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The comet assay as a tool in human biomonitoring exposure to combustion-derived air pollution – A systematic review and meta-analysis

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ABSTRACT

Humans are exposed to environmental or occupational air pollution from combustion emissions in outdoor and indoor environments. Irrespective of the sources, combustion emissions are characterized by being a complex mixture of particles, volatile compounds and gases. The present systematic review summarizes results on DNA strand breaks measured by the comet assay in leukocytes, from studies on human exposure to traffic-related vehicle exhaust, biomass combustion and coke oven work environments. These exposures have in common the combustion of fuel, which generates particles and polycyclic aromatic hydrocarbons. Standardized mean differences (SMDs) have been calculated by random effects models. Meta-analyses show increased levels of DNA strand breaks in studies on traffic-related exhausts (SMD = 0.62, 95 % CI: 0.36, 0.89, n = 21), biomass combustion (1.73, 95 % CI: 0.72, 2.74, n = 10) and coke oven emission (0.84, 95 % CI: 0.30, 1.37, n = 10). Studies from high-income countries have reported much smaller differences in DNA strand break levels than have studies from middle-income countries. These differences may be attributed to higher exposures related to less strict emission control, and more susceptible populations in middle-income populations; unrecognized confounding despite efforts to match subjects on traditional confounders; or higher risk of comet assay measurement bias and exposure misclassification. In conclusion, this systematic review and meta-analysis show that exposure to combustion-derived air pollution, with clear exposure gradients in terms of particulate matter or polycyclic aromatic hydrocarbons, is associated with increased levels of DNA strand breaks in human leukocytes.

1. Introduction

The comet assay has been used extensively to assess DNA-damaging effects of environmental and occupational exposures in humans, using mainly white blood cells (whole blood) or subsets thereof, such as peripheral blood mononuclear cells (sometimes just called lymphocytes) [1]. The standard comet assay measures DNA strand breaks and alkali-labile sites; for simplicity, these lesions are typically called DNA strand breaks [2]. The first study on relationships between air pollution exposure and DNA strand breaks, measured by the comet assay, was

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published in 1996 [3]. In this study, DNA strand breaks were assessed from blood samples of female postal workers in two different districts of Bohemia, Czechia. Studies on children in different parts of Mexico City also belong to the group of investigations where the comet assay was used as a new and promising test for genotoxicity in human cells [4]. Subsequently, a relatively large number of studies have been published on various types of air pollution sources from different locations in the world. The majority of studies entail combustion emissions in environmental and occupational settings [1,5]. Based on the latest WHO air quality guidelines, more than 90 % of the urban population is exposed to air pollution higher than recommended [6], which then increases risks for heart diseases, stroke, chronic obstructive pulmonary disease, and lung cancer, and leads to an estimated 8.3 million deaths annually [7,8].

Air pollution is a complex mixture of gases, volatile organic compounds (VOCs), and particulate matter (PM). Measurements of polycyclic aromatic hydrocarbons (PAHs) and benzo[*a*]pyrene (B[*a*]P) in air or PM are reliable markers of inhalation exposure to combustion-derived air pollutants. PM is measured as mass concentration (i.e. μg/m^3) of particles in specific size fractions, including particles with less than 2.5 μm in aerodynamic diameter ($PM_{2.5}$). Many studies report particle exposure as $PM_{2.5}$ or PM_{10} mass concentration, which might be due to their use in monitoring air pollution levels. Alternatively, it is possible to measure the particle number concentration (PNC, unit: particles/cm^3). The PNC is considered to represent ultrafine particles (UFPs) with diameters less than 0.1 μm, although the equipment used for these measurements typically detects slightly larger particles too. Combustion processes generate a high number of UFPs. Measurements of UFPs have been introduced at a later stage in monitoring air pollution, and relatively few biomonitoring studies on comet assay results have used this type of information to assess exposure. Nevertheless, measurements of UFPs are highly relevant in toxicology because they can deposit deep in the airways, and small particles are considered more hazardous than larger particles [9].

This review aims to assess the association between exposure to combustion-derived air pollution and DNA strand breaks in human biomonitoring studies. It is a continuation of a previous scoping review on environmental and occupational exposure, including air pollution [1]. The objective of the scoping review was to collect studies on air pollution exposures, knowing very well that the studies were heterogeneous with respect to sources of pollutants. Unlike the scoping review, the present systematic review uses meta-analyses, with the purpose of incorporating comparable studies in the same statistical analysis. To this end, we have selected studies on traffic-related combustion sources, biomass combustion, and coke oven emissions.

2. Methods

The review is segregated into meta-analyses of specific combustion particle emissions. A detailed description of the stepwise review process is available in the supplement. Briefly, associations between air pollution exposure and DNA strand breaks are assessed in (i) the full dataset of included papers (using statistical significance in the original paper as outcome), (ii) meta-analysis of results from papers with information on mean/median and corresponding variability results, (iii) generalizability of the meta-analysis findings to all studies on the same type of air pollutants, (iv) subgroup analysis, and (v) sensitivity analysis. The systematic review protocol has been registered in PROSPERO (CRD42025647927).

2.1. Literature search

The literature search follows the strategy laid out in our previous scoping review [1]. However, the literature search in the scoping review revealed limitations when combining diversity (i.e. many different types of combustion emissions and exposure situations) and specificity (i.e. only human biomonitoring studies). There tend to be too few search results if “biomonitoring” is a specific term and too many results if “human” is not included in the search string. Therefore, we have used relatively broad search terms and screened studies for relevance, using the title (1st step) and abstract (2nd step). Based on the identified papers in the scoping review [1], we extended the search terms to include biomass and coke oven emissions. The search string was as follows: (Human OR Human Biomonitoring OR monitoring) AND comet assay AND (air pollution OR diesel exhaust OR dust OR ozone OR particulate matter OR ultrafine particles OR hydrocarbon OR wood smoke OR biomass OR coke oven). Fig. 1 shows a flow diagram of the search, screening and selection of papers for the review and meta-analysis. Certain studies have been included based on knowledge of the relevance from previous reviews [10,11], or they were found in reference lists of identified studies. The literature search was conducted in January 2025, encompassing the period from January 1st 2000 to December 31st 2024.

2.2. Inclusion criteria (in the review)

We have only included studies on inhalation exposures to combustion-derived air pollution. In addition, only results on DNA strand breaks in white blood cells are included. This encompasses studies that have described results on whole blood, white blood cells, leukocytes, peripheral blood mononuclear cells, lymphocytes and polymorphonuclear granulocytes.

In general, studies have been considered to be excluded from the review if they (i) were written in non-English language, (ii) were suspected to have selection bias due to comparison of dissimilar study populations in the exposure and control groups, (iii) had inadequate information on population characteristics such as age, sex, smoking and location of living, (iv) were influenced by effects of confounders such as age, sex and smoking, (v) had no exposure gradient, (vi) had much larger exposure gradient of co-exposures [e.g. an issue in occupational exposure studies where the work category may entail complex exposures such as welders], (vii) were double publication of results, (viii) lacked information on the cell type used for the comet assay, or (ix) had results that do not follow the state-of-the-art for studies on the comet assay [e.g. studies that have not reported the pH of electrophoresis solution or used neutral pH solution; studies where all scored comets have been used in statistical analysis; or studies where the distribution of comet descriptors such as χ^2 degrees of freedom has been used rather than the mean/SD or median/IQR]. Excluded studies are summarized in Supplementary Tables S1-S3.

We have not applied specific inclusion or exclusion criteria for measurements of combustion-derived air pollution. This is due to the complexity and diversity of air pollution exposures and the heterogeneous ways used to assess levels of specific air pollutants. In addition, measurements of certain air pollutants have evolved over the period, such as equipment for the measurement of particle number concentration. We have included studies with study designs that generate an exposure gradient (i.e. studies with controls and presumably exposed subjects), irrespective of how elaborate the exposure assessment has been. In general, the certainty of exposure has been grouped into studies with (i) little information, (ii) moderate information based on air measurements, and (iii) sufficient information based on biomarkers of exposure or controlled exposure study design. For verification of combustion sources, we have considered measurements of particles (PM or UFPs) as indicators of combustion sources of exposure. Other indicators of combustion processes include PAHs, B[*a*]P or PAH-metabolites (e.g. 1-hydroxypyrene (1-OHP) in urine). Nitrogen oxides (NO and NO_2) in the air are also considered to originate from combustion sources. Measurements of PAHs, B[*a*]P and 1-OHP in biological material are not specific indicators of inhalation exposure to combustion emissions as they can derive from the diet (e.g. smoked or barbecued food). Certain studies have been included - even though they have not assessed exposure to particles or PAHs - because subjects have been recruited from

