.00;1.04)	12	1.03 (1.01;1.05)
		Circulatory	High	10	1.04 (1.00;1.09)	9	1.02 (1.00;1.04)	11	1.04 (1.01;1.08)
		Respiratory	Moderate	8	1.05 (1.00;1.09)	8	1.01 (0.98;1.05)	7	1.03 (0.97;1.10)
		Lung cancer	Moderate-to-high	5	1.04 (1.01;1.07)	3	1.02 (0.88;1.19)	6	1.06 (0.99;1.13)
		Ischemic heart disease	High	6	1.05 (1.03;1.08)	6	1.05 (0.99;1.11)	7	1.07 (1.04;1.10)
		Stroke	Low-to- moderate	6	1.01 (0.98;1.04)	<3	NA	3	1.04 (1.01;1.07)
		Chronic obstructive pulmonary disease	Low	3	1.03 (1.00;1.05)	<3	NA	<3	NA

[1] Incidence.
[2] Prevalence.
[3] Mean difference in g. NA = not applicable.

the last 12 months. For most of the other respiratory outcomes investigated, including incidence of chronic obstructive pulmonary disease, acute lower respiratory infections in adults, wheeze outcomes as well as exacerbation of asthma and chronic obstructive pulmonary disease in diseased adults, the confidence was very low or low for an association with TRAP, hampered in part by the small number of qualifying studies.

5.3. Cardiometabolic outcomes

The summary estimates were consistent with an association of PM_{10} with ischemic heart disease: 1.14 (95% CI: 0.99; 1.31) per 10 μg/m^3, with evidence suggesting a monotonic exposure–response function. Evidence was suggestive for EC and $PM_{2.5}$, but was less consistent overall. Associations were reported between NO_2 and diabetes prevalence with a summary estimate of 1.09 (95% CI: 1.02; 1.17) per 10 μg/m^3, supported by consistent but imprecise estimates for the other pollutants. The summary estimates of EC, PM_{10} and $PM_{2.5}$ with stroke incidence were slightly less precise, but the evidence was strengthened by several high-quality studies with a monotonic exposure–response function. Studies that were not included in meta-analyses provided additional support for an association between TRAP and ischemic heart disease, diabetes and stroke. In contrast, for coronary events, the number of studies was smaller and insufficient for meta-analyses, except for NO_2, which yielded a positive, though imprecise association.

Because cardiometabolic outcomes are likely influenced by traffic noise, some studies investigated possible confounding or effect modification by noise with mostly similar results after adjustment for co-exposure to noise.

The Panel had overall moderate confidence in the evidence for an association between long-term exposure to TRAP and ischemic heart disease, and diabetes, low-to-moderate confidence in the evidence for an association of TRAP with stroke, and low confidence in the evidence for an association of TRAP with coronary events.

5.4. Mortality

The summary estimates showed that NO_2, EC, and $PM_{2.5}$ were associated with all-cause, circulatory, ischemic heart disease, respiratory and lung cancer mortality, with relative risks ranging from 1.01 to 1.07 (Table 1). Associations of those pollutants with stroke and COPD mortality were less certain because fewer studies were available for consideration. The studies on pollutants not included in the meta-analyses and the studies with indirect traffic measures supported those associations. All studies on mortality had cohort designs, with outcome during follow-up determined by linkage with mortality registries. Most studies were conducted in North America and Europe; some were set in Asia. The majority of studies accounted for a large number of individual and area-level covariates, including smoking, body mass index and individual and area-level socio-economic status, and were judged at a low or moderate risk for bias.

The overall confidence in the evidence for an association between TRAP exposure and mortality was high for all-cause, circulatory, and IHD mortality. The Panel's overall confidence was moderate-to-high for lung cancer, moderate for respiratory, low-to-moderate for stroke, and low for COPD mortality.