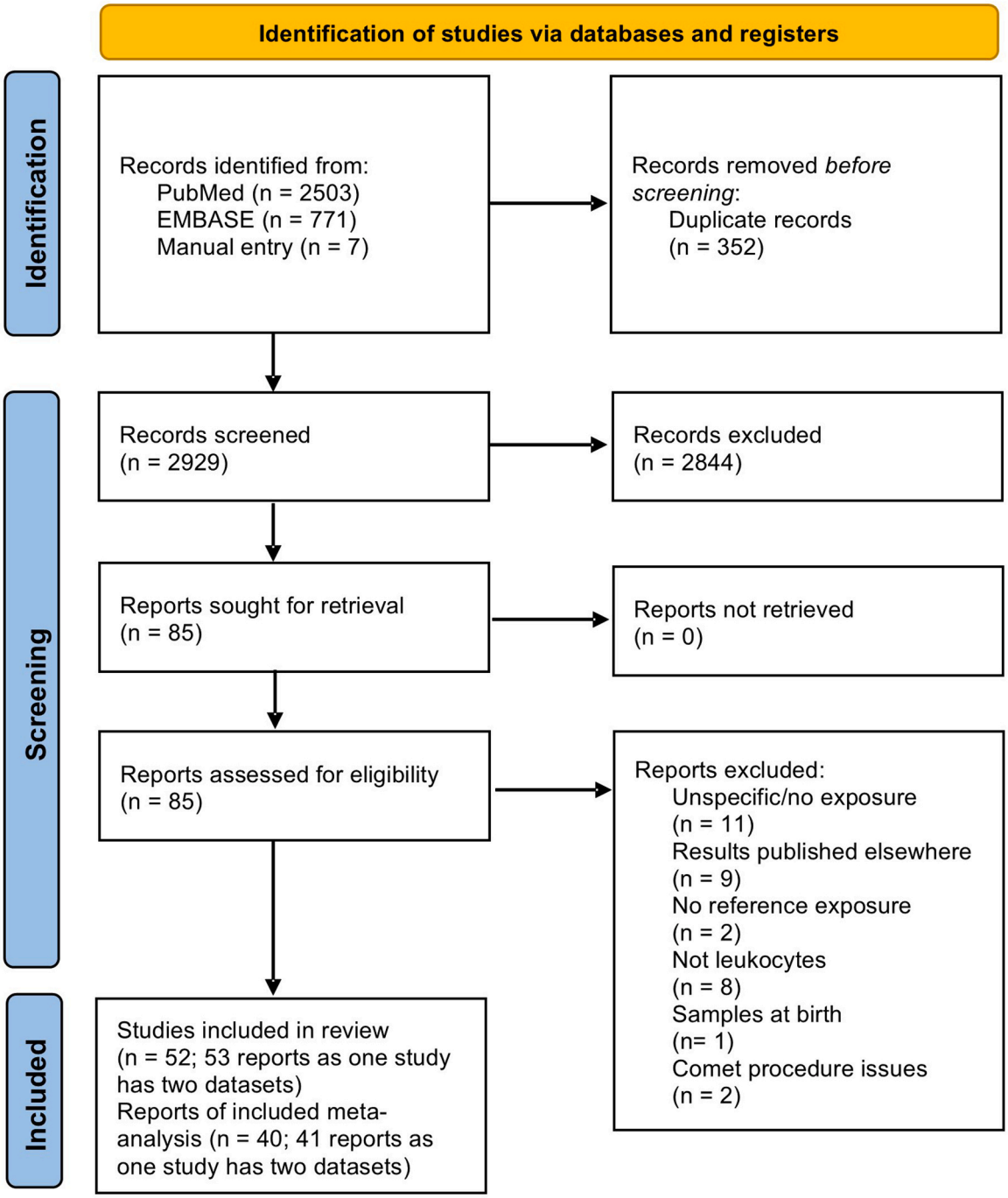

Fig. 1. Flow chart of search and inclusion of studies.

populations that are known to be exposed to particle-rich vehicle exhaust (e.g. taxi drivers). Ozone is a relevant air pollutant, but not a specific indicator of combustion-related air pollution, because it is generated by solar radiation and partially removed through reactions with NO from combustion processes. Some studies have assessed benzene as an air pollutant. However, benzene is not sufficiently specific for combustion processes to be used as a stand-alone indicator of engine exhaust emissions.

According to these considerations, studies on traffic-related combustion sources encompass subjects exposed to (i) diesel engine exhaust, (ii) air near traffic-intense streets, and (iii) urban air (assuming living in urban *vs* rural areas provides a difference in traffic vehicle exhaust in subjects who are matched for relevant confounders). A few studies are clearly related to combustion sources, but there is only one of each kind, which precludes a meta-analysis. Examples include jet fuel combustion emission [12] and candlelight combustion particles [13].

2.3. *Generalizability*

Certain studies have sufficient relevance to be included in the review, although the results are not applicable in the meta-analysis. This includes studies designed for correlation or regression analysis. In addition, results reported as geometric mean and standard deviation factor cannot be incorporated into a meta-analysis with results reported as mean and standard deviation from a Gaussian distribution of results. The same goes for binary data or results analysed by logistic regression.

Thus, the results in the meta-analyses of the present review are a subgroup of all included studies. The generalizability of the results in the meta-analyses to all studies in the review has been assessed by a Z-test for comparing two proportions, with correction for continuity (test results are reported as Z-value and corresponding P-value level).

2.4. Meta-analysis

Some studies have compared levels of DNA strand breaks in exposed subjects to a control group, whereas other studies have more than two exposure groups. For the latter studies, we have defined controls as the group of subjects with the lowest exposure. We have dichotomized exposures in studies where the subjects have been segregated into more than two groups. This encompasses studies that have included multiple samples from different locations or different seasons.

All studies with mean and standard deviation (or standard error of the mean) and median and inter-quartile range have been included in the meta-analysis. The median and inter-quartile range (i.e. the difference between 25 % and 75 % percentile) have been included in the meta-analysis as a proxy of mean and standard deviation [14]. Studies using other central tendencies and variability are not included in the meta-analysis.

For the meta-analysis, we have used standardized mean difference (SMD) as an effect measure because the studies have used different comet descriptors (i.e. tail length, tail intensity (i.e. percentage of total DNA fluorescence in the tail), tail moment and visual score). Values of the same comet descriptor in different studies do not correspond to the same number of DNA strand breaks because studies use different comet assay procedures. SMD is the difference between groups in standard deviation units. For instance, SMD = 1 means that the difference between two groups is the same as the pooled standard deviation. The 95 % confidence interval (95 % CI) of SMD is not statistically significant if it includes zero. For graphical purposes, we have reproduced Forest plots in GraphPad Prism from Review Manager. Original Forest plots and accompanying Funnel plots from the Review Manager are reported as Supplementary Figures S1-S6.

We have calculated SMD and 95 % CI in random effects models using Review Manager 5.4 (The Nordic Cochrane Centre, The Cochrane Collaboration). The random effects model assumes that the induction of DNA damage can vary across studies because of real differences in the treatment effect and sampling variability. I^2 values are used as a measure of heterogeneity between studies. The I^2 value describes the percentage of the variability in an effect estimate that is due to heterogeneity rather than sampling error (chance). Formally, it is calculated as [(Q-df)/Q] *100 %, where Q is the Chi-squared statistic, and df is its degrees of freedom. The Cochrane Handbook uses these descriptions of I^2 values: 0–40 % "might not be important", 30–60 % "may represent moderate heterogeneity", 50–90 % "may represent substantial heterogeneity", and 75–100 % "considerable heterogeneity" (https://training.cochrane.org/handbook).

We have used Egger's test to test Funnel plot asymmetry; statistical significance at $p < 0.05$ level is an indicator of publication bias. Statistical tests have been done in Stata 15 (StataCorp LCC, College Station, TX, USA) because the Eggers's test is not included in the RevMan program. We have used *esize(cohensd)* and *meta bias, egger* commands. The individual study SMDs are the same in RevMan and Cohen's d test [*esize (cohensd)*] in Stata. The two programs generate slightly different overall effect size and measures of inter-study heterogeneity. However, the differences are too small to affect the interpretation of results.

Heterogeneity between studies may arise from differences in biological effects due to factors such as age, sex and exposure situation. Some differences, such as those between occupational and environmental exposure studies, may be relatively straightforward to explain. Heterogeneity might also be related to differences between workplaces in their ability to implement and enforce protection procedures to minimize exposure of workers to hazardous compounds. It is virtually impossible to assess the magnitude of exposure between studies, except maybe by comparing $PM_{2.5}$ concentrations in air samples. In addition, heterogeneity in effect sizes might be dependent on procedures to control random variation that occurs in biological techniques such as the comet assay. This applies to both blinded scoring of samples and inclusion of samples with contrasting exposures in the same comet assay experiment (i.e. analysis of matched pairs of pre- and post-samples or exposed/controls from the same comet assay experiment).

The meta-analyses in this review have a high degree of heterogeneity ($I^2 > 75$ %). Visual inspection of Forest plots does not reveal a strongly skewed distribution of SMDs to the right (i.e. the central tendency being influenced by studies with high effect size). It suggests that the dataset is not strongly affected by small studies with high effect (which would indicate possible publication bias). Nevertheless, the SMD is calculated by parametric test, assuming a normal distribution of individual SMDs from each study. In order to assess the robustness of the meta-analysis, we have also used non-parametric analysis to calculate the overall central tendency. For this analysis, we have used the SMDs from each study for the calculation of the median and 95 % CI. The 95 % CI has been calculated by the equation as follows: rank number = n*q ± z* [SQRT(n*q*(1-q)], where n = sample size, q = median (0.5), z = critical value (1.96 for $p < 0.05$). The rank number has been rounded down and up to the nearest whole number for the lower and upper 95 % CI, respectively. These ranks have subsequently been converted to absolute values. We refer to this calculation of effect size as SMD_{median} to distinguish it from the regular SMD.

2.5. Subgroup analyses

The studies have been segregated into populations from high-income and middle-income countries. We have determined the origin of the study population from information on the location of the study population; it is not based on the country of the first author or the laboratory/country where the comet assay has been done. We have used the World Bank classification for the segregation of populations into high-income and middle-income countries (https://data.worldbank.org/, downloaded March 2025). The World Bank uses the Gross National Income per capita for its classification of income groups. Some high-income countries have been upgraded from the middle-income group in the period 2000–2025. In these cases, we have used the highest possible rank because these countries have most likely made progress to become a high-income country prior to the upgrade. The World Bank ranking has been used as a proxy-measure of countries regulation of environmental and occupational exposures (including economic means to uphold control over emissions) and research (including equipment and organisation of scientific work). High-income countries represented in the present dataset are Bulgaria, Czechia, Denmark, Germany, Greece, Italy, the Netherlands, Poland, Portugal, Slovak Republic, Sweden and South Korea. Countries in the group of middle-income economics are Benin, Brazil, China, Colombia, Iran, India, Mexico, Pakistan and Thailand. Countries in the lower-middle and upper-middle categories have been pooled into one group.

2.6. Sensitivity analyses

Uncertainty (potential bias) related to comet assay experiments and exposure assessment has been assessed on a scale with low, moderate or high risk of bias/exposure misclassification. The classification system is described in detail in the supplementary material. The description of comet assay procedures has been rated according to the recommended Minimum Information for Reporting on the Comet Assay (MIRCA) [15], the inclusion of assay controls and coded/blinded analysis of samples or slides. We refer to this as a marker of risk of comet assay measurement bias.

The studies on combustion emissions can be grouped into controlled exposure studies and cross-sectional (or field) studies. By analogy with

epidemiological study designs, controlled exposure studies are experimental, whereas cross-sectional studies have observational study designs. There is a low risk of exposure misclassification in controlled exposure studies because the researchers allocate subjects to groups with contrasting levels of exposure. In contrast, the risk of exposure misclassification in cross-sectional studies is more complex, encompassing the categorization of subjects into exposure groups, measurements of air pollution compounds and/or biomarkers of exposure. We have used measurements as follows to assess the certainty of inhalation exposure to air pollution in cross-sectional studies:

(i) Grouping based on work categories or areas.

(ii) Environmental monitoring assessment, including PM mass concentration, PNC (for UFPs) and concentration of PAHs (e.g. extracted from respirable particles). Other air pollution constituents have been used as indicators of combustion emissions from vehicles, although they may not have DNA-damaging properties (e.g. NOx). Certain constituents are not considered to be sufficiently specific, including ozone (generated by solar radiation), and benzene (industry emissions).

(iii) Biomarkers of exposure *and* environmental monitoring assessment: Alternatively, biomarkers of exposure *and* exclusion of confounding factors (e.g. diet). It should be noted that biomarkers of internal/effective doses of combustion-derived air pollutants are not specific for inhalation exposure because a significant contribution comes from dietary sources such as smoked food items. Biomarkers of internal/effective dose cannot be used alone to confirm inhalation exposure with certainty.

For visual presentation, we have used traffic light plots where red, yellow and green colours refer to studies with high, moderate and low risk of bias/exposure misclassification. The traffic light plots have been generated in robvis (https://mcguinlu.shinyapps.io/robvis/) [7]. Difference in distributions has been tested by the χ^2-test.

3. Results

The literature search identified 52 studies, of which 40 are included in meta-analyses. The studies are grouped into traffic-related air pollution (Table 1), biomass fuel smoke (Table 2), and coke oven emission (Table 3). Table 4 summarises effect sizes in each exposure group and subgroup analyses. Table 5 shows results from sensitivity analyses related to risk of comet assay measurement bias and exposure misclassification.

3.1. Traffic-related combustion

Table 1 summarizes the results from the studies included in the review. The meta-analysis includes 21 studies [16–36]. Additionally, six studies have been included in the review [37–42].

The included studies on traffic-related emission can be grouped into four different types of study depending on the source of exposure (i.e. diesel engine exhaust or road traffic emission), and study design (i.e. controlled exposure or cross-sectional studies). In controlled exposure studies, the same subjects are exposed to different types of air in either a chamber or a setting in the field where the exposure can be controlled. In cross-sectional studies, by contrast, exposure gradients are obtained by comparing different groups of exposed subjects.

(i) Controlled exposure studies on diesel engine exhaust emissions. A chamber study showed unaltered levels of DNA strand breaks after 3 h exposure to diesel engine exhaust from fossil fuel compared to clean air (PM_1: 276 vs 2 μg/m^3) [28]. The same research group also found unaltered levels of DNA strand breaks at 3 and 24 h after 3 h exposure to exhaust from biofuel combustion (i.e. hydrogenated vegetable oil; $PM_{2.5}$: 93 vs 1 μg/m^3) [34]. However, a third controlled exposure study showed an increased level of DNA strand breaks after exposure to diesel engine exhaust in a passenger compartment of a diesel-powered train for three consecutive days as compared to the same exposure time in an electric train (PNC: 133,400 vs 9100 particles/cm^3) [16].

(ii) Cross-sectional studies on diesel exhaust emissions. The first study on diesel engine exhaust found higher levels of urinary 1-OHP excretion and DNA strand breaks in automobile emission inspectors from South Korea [32]. A study from China showed that diesel engine testing workers, who were exposed to diesel engine exhaust (assessed by air concentrations of $PM_{2.5}$ and elemental carbon as well as urinary excretion of PAH metabolites), had higher levels of DNA strand breaks than water pump operators ($PM_{2.5}$: 288 vs 92 μg/m^3) [35]. Another study by the same research group in China showed an increased level of DNA strand breaks from subjects in a diesel engine testing department. The subjects in the exposure group worked in areas with high air concentration of $PM_{2.5}$ and had higher levels of 1-OHP and PAH-metabolites in urine as compared to a control group (i.e. water pump operators) [25]. These two Chinese studies have similar levels of $PM_{2.5}$ air concentrations, subject characteristics and DNA strand break levels, but it is not the exact same number of subjects in the two publications (see supplemental material for further details on the similarities of the two studies). A fourth study showed an increased level of DNA strand breaks in mechanics as compared to a reference group from "Departamento del Atlantico" [30]. The exposed group had relatively high exposure levels in the workplace ($PM_{2.5}$ = 250 μg/m^3). However, there was no personal exposure assessment of the workers, and the levels of exposure in the control group are not reported. Lastly, one study on workers in bakeries has shown an increased level of DNA strand breaks among subjects who use diesel-powered ovens as compared to a control group, consisting of university staff employees [29]. As the study does not have PAH exposure measurement, confounding cannot be ruled out due to co-exposures and non-comparable populations (i.e. bakers and university staff).

One cross-sectional study on diesel engine exhaust has been included in the review, although excluded from the meta-analysis. This study assessed diesel engine exhaust exposure in underground mine workers compared to surface workers. The underground workers had higher exposure to PAHs (1-nitropyrene in respirable particles) and benzene, but there was no difference in levels of DNA strand breaks [39].

(iii) Controlled exposure studies on traffic-related emissions. Three studies have been conducted in Copenhagen (Denmark). The first study showed no effect on DNA strand breaks when subjects were exposed to traffic-related emissions (bicycling on busy streets: 32,400 particles/cm^3, measured by person-borne samplers) as compared to a reference period (bicycling in a laboratory: 13,400 particles/cm^3) [36]. The bicycle route was designed to pass two curb side busy street stationary monitoring stations that measured UFPs (30,400 ± 13,800 particles/cm^3) and PM_{10} (23.5 ± 14.8 μg/m^3). A later study used a chamber to expose subjects to air from a busy street for 24 h. The study showed increased levels of DNA strand breaks when subjects were exposed to non-filtered air from traffic-related emissions (10,067 particles/cm^3) as compared to particle-filtered air (235 particles/cm^3) [20]. Interestingly, the same study also showed a correlation between a 57 nm size mode of PNCs that represent carbonaceous soot from diesel engines and DNA strand breaks, whereas other size modes did not correlate with DNA strand breaks [20]. Lastly, a chamber study did not find differences in DNA strand break levels after exposure to non-filtered air ($PM_{2.5}$ = 24 μg/m^3 and 23,000 particles/cm^3) compared to particle-filtered air ($PM_{2.5}$ = 3 μg/m^3 and 1800 particles/cm^3) from a traffic-intense street [27].

One study, using personal PM exposure, has been included in the review, but excluded from the meta-analysis. The study assessed DNA strand break levels in subjects from Copenhagen four times over one year to obtain differences in exposure within the same subject. There was no association between personal $PM_{2.5}$ exposure and DNA strand breaks [40]. There was a significant effect of the season, with the lowest level of DNA strand breaks in the winter as compared to the summer. However, this association was attributed to a seasonal effect as demonstrated by a correlation between ambient temperature and DNA strand break levels. A similar effect of the season has been observed in Denmark, although it has been attributed to solar radiation in other

Table 1
Summary of findings from the included studies on traffic-related air pollution.

Author	Year	Main Chemical Exposure	Country	Exposure Assessment or Biomarkers of Exposure	Population Characteristics	DNA Damage	Reference
Andersen	2019	Diesel engine exhaust (PAH)	Denmark	**PNC**: 133,400 vs 9100 (NanoTracer), 189,200 vs. 8100 (DiscMini) Air (black carbon, NOx) and urine (1-OHP, 2-OHF, 1-NAPH, and 2-NAPH).	83 healthy volunteers (54 exposed to diesel, 29 exposed in electric train)	• **VS:** exposed/diesel train (0.18 ± 0.13) vs. control/electric train (0.12 ± 0.13); **sig.** (Mean and SD). Results reported as lesions/10^6 bp	[16]
Avogbe[1]	2005	Outdoor air (UFP, benzene)	Benin	**PNC**: 265,145 (busy street), 19,580 (suburban), 6961 (rural) (stationary measurement) Urine (S-PMA)	135 city traffic exposure (29 drivers, 37 roadside residents, 42 suburban, 27 rural)	• **TI**: drivers (6.09 ± 3.46) vs. roadside residents (6.32 ± 4.00) vs. suburban (5.42 ± 2.28) vs. rural (4.26 ± 1.76); **sig.** (Mean and SD)	[17]
Bagryantsava[2]	2010	Outdoor air (PAH, VOC)	Czechia	Air (PAH abstracted from filters, personal samplers)	120 (50 bus drivers, 20 garagemen, 50 controls)	• **TI:** bus drivers (1.60 ± 0.90), garagemen (2.42 ± 2.19), controls (1.31 ± 0.88); **sig.** (Mean and SD)	[18]
Barth	2016	Outdoor air (PAH)	Brazil	Urine (1-OHP)	82 (45 taxi drivers, 37 controls)	• **TI:** exposed (11.58 ± 0.35) vs. controls (8.28 ± 0.21); **sig.** (Mean and SEM) • **TM:** exposed (2.64 ± 0.17) vs. controls (1.83 ± 0.20); **sig.** (Mean and SEM) • ***Combined:*** *exposed (1.42 ± 0.45) vs. controls (1 ± 0.41)*	[19]
Brauner	2007	Outdoor air (chamber study)	Denmark	**PNC**: 10,067 vs 235 particles/cm^3 Air (NOx, CO, O_3)	29 (before and after 24 h exposure period)	• **VS**: exposed/non-filtered air (0.24, 0.14–0.35) vs. controls/particle-filtered air (0.16, 0.09–0.25). **Sig**. (Median and 25th–75th percentile). Results reported as lesions/10^6 bp	[20]
Carere	2002	Outdoor air (benzene)	Italy	Air (benzene, personal samplers)	190 (133 traffic policemen, 57 office workers as controls)	• **TM:** exposed (0.46 ± 0.46), controls (0.36 ± 0.32); **non-sig.** (Mean and SD)	[21]
Cebulska-Wasilewska[3]	2005	Outdoor air (PAH)	Czechia	Air (PAH abstracted from filters, personal samplers)	78 (40 policemen, 38 controls)	• **TI:** exposed (winter: 2.72 ± 1.70, summer: 2.91 ± 1.05) vs. controls (winter: 2.64 ± 1.37, summer: 2.62 ± 1.04); **non-sig.** (Mean and SD)	[22]
Cebulska-Wasilewska	2007	Outdoor air (PAH)	Slovak Republic and Bulgaria	Air (PAH abstracted from $PM_{2.5}$ filters, personal samplers)	174 policemen (99 exposed, 75 controls)	• **TI:** controls (4.06 ± 1.40), exposed (3.86 ± 1.28); **non-sig.** (Mean and SD)	[23]
Cetkovic	2023	Outdoor air ($PM_{2.5}$)	Bosnia and Herzegovina	**$PM_{2.5}$**: 46 μg/m^3 (winter) vs 20 μg/m^3 (summer)	33 volunteers (summer and winter sampling)	• **TL:** winter (2.20 ± 0.14); summer (2.25 ± 0.17); **Sig** (Mean and SD, positive correlation with $PM_{2.5}$ in winter samples) • **TI:** winter (1.14 ± 0.23); summer (1.19 ± 0.19); **non-sig.** (Mean and SD) • **TM:** winter (1.03 ± 0.29); summer (1.07 ± 0.25); **non-sig.** (Mean and SD)	[37]
Chu[4]	2015	Outdoor air ($PM_{2.5}$)	China	**$PM_{2.5}$**: 68 (Zhuhai), 115 (Wuhan), and 147 μg/m^3 (Tianjin) (personal exposure)	301 (108 from Zhuhai, 114 from Wuhan, 79 from Tianjin)	• **TI**: Tianjin (2.97, 1.47–6.32), Wuhan 2.15 (0.77, 4.63), Zhuhai 1.36 (0.67, 2.66); **sig.** (Median and 25th–75th percentile)	[24]
Duan	2016	Diesel engine exhaust	China	**$PM_{2.5}$**: 288 vs 92 μg/m^3 (stationary measurement) Air (elemental carbon, NO_2, SO_2, and airborne PAHs) and urine (1-OHP)	207 (101 exposed workers and 106 controls)	• **TI:** exposed (60.02 ± 28.59) vs. controls (18.75 ± 28.29); **sig.** (Mean and SD) • **TM:** exposed (4.68 ± 2.55) vs. exposed (1.06 ± 2.33); **sig.** (Mean and SD) • ***Combined:*** *exposed (3.81 ± 1.97) vs. controls (1 ± 1.85)*	[25]
Geric	2024	Outdoor air	Croatia	**$PM_{2.5}$**: 24 μg/m^3, range: 3–73 μg/m^3, 24 h before sampling) Air (PM_{10}, gases)	123 (students)	• **TL:** 14.32 ± 1.40; **non-sig** (Mean and SD, correlation analysis) • **TI:** 1.62 ± 0.86; **non-sig** (Mean and SD, correlation analysis) • **TM:** 0.21 ± 0.12; **non-sig** (Mean and SD, correlation analysis)	[38]
Göethel[5]	2014	Outdoor air (benzene and CO)	Brazil	Urine (t,t-muconic acid)	99 (43 gas station staff, 34 drivers, 22 unexposed)	• **VS:** gas station staff (89.8 ± 21.5), drivers (94.2 ± 12.8),	[26]