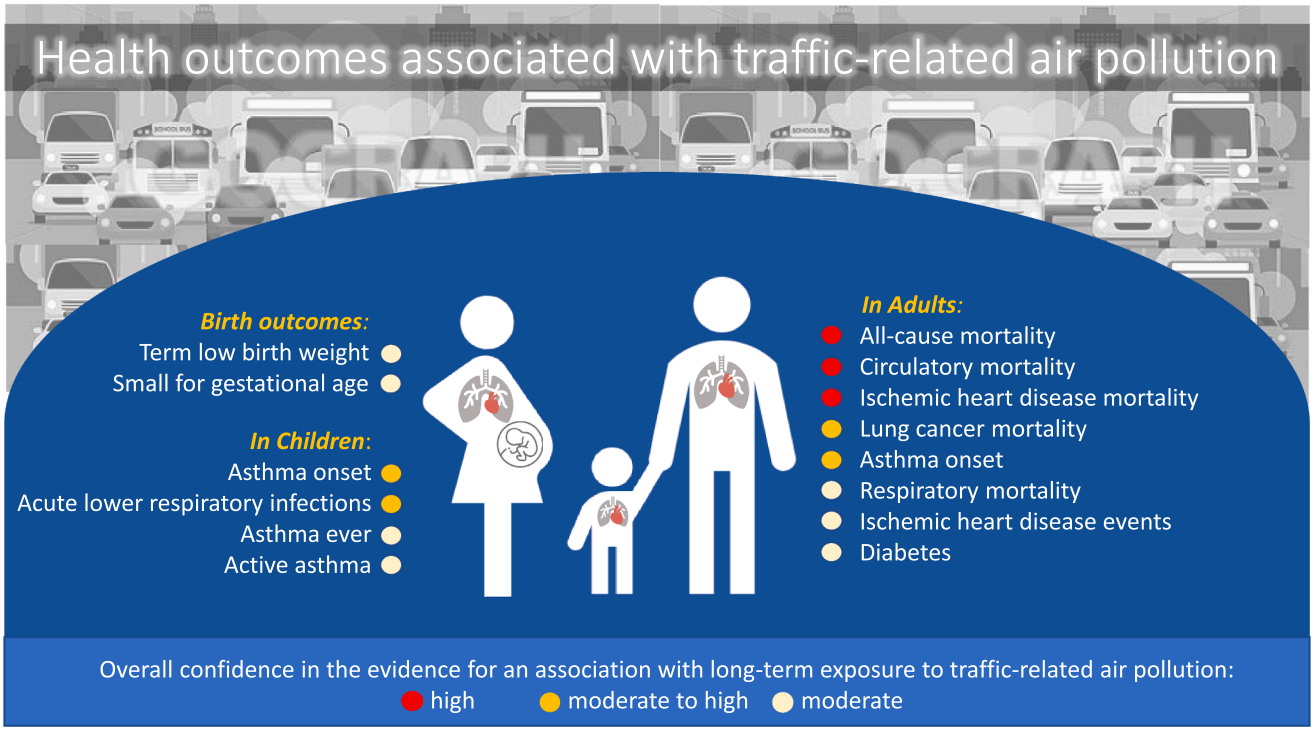


Fig. 1. Overall confidence in the evidence for an association between long-term exposure to ambient TRAP and selected health outcomes. Footnote: health outcomes for which the overall confidence in the evidence was low-to-moderate, low or very low are not in Fig. 1.

Table 2
Overall confidence assessment – Descriptions of the level of confidence in the evidence for an association.[1]

High	Evidence is sufficient to conclude that the strength of the evidence for an association is high, that is, the exposure has been shown to be associated with health effects in studies in which chance, confounding, and other biases could be ruled out with reasonable confidence. The determination is based on multiple high-quality studies conducted in different populations and geographical areas with consistent results for multiple exposure indicators. High confidence in the association between exposure and the outcome.
Moderate	Evidence is sufficient to conclude that an association is likely to exist, that is, the exposure has been shown to be associated with health effects in studies where results are not explained by chance, confounding, and other biases, but uncertainties remain in the evidence overall. The determination is based on some high-quality studies in different populations and geographical areas, but the results are not entirely consistent across areas and for multiple exposure indicators. Moderate confidence in the association between exposure and the outcome.
Low	Evidence is suggestive but limited, and chance, confounding, and other biases cannot be ruled out. Generally, the body of evidence is relatively small, with few high-quality studies available and at least one high-quality epidemiologic study shows an association with a given health outcome and/or when the body of evidence is relatively large but the evidence from studies of varying quality and across multiple exposure indicators is generally supportive but not entirely consistent. Low confidence in the association between exposure and the outcome.
Very low	Evidence is inadequate to determine if an association exists with the relevant exposures. The available studies are of insufficient quantity, quality, consistency, or statistical power to permit a conclusion regarding the presence or absence of an association. Very low confidence in the association between exposure and the outcome.