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Table 1 (*continued*)

Author	Year	Main Chemical Exposure	Country	Exposure Assessment or Biomarkers of Exposure	Population Characteristics	DNA Damage	Reference
						unexposed (48.6 ± 35.9); **sig.** (Mean and SD)	
Hemmingsen	2015	Diesel engine exhaust	Sweden	**PM_1**: 276 vs 2 μg/m^3 **PNC**: 390,000 particles/cm^3 (during exposure)	18 individuals with controlled exposure (3 h)	• **VS:** exposed (after: 0.30 ± 0.04, before: 0.32 ± 0.04) vs. control/ after (after: 0.24 ± 0.06, before: 0.30 ± 0.07); **non-sig.** (Mean and SEM)	[28]
Hemmingsen	2015	Outdoor air (chamber study)	Denmark	**$PM_{2.5}$**: 24 vs 3 μg/m^3 **PNC**: 23,000 vs 1800 particles/cm^3	60 overweight subjects with controlled exposure (5 h)	• **VS:** exposed/non-filtered air (0.59 ± 0.05) vs. controls/ particle-filtered air (0.57 ± 0.04); **non-sig**. (Mean and SEM). Results reported as lesions/10^6 bp	[27]
Kianmehr	2017	Diesel engine exhaust (bakers)	Iran	No exposure assessment	55 (11 diesel engine exhaust, 11 unexposed)	• **TL**: exposed (12.31 ± 4.51) vs. controls (2.89 ± 1.22); **sig.** (Mean and SD) • **TI**: exposed (4.03 ± 1.95) vs. controls (6.21 ± 1.88); **sig.** (Mean and SD) • **TM:** exposed (1.85 ± 1.33) vs. controls (0.17 ± 0.23); **non-sig.** (Mean and SD) • ***Combined:*** *exposed (6.11 ± 3.64) vs. control (1 ± 0.74)*	[29]
León-Mejía	2019	Diesel exhaust (gases, PAH, PM)	Colombia	**$PM_{2.5}$**: 250 μg/m^3 in workplace (stationary sampling; no information about exposure in controls)	220 (120 exposed mechanics and 100 controls)	• **TI:** exposed (30.91 ± 17.52) vs. controls (23.39 ± 9.18); **sig.** (Mean and SD) • **VS:** exposed (131.22 ± 48.15) vs. controls (107.05 ± 27.88); **sig.** (Mean and SD) • ***Combined:*** *exposed (1.27 ± 0.60) vs. controls (1 ± 0.33)*	[30]
Novotna[6]	2007	Outdoor air	Czechia	**$PM_{2.5}$**: 33.2 (January) and 14.5 μg/m^3 (September) (stationary sampling) Air (PAH abstracted from filters, personal samplers)	65 non-smoking city policemen (54 outdoor policemen, 11 indoor policemen)	• **TI:** exposed (January: 7.04 ± 0.38, September (4.72 ± 0.29) vs. unexposed (January: 3.75 ± 0.85, September (2.65 ± 0.18); **sig.** (Mean and SEM)	[31]
Oh	2006	Automobile emission (PAH)	South Korea	Urine (1-OHP and 2-naphthol)	138 (54 automobile emission inspectors, 84 controls)	• **TI:** exposed (mononuclear cells: 14.91 ± 2.37, polynuclear cells: 15.58 ± 3.58) vs. controls (mononuclear cells: 9.17 ± 2.22, polynuclear cells: (13.35 ± 2.44); **sig.** (Mean and SD) • **TM:** exposed (mononuclear cells: 1.71 ± 0.23, polynuclear cells: 3.21 ± 0.42) vs. controls (mononuclear cells: 1.34 ± 0.16, polynuclear cells: 2.76 ± 0.38); **sig.** (Mean and SD) • ***Combined:*** *exposed (1.31 ± 0.21) vs. controls (1 ± 0.21)*	[32]
Piperakis	2000	Outdoor air	Greece	No exposure assessment	80 healthy individuals living in urban and rural areas with different smoking habits	• **VS:** urban non-smokers (78 ± 10.2), urban smokers (99 ± 10.9), rural non-smokers (71 ± 7.8), rural smokers (98 ± 12.5); **sig.** (Mean and SD)	[33]
Scheepers	2002	Diesel engine exhaust (benzene, PAH)	Estonia, Czechia	Air (1-nitropyrene on respirable particles) and urine (1-OHP and metabolites of PAH and benzene)	92 underground miners (drivers of diesel-powered excavators) (46 underground workers, 46 surface workers)	• **VS**: exposed (134) vs controls (104); **non-sig.** (Mean, variation not reported)	[39]
Scholten	2021	Diesel engine exhaust (chamber study)	Sweden	**$PM_{2.5}$**: 93 vs 1 μg/m^3 Air (PM_1, elemental carbon, NOx, CO)	19 subjects with controlled exposure (3 h) to biodiesel or filtered air	• **VS:** exposed (0.014 ± 0.009) vs. controls (0.018 ± 0.017); **non-sig**. (Mean and SD, estimated from the graph, mean of 3 and 24 h post-exposure). Results reported as lesions/10^6 bp	[34]
Shen	2016	Diesel engine exhaust	China	Air (elemental carbon (267 vs 96 μg/m^3) and urine 1-OHP and other PAH metabolites)	185 (86 exposed diesel engine testing workers, 99 unexposed)	• **TI:** exposed (66.44 ± 25.93) vs. controls (20.20 ± 29.45); **sig.** (Mean and SD) • **TM:** exposed (5.29 ± 2.30) vs. controls (1.16 ± 2.45); **sig.** (Mean and SD)	E7015

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Table 1 (*continued*)

Author	Year	Main Chemical Exposure	Country	Exposure Assessment or Biomarkers of Exposure	Population Characteristics	DNA Damage	Reference
						• ***Combined:*** *exposed (3.92 ± 1.63) vs. controls (1 ± 1.78)*	
Sørensen	2003	Outdoor air (PM)	Denmark	**$PM_{2.5}$**: 16.1 μg/m^3 (quartiles: 10.0–24.5 μg/m^3, personal exposure), 9.2 μg/m^3 (quartiles: 5.3–14.8 μg/m^3, monitoring station from urban background location) Air (black smoke) and urine (1-OHP)	50 students (samples collected during four seasons)	• **VS:** 4.5, 2–10; **non-sig** (Median and 25th-75th percentile, correlation analysis)	[40]
Tovalin	2006	Outdoor air ($PM_{2.5}$, ozone, VOC)	Mexico	**$PM_{2.5}$**: 133/86.6 μg/m^3 (Mexico City) and 122/78.3 μg/m^3 (Puebla) (outside/inside). Air (O_3 and VOC, personal exposure)	55 City traffic exposure (28 outdoor workers, 27 indoor workers)	• **TL**: exposed (median: 46.80, maximum: 132.41) vs. controls (Median 30.11, maximum 51.47); **sig.**	[41]
Ullah	2021	Outdoor air (traffic)	Pakistan	No exposure assessment	240 (60 participants exposed to traffic pollution, 60 controls)	• **TL:** exposed (28.69, 26.83–30.55) vs. controls (8.62, (7.98–9.26); **sig.** (Mean, min-max)	[42]
Vinzents	2005	Outdoor air (PM_{10}, UFP, NOx, CO)	Denmark	**PNC**: 32,400 vs 13,400 particles/cm^3 (personal exposure) **PNC**: 30.400 particles/cm^3 (stationary monitoring along the bicycle route) **PM_{10}**: 23.5 μg/m^3	15 subjects bicycling in traffic or indoors on six occasions (controlled exposure)	• **VS:** exposed (0.06, 0.03–0.11) vs. controls (0.06, 0.02–0.12); **non-sig.** (Median and 25th–75th percentile). Results reported as lesions/10^6 bp	[36]

Comet descriptors are segregated into visual score (VS), tail length (TL; sometimes also called comet tail length), tail intensity (TI; percentage of total DNA fluorescence in the tail), tail moment (TM; sometimes also called comet tail moment), Olive tail moment (OTM). Results have been combined for studies with more than one comet descriptor. Abbreviations: 1-hydroxypyrene (1-OHP), particle number concentration (PNC), polycyclic aromatic hydrocarbon (PAH), volatile organic compounds (VOC), ultrafine particles (UFP), S-phenylmercapturic acid (S-PMA), 2-hydroxyfluorene (2-OHF), 1- and 2-naphthol (1-NAPH and 2-NAPH).

[1] Results from taxi-motor drivers, roadside and suburban have been pooled for meta-analysis (5.91 ± 3.27, n = 108). Levels of ultrafine particles have been assessed in representative areas where the subjects are located. The levels are midday hourly measurements, using portable monitors.

[2] Results from bus drivers and garagemen have been pooled for meta-analysis (2.01 ± 1.55, n = 70).

[3] Results from summer and winter have been pooled for meta-analysis (exposed: 2.82 ± 1.41, n = 86; controls: 2.63 ± 1.28, n = 58).

[4] Results from Wuhan and Tianjin have been pooled for the meta-analysis (2.56 ± 4.31, n = 193). The paper does not report whether the results are statistically significant. A Student's *t*-test indicates a statistical significance (t-value =2.68, $P < 0.01$). We have considered the results to be statistically significant.

[5] Results from gas station attendants and taxi drivers have been pooled for meta-analysis (91.7 ± 18.2, n = 77). Results have been estimated from the graph.

[6] Results from January and September have been pooled for meta-analysis (exposed: 3.37 ± 1.91, n = 54; controls: 1.91 ± 1.38, n = 11, mean and SD).

studies [43,44].

(iv) Cross-sectional studies on traffic-related emissions. These studies examine populations with different air pollution exposure, such as subjects occupationally exposed to vehicle engine exhaust (e.g. taxi drivers) or those living in locations or cities with different traffic intensities. Studies on taxi or bus drivers have shown higher levels of DNA strand breaks as compared to control groups [17–19,26]. Increased levels of DNA strand breaks have also been observed in outdoor working police officers as compared to subjects who worked indoors in Prague, Czechia [31]. However, other studies on police officers with well-documented PAH or benzene exposure from Prague [22], Kosice (Slovak Republic), Sofia (Bulgaria) [23], and Rome (Italy) [21] have not found different levels of DNA strand breaks between exposed subjects and controls. Two studies on subjects in different locations (city center in Athens, Greece *vs.* rural areas; Zhuhai, Wuhan and Tianjin in China with different $PM_{2.5}$ levels) showed higher levels of DNA strand breaks in exposed subjects [24,33].

Four cross-sectional studies on air pollution exposure have been included in the review but excluded from the meta-analysis. Two studies have shown null results between air pollution exposure and DNA strand breaks [37,38], whereas two other studies showed increased levels of DNA strand breaks in exposed subjects [41,42].

3.1.1. Generalizability

The generalizability of meta-analysis results to all included studies is somewhat statistically underpowered because most studies on traffic-related exposures are included in the meta-analysis. The distribution between positive and null results does not differ between the studies in the meta-analysis (67 %, 14 out of 21 studies) and studies that are only included in the review (50 %, 3 out of 6 studies, Z-value = 0.26, $P > 0.05$) (Supplementary Table S4).

3.1.2. Meta-analysis

Fig. 2 shows results from the meta-analysis of 21 studies. There is considerable inter-study heterogeneity (I^2 = 89 %), although Egger's text does not indicate asymmetry of Funnel plots (z = 0.57, P = 0.57). Effect sizes from the overall meta-analysis are summarized in Table 4. Overall, there is a positive association between exposure and levels of DNA strand breaks (SMD = 0.62, 95 % CI: 0.36, 0.89). The effect size is slightly lower when calculated by non-parametric analysis (SMD_{median} = 0.47, 95 % CI: 0.24, 0.79).

3.1.3. Subgroup analysis

Effect sizes from subgroup analysis are summarized in Table 4. The analysis indicates that the genotoxic effect is larger in studies on populations from middle-income countries (SMD = 1.11, 95 % CI: 0.66, 1.56, n = 8) as compared to studies from high-income countries (SMD = 0.32, 0.06, 0.58, n = 13).

3.1.4. Sensitivity analysis

Fig. 3 shows the risk of comet assay measurement bias and exposure misclassification. With the exception of a few studies, there is a low or moderate risk of comet assay measurement bias and exposure misclassification. However, the sensitivity analysis indicates that studies with

Table 2
Summary of findings from the included studies on biomass combustion.

Author	Year	Main Chemical Exposure	Country	Exposure Assessment or Biomarkers of Exposure	Population Characteristics	DNA Damage	Reference
Abreu	2017	Wildland fires	Portugal	No exposure assessment	126 (63 firefighters, 63 controls)	• **TI:** exposed (11.23 ± 0.36) vs controls (6.38 ± 0.42). **Sig.** (Mean and SEM)	[45]
Andersen	2018	PAH (controlled exposure)	Denmark	Skin (PAH), urine (1-OHP)	22 professional firefighters	• **VS:** exposed (0.30 ± 0.20) vs. unexposed/before (0.23 ± 0.10); **non-sig.** (Mean and SD). Results reported as lesions/10^6 bp	[46]
Danielsen	2008	Wood smoke	Sweden	Air (PM: 279 and 243 in two different exposure sessions; UFP: 180,000 and 95,000 particles/cm^3)	13 never-smoking subjects	• **VS:** exposed (20 h: 0.035 ± 0.019, 3 h: 0.042 ± 0.036) vs. filtered air (20 h: 0.085 ± 0.043, 3 h: 0.071 ± 0.053); **non-sig.** (Mean and SD). Results reported as lesions/10^6 bp • ***Combined:*** *exposed (0.039 ± 0.028) vs. control (0.078 ± 0.048)*	[47]
Forchhammer	2012	Wood smoke (controlled exposure)	Denmark	Air ($PM_{2.5}$: 14, 220, or 354 μg/m^3; PNC: 222, 29,112, or 71,306 particles/cm^3) from a well-burning modern wood stove for 3 h in a climate-controlled chamber with 2-week intervals)	20 healthy non-smoking subjects (controlled exposure)	• **VS**: High (20 h: 0.034 ± 0.030, 6 h: 0.075 ± 0.042, 0 h: 0.072 ± 0.102), low (20 h: 0.033 ± 0.034, 6 h: 0.037 ± 0.041, 0 h: 0.043 ± 0.043), filtered air (20 h: 0.048 ± 0.072, 6 h: 0.042 ± 0.052, 0 h: 0.037 ± 0.030); **non-sig.** (Mean ± SD). Results reported as lesions/10^6 bp • ***Combined:*** *exposed (0.049 ± 0.072) vs. controls (0.042 ± 0.054)*	[48]
Jensen	2014	Wood smoke exposure	Denmark	Exposure to high indoor concentrations of $PM_{2.5}$ (700–3600 μg/m^3), CO (10.7–15.3 ppm), and NO_2 (140–154 μg/m^3) during 1 week.	11 university students	• **VS:** exposed/after (0.061 ± 0.0.46) vs. unexposed/before (0.0.51 ± 0.031); **non-sig.** (Mean ± SD). Results reported as lesions/10^6 bp	[49]
Kianmehr	2017	Fuel smoke (firewood)	Iran	No exposure assessment	55 (11 exposed bakers, 11 unexposed)	• **TL:** exposed (19.35 ± 5.97) vs. unexposed (2.89 ± 1.22); **sig.** (Mean and SD) • **TI**: exposed (6.21 ± 1.88) vs. controls (6.21 ± 1.88); **sig.** (Mean and SD) • **TM:** exposed (4.40 ± 1.98) vs. controls (0.17 ± 0.23); **sig.** (Mean and SD) • ***Combined:*** *exposed (12.49 ± 5.06) vs. controls (1 ± 0.74)*	[29]
Miglani[1]	2019	PAH (biomass burning)	India	Urine (1-OHP)	178 (79 tandoor workers, 79 controls)	• **TL:** exposed (tobacco users: 5.82 ± 0.61, non-tobacco: 5.62 ± 0.92) vs. controls (tobacco users: 1.42 ± 0.19, non-tobacco users: 1.35 ± 0.34); **sig.** (Mean and SD)	[50]
Mondal	2010	Fuel smoke (biomass and liquefied petroleum)	India	$PM_{2.5}$ and PM_{10} (stationary sampling). $PM_{2.5}$: 312 vs 77 μg/m^3 during cooking period and 82 vs 45 μg/m^3 in non-cooking periods	217 (132 biomass users, 85 liquefied petroleum gas users)	• **TL:** biomass users (46.6 ± 4.7) vs. gas users (44.1 ± 4.6); **sig.** (Mean and SD) • **TI:** biomass users (21.6 ± 5.2), gas users (16.8 ± 3.3); **sig.** (Mean and SD) • **TM**: biomass users (4.2 ± 1.0) vs. gas users (4.2 ± 1.0); **sig.** (Mean and SD) • ***Combined:*** *exposed (1.99 ± 0.42) vs. controls (1 ± 0.23)*	[51]
Pandey	2005	Fuel smoke (biomass fuel, liquefied petroleum gas)	India	No exposure assessment	144 volunteers (70 biomass fuel (BMF) users, 74 liquefied petroleum gas (LPG) users)	• **TL:** exposed/BMF users (51.20 ± 1.57) vs controls/LPG users (40.12 ± 0.92) vs.; **sig.** (Mean and SEM) • **TI:** exposed/ BMF users (11.29 ± 0.7) vs. controls/LPG users (8.22 ± 0.20); **sig.** (Mean and SEM) • **TM:** exposed/ BMF users (3.90 ± 0.16) vs. controls/LPG users (2.68 ± 0.07); **sig.** (Mean and SEM)	[52]

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Table 2 (*continued*)

Author	Year	Main Chemical Exposure	Country	Exposure Assessment or Biomarkers of Exposure	Population Characteristics	DNA Damage	Reference
Panumasvivat	2024	Wildland fires	Thailand	Air ($PM_{2.5}$: 35.3 vs 13.1 μg/m^3)	54 (firefighters)	• ***Combined:*** *exposed (1.37 ± 0.40) vs. controls (1 ± 0.21)* • **TL:** −0.394 (-0.230, 0.152). **Non-sig.** (Mean change for the season as a factor and 95 % CI, multivariate regression analysis). • **TM:** −0.024 (-0.01, 0.051). **Non-sig.** (Mean change for the season as a factor and 95 % CI, multivariate regression analysis)	[54]
Torres-Dosal	2008	Biomass (indoor air pollution)	Mexico	Urine (1-OHP)	20 (before and after the wood smoke intervention program)	• **TM**: exposed/before (6.58 ± 2.78) vs. before (2.96 ± 1.14). **Sig**. (Mean and SD, estimated from the graph)	[53]

Comet descriptors are segregated into visual score (VS), tail length (TL; sometimes also called comet tail length), tail intensity (TI; percentage of total DNA fluorescence in the tail), tail moment (TM; sometimes also called comet tail moment), Olive tail moment (OTM). Results have been combined for studies with more than one comet descriptor.