[1] The overall confidence assessment of the association of each health outcome with long-term exposure to TRAP is a combination of the narrative assessment and the modified OHAT assessment. The descriptors are modified from U.S. EPA (2015) and OHAT (2019).

6. Overall conclusions

The findings from the systematic review, meta-analyses, and evaluation of the quality of the studies and potential biases provided an overall high or moderate-to-high level of confidence in an association between long-term exposure to TRAP and the adverse health outcomes all-cause, circulatory, ischemic heart disease and 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. The findings add to the growing evidence base of a range of other health outcomes associated with long-term exposure to TRAP.

Tailpipe emissions from motor vehicles and ambient concentrations of most monitored traffic-related pollutants have decreased steadily over the last several decades in most high-income countries. The Panel's main findings were derived from studies conducted when exposure levels were generally higher than present-day levels in high-income countries, and comparable to or lower than present-day levels in low-income countries.

In light of the large number of people exposed to TRAP – both in and beyond the near-road environment - the Panel concluded that the overall high or moderate-to-high confidence in the evidence for an association between long-term exposure to TRAP and several adverse health outcomes indicates that exposures to TRAP remain an important public

health concern and deserve greater attention from the public and from policymakers.

Credit authorship contribution statement

H. Boogaard: Conceptualization, Methodology, Writing, Supervision. **A.P. Patton:** Methodology, Writing. **R.W. Atkinson:** Conceptualization, Methodology, Formal analysis, Writing. **J.R. Brook:** Conceptualization, Methodology, Writing. **H.H. Chang:** Conceptualization, Methodology, Writing. **D.L. Crouse:** Writing. **J.C. Fussell:** Writing. **G. Hoek:** Conceptualization, Methodology, Writing. **B. Hoffmann:** Conceptualization, Methodology, Writing. **R. Kappeler:** Investigation. **M. Kutlar Joss:** Investigation. **M. Ondras:** Visualization, Writing. **S.K. Sagiv:** Conceptualization, Methodology, Writing. **E. Samoli:** Conceptualization, Methodology, Formal analysis, Writing. **R. Shaikh:** Writing. **A. Smargiassi:** Conceptualization, Methodology, Writing. **A.A. Szpiro:** Conceptualization, Methodology, Writing. **E.D.S. Van Vliet:** Writing. **D. Vienneau:** Conceptualization, Methodology, Writing. **J. Weuve:** Conceptualization, Methodology, Writing. **F.W. Lurmann:** Conceptualization, Methodology, Writing. **F. Forastiere:** Conceptualization, Methodology, Writing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

HEI is indebted to the Panel, the consultants to the Panel, external peer reviewers and contract team for its expertise, cooperation, and enthusiasm. We would specifically thank Frank Kelly, Tim Nawrot, and Greg Wellenius as consultants to the Panel, and Eva Tanner for help with the outside peer review process. In addition, we would like to thank Bert Brunekreef, Dan Greenbaum, Robert O'Keefe and Annemoon Van Erp for valuable guidance. In addition, we would like to thank Alan da Silveira Fleck, Pascale Haddad, Leonie Hoffmann, Lara Stucki, Margaux Sadoine, Zoe Roth, and Elina Wüthrich for their help with data extraction.

Research described in this article was conducted under contract to the HEI, an organization jointly funded by the United States Environmental Protection Agency (EPA) (Assistance Award No. CR-83998101) and certain motor vehicle and engine manufacturers. The views expressed in this article are those of the authors and do not necessarily reflect the views of the Health Effects Institute or its sponsors.

References

Beelen, R., Hoek, G., Raaschou-Nielsen, O., Stafoggia, M., Andersen, Z.J., Weinmayr, G., et al., 2015. Natural-cause mortality and long-term exposure to particle components: an analysis of 19 European cohorts within the multi-center ESCAPE project. Environ. Health Perspect., https://doi.org/10.1289/ehp.1408095.

Beelen, R., Raaschou-Nielsen, O., Stafoggia, M., Andersen, Z.J., Weinmayr, G., Hoffmann, B., et al., 2014. Effects of long-term exposure to air pollution on natural-cause mortality: an analysis of 22 European cohorts within the multicentre ESCAPE project. Lancet. https://doi.org/10.1016/S0140-6736(13)62158-3.