[1] Combined tobacco user status: exposed (5.72 ± 0.77, n = 76) and controls (1.39 ± 0.27, n = 79).

moderate/high risk of comet assay measurement bias have a higher effect size as compared to studies with low risk (Table 5). In contrast, it seems that studies with moderate/high risk of exposure misclassification have lower effect sizes as compared to low-risk studies (Table 5). The combined categorization indicates a slightly lower effect size in the group of studies with the lowest risk of comet assay measurement bias/exposure misclassification (SMD = 0.42, 95 % CI: −0.00, 0.84) as compared to the groups with moderate (SMD = 0.74, 95 % CI: 0.37, 1.12) and high risk of bias (SMD = 0.73, 95 % CI: −0.27, 1.73).

3.1.5. Summary of studies on traffic-related emissions

Collectively, the meta-analysis shows that exposure to traffic-related combustion emissions is associated with increased levels of DNA strand breaks. Studies from high-income countries have reported lower effect sizes than have studies from middle-income countries.

3.2. Biomass combustion

Ten studies with results on DNA strand breaks after exposure to wood smoke have been included in the review and meta-analysis [29,45–53] (Table 2). One additional study has been included in the review [54]. The studies are segregated into controlled exposure studies and cross-sectional studies. The controlled exposure studies have used relatively clean fuel, whereas cross-sectional studies have more complex exposures in regard to the type of biomass fuel, exposure scenario and combustion condition.

(i) Controlled exposure studies on biomass combustion emissions. A number of controlled exposure studies have been conducted by the same research group (i.e. comet assay results originate from the same laboratory). The first study of its kind exposed subjects to smoke from birch and spruce wood for 4 h in an exposure chamber (PM mass: 279 and 241 μg/m^3, PNC: 180,000 and 95,000 particles/cm^3 on two different days of exposure). Surprisingly, there was a lower level of DNA strand breaks after wood smoke exposure as compared to filtered air (<30 μg/m^3) [47]. The authors hypothesized that lower levels of DNA damage correspond to increased DNA repair activity as the hOGG1-mediated repair activity was slightly increased in peripheral blood mononuclear cells, and there was elevated urinary excretion of 8-oxoguanine (repair product of hOGG1-mediated DNA repair). A later study with a cross-over design exposed the same human subjects for 3 h to filtered air (control; 14 μg/m^3 or 222 particles/cm^3, $PM_{2.5}$ and PNC, respectively), or to low (220 μg/m^3 or 29,112 particles/cm^3) or high (354 μg/m^3 or 71,036 particles/cm^3) concentrations of smoke from beech wood. Blood samples were obtained immediately, 6 and 20 h after the exposure. There were no differences in levels of DNA strand breaks [48]. A third study assessed DNA strand breaks in conscripts who were included in fire extinction exercises of a firefighters' training program. As the volunteers were wearing personal protective equipment when extinguishing fires (mainly European Union wood pallets), the primary period of exposure was considered to be during by-stander position (e.g. while waiting their turn to extinguish fires, receiving specific instructions or getting feedback on their performance). There was a positive correlation between personal exposure (i.e. PAHs in skin wipes and urinary 1-OHP) and DNA strand breaks. However, DNA strand break levels did not significantly differ between fire extinguishing exercises, and control periods before and after the exposure [46]. The fourth study from this research group was a somewhat opportunistic study where subjects lived for a week in a reconstructed Viking Age house with an indoor fireplace for heating and cooking (using mainly beech wood). The mean estimated personal $PM_{2.5}$ exposure level was 471 μg/m^3 (range from 275 to 821 μg/m^3 during the stay). Despite the high level and long exposure period, there was no difference in DNA strand break levels before and after the exposure period [49]. It should be noted that the study was not controlled for exposure misclassification because the personal $PM_{2.5}$ exposure was modelled from information on indoor stationary measurement and time spent in the Viking Age house.

(ii) Cross-sectional studies on biomass combustion emissions. A group of studies was conducted in villages in West Bengal (India), where exposure contrasts were assessed by comparing women living in homes with biomass burning of wood, cow dung and agricultural waste, to those using liquefied petroleum gas in their homes (controls). The first set of studies showed increased levels of DNA strand breaks in the group using biomass fuel [51]. The indoor $PM_{2.5}$ levels in the kitchen were higher during cooking compared with non-cooking periods (biomass: 312 and 82 μg/m^3; liquefied petroleum gas: 77 and 45 μg/m^3). Another research group from India also showed an increased level of DNA strand breaks in women using biomass combustion (wood, cow dung and unspecified cake fuel) as compared to those using liquefied petroleum gas [52]. Iranian bakery workers, using wood-fuelled ovens, had a higher level of DNA strand breaks as compared to a control group of university staff employees [29]. Lastly, a study on wood smoke showed that tandoor workers (i.e. a clay oven fired by wood) had higher levels of DNA strand breaks than the control group [50].

A study of rural populations in Mexican villages showed decreased levels of DNA strand breaks compared to controls, after an intervention in which indoor surfaces were cleaned, dirt floors paved, and new wood stoves installed in the dwellings to reduce wood smoke exposure [53]. Wildland firefighters in Portugal had higher levels of DNA strand breaks compared to controls [45]. The exposure assessment only included questionnaire data on years of firefighting activity and hours spent in

Table 3
Summary of findings from the included studies on coke oven workers.

Author	Year	Main Chemical Exposure	Country	Exposure Assessment or Biomarkers of Exposure	Population Characteristics	DNA Damage	Reference
Chen	2006	PAH	China	Air (PAH)	363 (240 coke-oven workers and 123 controls, all males)	• **TM:** exposed (1.23 ± 1.12) vs. control (0.58 ± 0.92), **sig.** (Mean and SD)	[55]
Cheng	2009	PAH	China	Urine (1-OHP)	158 (94 coke-oven workers and 64 controls)	• **TM:** exposed (0.86; 0.77–0.97) vs. controls (0.43; 0.35–0.52); **sig.** (Geometric mean and 95 % CI)	[56]
Gao	2014	PAH	China	Urine (1-OHP)	204 (126 coke-oven workers and 78 controls)	• **TL:** exposed (7.49 ± 0.89) vs. controls (3.16 ± 0.58); **sig.** (Mean and SD) • **TM**: exposed 10.48 ± 3.52) vs. controls (0.85 ± 0.23); **sig.** (Mean and SD) • ***Combined:*** *exposed (7.35 ± 2.21) vs. controls (1 ± 0.23)*	[57]
Huang[1]	2012	PAH	China	Air (PAH)	298 (202 exposed coke-oven workers: bottom 67, side 57, top 78 of the coke-oven; 96 controls)	• **TM:** exposed (bottom: 0.98 ± 1.07); side: 1.37 ± 1.07; top: 1.39 ± 1.09) vs. controls (0.55 ± 0.93); **sig.** (Mean and SD)	[58]
Leng	2004	PAH	China	Urine (1-OHP)	193 (143 coke-oven workers, 50 controls)	• **TM**: exposed (2.6, 2.1–3.3) vs. controls (1.0, 0.8–1.2); **sig.** (Geometric mean and 95 % CI)	[59]
Marczynski[2]	2002	PAH	Germany	Air (PAH) and urine (1-OHP and other PAH metabolites)	51 (19 coke-oven workers, 32 controls	• **TM:** exposed (3.5 ± 1.72) vs. controls (2.54 ± 0.68); **non-sig.** (Mean and SD)	[60]
Marczynski	2009	PAH	Germany	Air (PAH) and urine (1-OHP and other PAH metabolites)	85 (34 coke-oven workers, 48 controls)	• **TM:** exposed (2.2, 1.7–2.7) vs. controls (1.3, 1.2–1.8); **Sig.** (median and inter-quartiles)	[61]
Siwińska	2004	PAH	Poland	Urine (1-OHP)	98 (49 coke-oven workers, 49 controls)	• **TL:** exposed: (32.3, 29.0–37.3) vs. controls (34.6, 31.4–40.4); **sig.** (Median and 25th–75th percentile)	[62]
van Delft	2001	PAH	Netherlands	Urine (1-OHP)	72 (28 coke-oven workers, 37 controls)	• **VS:** exposed (1.3 ± 0.4) vs. controls (1.4 ± 0.4); **non-sig.** (Mean and SD)	[63]
Wang	2010	PAH	China	Air (B[*a*]P) and urine (1-OHP)	475 workers (157 low, 160 intermediates, 158 high exposure)	• **TM:** all 0.36 (0.13–1.24), low 0.33 (0.12–1.06), intermediate 0.38 (0.17–1.74), high 0.40 (0.14–3.17); **sig.** (Median, 5th–95th percentiles	[65]
Wilhelm	2007	PAH	Germany	Air (total suspended particles: ≤30 μg/m3 and >45 μg/m^3 in Borken and Duisburg North, respectively) and urine (1-OHP)	218 children (151 in Duisburg North, 67 in Borken)	• **TM:** exposed (1.99, 0.55–10.65) vs. control (1.32, 0.73–2.47). **Sig.** (Median and range)	[64]
Xiao	2002	PAH	China	Air (B[*a*]P)	83 (43 coke-oven workers, 40 controls)	• **VS:** exposed (67000 ± 64934) vs. controls (28936 ± 20874); **Sig.** (Mean and SD)	[66]
Yu[3]	2022	PAH	China	Urine (1-OHP and other PAH metabolites)	332 (coke-oven workers)	• **TL:** 3.61 (3.24–4.88); **sig** (Median and 25th–75th percentile) • **TI:** 3.20 (2.14, 5.18); **non-sig.** (Median and 25th–75th quartiles) • **TM:** 0.14 (0.08, 0.33); **sig.** (Median and 25th–75th percentile) • **OTM:** 0.44 (0.30, 0.75); **non-sig.** (Median and 25th–75th percentile)	[69]
Zhang	2015	PAH	China	Air (B[*a*]P) and urine (1-OHP)	121 (74 coke-oven workers, 47 controls)	• **TM:** exposed (0.41 ± 0.25) vs. controls (0.32 ± 0.12 20874); **Sig.** (Mean and SD)	[67]
Zhang	2021	PAH	China	Urine (1-OHP)	256 (173 male coke-oven workers, 83 male hot-rolling workers not exposed as a control group)	• **TI:** exposed (40.8, 20.4–51.1) vs. controls (4.92 (3.32–6.22); **Sig.** (Median and 25th–75th percentile) • **TM:** exposed (22.1, 11.7–32.5) vs. controls (3.73, 1.32–5.72); **sig.** (Median and 25th–75th percentile) • ***Combined:*** *exposed (7.11 ± 5.91) vs. controls (1 ± 0.88)*	[68]

Comet descriptors are segregated into visual score (VS), tail length (TL; sometimes also called comet tail length), tail intensity (TI; percentage of total DNA fluorescence in the tail), tail moment (TM; sometimes also called comet tail moment), Olive tail moment (OTM). Results have been combined for studies with more than one comet descriptor. Abbreviations: 1-hydroxypyrene (1-OHP), benzo[*a*] pyrene (B[*a*]P), polycyclic aromatic hydrocarbon (PAH)

[1] Coke oven exposure groups have been pooled for the meta-analysis (tail moment = 1.25 ± 1.08, n = 202).

[2] The study contains also a group of PAH-exposed graphite-electrode-producing workers. PAH exposure has only been assessed in exposed workers (not in controls).

[3] Correlation between PAH metabolites and DNA strand breaks. In general, there are positive associations between urinary PAH metabolites and DNA strand breaks,

although it is only statistically significant for tail length and tail moment. The study is considered to show a genotoxic effect of exposure in coke oven workers. Excluded from the meta-analysis.

Table 4
Summary of meta-analysis of exposure to combustion-derived emissions.

Metal	Papers (No)	Subjects (No)	Overall analysis (SMD)	Subgroup analysis (SMD)	Median (SMD_{median})
Traffic-related exhausts	21	2481	0.62 (0.36, 0.89)	High-income: 0.32 (0.06, 0.58) Middle-income: 1.11 (0.66, 1.56)	0.47 (0.24, 0.79)
Biomass	10	891	1.73 (0.72, 2.74)	High-income: 0.34 (-0.43, 1.11) Middle income: 3.21 (1.49, 4.92)	1.37 (-0.95, 3.06)
Coke oven	10	1622	0.84 (0.30, 1.37)	High-income: 0.29 (-0.35, 0.94) Middle-income: 1.18 (0.48, 1.89)	0.73 (-0.26, 1.07)

Standardized mean difference (SMD) is reported with a 95 % confidence interval.

Table 5
Sensitivity analysis of effect sizes in studies according to the use of blinded analysis, the inclusion of assay controls and description of the comet assay procedure.

Item (risk of bias)	Traffic-related emission	Biomass	Coke oven
Blinding/coding			
High	0.71 (0.30, 1.13) (11)	3.96 (1.18, 6.74) (3)	0.86 (0.22, 1.51) (9)
Low	0.50 (0.18, 0.82) (10)	0.75 (0.12, 1.38) (7)	0.61 (0.39, 0.84) (1)
Inclusion of assay controls			
High	0.67 (0.31, 1.03) (11)	2.91 (1.60, 4.23) (6)	0.84 (0.30, 1.37) (10)
Moderate	0.84 (0.24, 1.45) (6)	-0.95 (-1.85, −0.06) (1)	NA
Low	0.13 (-0.15, 0.40) (4)	0.33 (0.03, 0.64) (3)	NA
Comet assay description			
High	1.01 (-0.34, 2.37) (2)	7.35 (6.62, 8.34) (1)	1.15 (0.52, 1.77) (7)
Moderate	1.87 (0.84, 2.91) (1)	2.44 (1.63, 3.26) (3)	NA
Low	0.53 (0.26, 0.81) (18)	0.50 (-0.11, 1.11) (6)	0.07 (-0.56, 0.70) (3)
Exposure assessment			
High	0.51 (0.12, 0.89) (4)	1.64 (0.99, 2.28) (3)	NA
Moderate	0.26 (-0.00, 0.52) (5)	1.59 (0.15, 3.04) (3)	0.66 (0.50, 0.81) (3)
Low	0.77 (0.36, 1.18) (12)	1.77 (-1.10, 4.63) (4)	0.91 (0.01, 1.80) (7)
Combined			
High	0.73 (-0.27, 1.73) (3)	3.96 (1.18, 6.74) (3)	1.24 (0.46, 2.02) (6)
Moderate	0.74 (0.37, 1.12) (10)	1.64 (0.99, 2.28) (3)	0.23 (-0.32, 0.77) (4)
Low	0.42 (-0.00, 0.84) (8)	0.05 (-0.49, 0.58) (4)	NA

Results are mean and standard deviation of standard mean differences of studies (the number of studies is shown in brackets). Not applicable (NA).

recent firefighting activities. The inclusion of the latter in statistical models did not influence effects on DNA strand break levels between firefighters and controls.

One study of wildland firefighters has been included in the review, although excluded from the meta-analysis [54]. There was no difference in DNA strand break levels between the peak and pre-peak seasons of forest fires in Thailand ($PM_{2.5}$: 35.3 and 13.1 μg/m^3, respectively) [54].

3.2.1. Generalizability

The generalizability of meta-analysis results to all included studies is not applicable because all but one study on biomass combustion are also included in the meta-analysis. (Supplementary Table S5).

3.2.2. Meta-analysis

Fig. 4 shows the results of the meta-analysis of biomass combustion exposure studies. Table 4 shows the effect sizes of the meta-analysis.

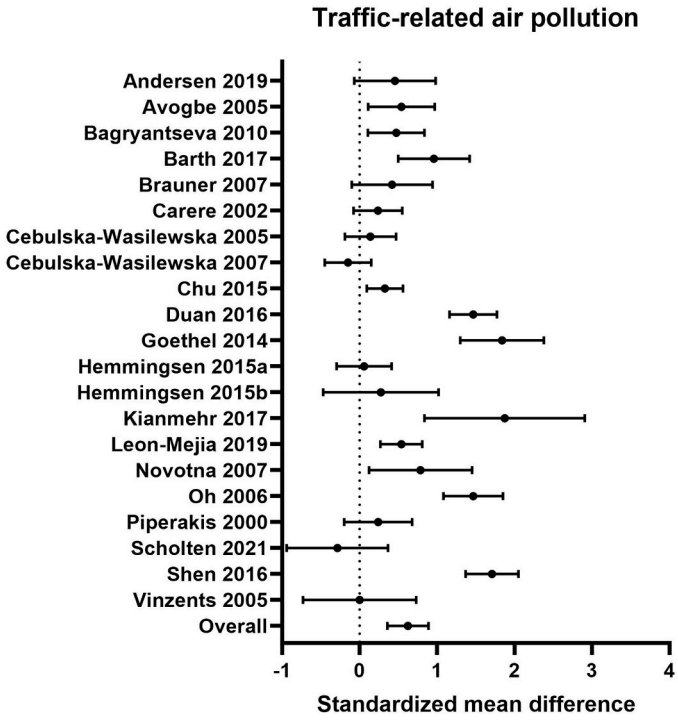

Fig. 2. Effect sizes in studies on traffic-related air pollution. Symbols and lines are mean and 95 % confidence intervals. Effects are statistically significant if they do not cross the vertical line at x = 0. The forest plot has been reproduced for graphical purposes by the Review Manager. Original Forest and Funnel plots are included in Supplementary Figs. S1 and S2, respectively.

There is considerable inter-study heterogeneity (I^2 = 97 %), although Egger's text does not indicate asymmetry of Funnel plots (z = 0.77, P = 0.44). Overall, the studies on biomass combustion emissions show a relatively strong effect (SMD = 1.73, 95 % CI: 0.72, 2.74). This is lower when using a non-parametric test to calculate the central tendency (SMD_{median} = 1.37, 95 % CI: 0.–0.95, 3.06).

3.2.3. Subgroup analysis

Effect sizes from subgroup analysis are summarized in Table 4. Results from studies on populations from high-income countries show a much lower effect (SMD = 0.34, 95 %: −0.43, 1.11, n = 5) compared to populations in middle-income countries (SMD = 3.21, 95 % CI: 1.49, 4.92, n = 5).

3.2.4. Sensitivity analysis

Fig. 5 shows the risk of comet assay measurement bias and exposure misclassification for biomass emission studies. This overall

Fig. 3. Risk of comet assay measurement bias and exposure misclassification (traffic light plot) for traffic-related air pollution studies.

categorization indicates there is a low effect size in the group of studies with the lowest risk of comet assay measurement bias/exposure misclassification (SMD = 0.05, 95 % CI: −0.49, 0.58) as compared to the groups with moderate (SMD = 1.64, 95 % CI: 0.99, 2.28) and high risk of bias (SMD = 3.96, 95 % CI: 1.18, 6.74). Sensitivity analyses of individual items also follow the same relationship between the risk of comet assay measurement bias/exposure misclassification and effect size (Table 5).

3.2.5. *Summary of studies on biomass combustion emissions*

Collectively, the meta-analysis shows that exposure to biomass combustion emissions is associated with increased levels of DNA strand breaks. Studies from high-income countries have reported lower effect sizes than studies from middle-income countries.