Chen, J., Hoek, G., 2020. Long-term exposure to PM and all-cause and cause-specific mortality: A systematic review and meta-analysis. Environ. Int. https://doi.org/10.1016/j.envint.2020.105974.

Frey, H.C., 2018. Trends in onroad transportation energy and emissions. J. Air Waste Manag. Assoc. https://doi.org/10.1080/10962247.2018.1454357.

Harrison, R.M., Allan, J., Carruthers, D., Heal, M.R., Lewis, A.C., Marner, B., et al., Non-exhaust vehicle emissions of particulate matter and VOC from road traffic: A review. Atmos Environ; https://doi.org/10.1016/j.atmosenv.2021.118592.

HEI (Health Effects Institute), 2010. Traffic-Related Air Pollution: A Critical Review of the Literature on Emissions, Exposure, and Health Effects. Special Report 17. Boston, MA, US: Health Effects Institute.

HEI (Health Effects Institute), 2019. Protocol for a Systematic Review and Meta-Analysis of Selected Health Effects of Long-Term Exposure to Traffic-Related Air Pollution. Boston, MA. Available: *https://www.healtheffects.org/system/files/TrafficReviewProtocol.pdf*.

HEI (Health Effects Institute), 2022. Systematic Review and Meta-Analysis of Selected Health Effects of Long-Term Exposure to Traffic-Related Air Pollution. Special Report 23. Boston, MA, US: Health Effects Institute. (in press).

Health Canada, 2016. Human Health Risk Assessment for Diesel Exhaust. Health Canada, Ottawa, ON.

Huangfu, P., Atkinson, R., 2020. Long-term exposure to NO_2 and O_3 and all-cause and respiratory mortality: A systematic review and meta-analysis. Environ. Int. https://doi.org/10.1016/j.envint.2020.105998.

IARC (International Agency for Research on Cancer, World Health Organization), 2016. Outdoor Air Pollution. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. Vol. 109. Lyon, FR: IARC.

Khreis, H., Kelly, C., Tate, J., Parslow, R., Lucas, K., Nieuwenhuijsen, M., 2017. Exposure to traffic-related air pollution and risk of development of childhood asthma: A systematic review and meta-analysis. Environ. Int. https://doi.org/10.1016/j.envint.2016.11.012.

Khreis, H., Nieuwenhuijsen, M., Zietsman, J., Ramani, T., eds. 2020. Traffic-Related Air Pollution. 1st ed. Waltham, MA: Elsevier.

OHAT (Office of Health Assessment and Translation, National Toxicology Program, National Institute of Environmental Health Sciences, U.S. Dept. of Health and Human Services), 2019. Handbook for Conducting a Literature-Based Health Assessment Using OHAT Approach for Systematic Review and Evidence Integration. Available: *https://ntp.niehs.nih.gov/ntp/ohat/pubs/handbookmarch2019_508.pdf*.

U.S. EPA (U.S. Environmental Protection Agency), 2015. Preamble to the integrated science assessments. EPA/600/R-15/067. Research Triangle Park, NC.

U.S. EPA (U.S. Environmental Protection Agency), 2016. Integrated Science Assessment for Oxides of Nitrogen–Health Criteria. EPA/600/R-15/068. Washington, DC: U.S. EPA.

U.S. EPA (U.S. Environmental Protection Agency), 2019. Integrated Science Assessment for Particulate Matter (Final Report December 2019). EPA/600/R-19/188. Washington, DC; U.S. EPA.

WHO (World Health Organization), 2020. Risk of bias assessment instrument for systematic reviews informing WHO global air quality guidelines. Available: *https://www.euro.who.int/en/health-topics/environment-and-health/air-quality/publications/2020/risk-of-bias-assessment-instrument-for-systematic-reviews-informing-who-global-air-quality-guidelines-2020*.

WHO (World Health Organization), 2021. WHO Global Air Quality Guidelines: Particulate Matter ($PM_{2.5}$ and PM_{10}), Ozone, Nitrogen Dioxide, Sulfur Dioxide and Carbon Monoxide. World Health Organization. Available: *https://apps.who.int/iris/handle/10665/345329*.