3.3. *Coke oven emissions*

Fifteen studies have been included in the review [55–69] (Table 3). The majority of these studies have investigated occupational exposures. Only one study has assessed PAH exposure in children living near a coke oven facility [64]. In the coke oven exposure studies, the airborne concentrations of B[*a*]P or PAH are linked to biomarkers of exposure (1-OHP and other PAH metabolites). None of the studies have assessed exposures to inhalable particles or smaller size fractions.

Overall, 13 out of the 15 studies have reported a statistically significant association between exposure and DNA strand breaks [55–59, 61,62,64–69]. One of the null effect studies had a slightly higher level of

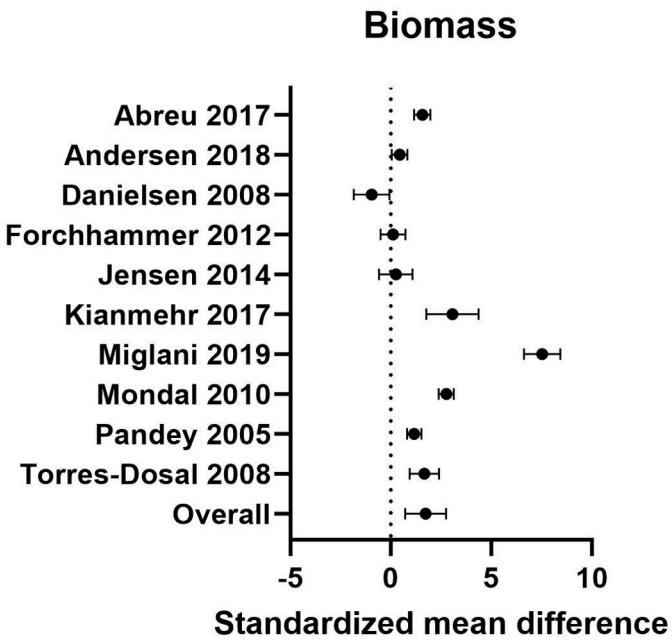

Fig. 4. Effect sizes in studies on biomass combustion emission. Symbols and lines are mean and 95 % confidence intervals. Effects are statistically significant if they do not cross the vertical line at x = 0. The forest plot has been reproduced for graphical purposes by the Review Manager. Original Forest and Funnel plots are included in Supplementary Figs. S3 and S4, respectively.

DNA strand breaks in coke oven workers compared to controls, with a borderline statistical significance (3.50 ± 1.72 vs 2.54 ± 0.68, P = 0.09, ANOVA) [60]. The other study showed increased urinary excretion of 1-OHP, but there were unaltered levels of DNA strand breaks as well as no effect on other biomarkers of genotoxicity (micronuclei, sister chromatid exchanges and PAH-DNA adducts) [63].

3.3.1. *Generalizability*

In general, there is a good generalizability between studies that have been included and those excluded from the meta-analysis. The distribution between positive and null effects does not differ between the studies in the meta-analysis (80 %, 8 out of 10 studies) and studies that have been excluded from the meta-analysis (100 %, 5 out of 5 studies, Z-value = 0.30, P > 0.05) (**Summary** Table S6).

3.3.2. *Meta-analysis*

Fig. 6 shows results from the meta-analysis of 10 studies. Table 4 shows the effect sizes in overall meta-analyses. There is considerable inter-study heterogeneity (I^2 = 96 %), although Egger's text does not indicate asymmetry of Funnel plots (z = 0.22, P = 0.82). Overall, there is a positive association between exposure and levels of DNA strand breaks (SMD = 0.84, 95 % CI: 0.30, 1.37). Using a non-parametric test to calculate the central tendency yields almost the same effect size, although the variability is larger (SMD_{median} = 0.73, 95 % CI: −0.26, 1.07).

3.3.3. *Subgroup analysis*

Table 2 shows the effect sizes in subgroup analyses. This indicates that the genotoxic effect is larger in studies from middle-income countries (SMD = 1.18, 95 % CI: 0.48, 1.89, n = 6) as compared to studies from high-income countries (SMD = 0.29, 95 % CI: −0.35, 0.94, n = 4).

3.3.4. *Sensitivity analysis*

Fig. 7 shows the risk of comet assay measurement bias and exposure misclassification for coke oven emission studies. The overall categorization can only be stratified into studies with moderate or high risk of

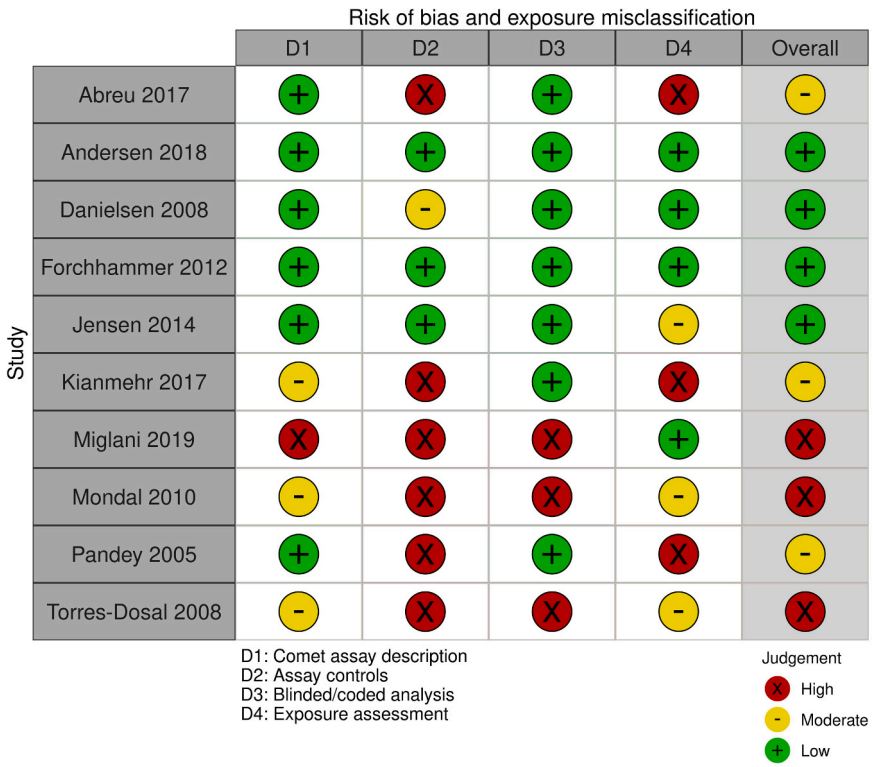

Fig. 5. Risk of comet assay measurement bias and exposure misclassification (traffic light plot) for studies on biomass combustion emission.

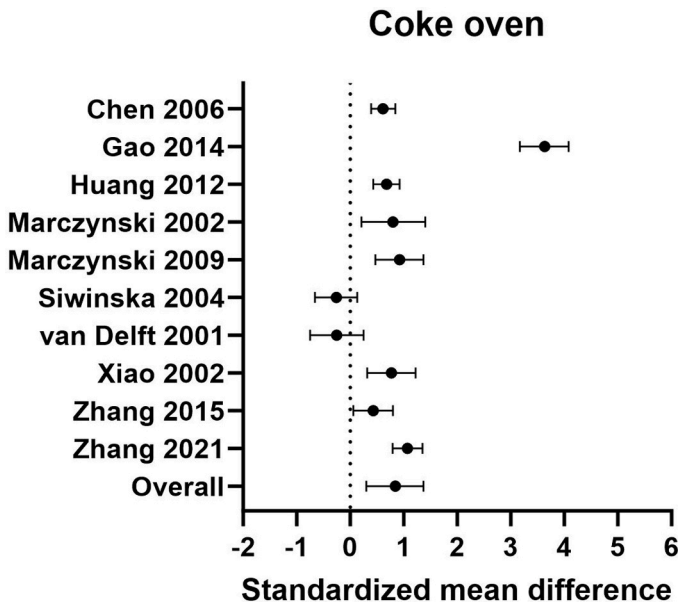

Fig. 6. Effect sizes in studies on coke oven emission. Symbols and lines are mean and 95 % confidence intervals. Effects are statistically significant if they do not cross the vertical line at x = 0. The forest plot has been reproduced for graphical purposes by the Review Manager. Original Forest and Funnel plots are included in Supplementary Figs. S5 and S6, respectively.

bias and exposure misclassification. This overall categorization suggests a lower effect size in the group of studies with a moderate risk of comet assay measurement bias/exposure misclassification (SMD = 0.23, 95 % CI: −0.32, 0.77) as compared to the groups with a high risk of bias (SMD = 1.24, 95 % CI: 0.46, 2.02). Sensitivity analyses of individual items also follow the same relationship between the risk of comet assay measurement bias/exposure misclassification and effect size (Table 5).

3.3.5. *Summary of studies on coke oven emissions*

Collectively, the meta-analysis shows that exposure to coke oven emissions is associated with increased levels of DNA strand breaks. Studies from high-income countries have reported a lower effect size than studies from middle-income countries.

4. Discussion

A number of previous reviews have summarized associations between outdoor air pollution exposures and levels of DNA strand breaks in human biomonitoring studies [10,70–74]. Overall, these reviews have concluded that there is a positive association between outdoor air pollution exposure and levels of DNA strand breaks in human blood cells. To the best of our knowledge, the present systematic review is the first study to assess effect sizes of air pollution exposure in a meta-analysis, covering specifically combustion-derived sources of emissions.

The meta-analyses in the present systematic review show increased levels of DNA strand breaks in leukocytes of humans by exposure to traffic-related air pollution (0.62, 95 % CI: 0.36, 0.89), biomass combustion (1.73, 95 % CI: 0.72, 2.74) and coke oven emission (0.84, 95 % CI: 0.30, 1.37). The effect sizes between the three types of combustion emissions appear to be different, but the difference is not so clear in the studies from high-income countries, which typically have a lower risk of comet assay measurement bias. The meta-analyses indicate a smaller effect size in studies from high-income countries as compared to studies from other countries. However, the group sizes tend to become small when the datasets are stratified into subgroups. Thus, in the discussion, we have used pooled datasets of traffic-related air pollution, biomass combustion and coke oven emissions to obtain larger group sizes and more robust findings [effect sizes of diesel and biomass combustion have been pooled in the study by Kianmehr et al., 2017 [29]]. The discussion adheres to the same flow as the text on individual sources of exposures, i.e. generalizability, subgroup analysis, and sensitivity analysis (results on merged datasets are reported in the supplementary material).

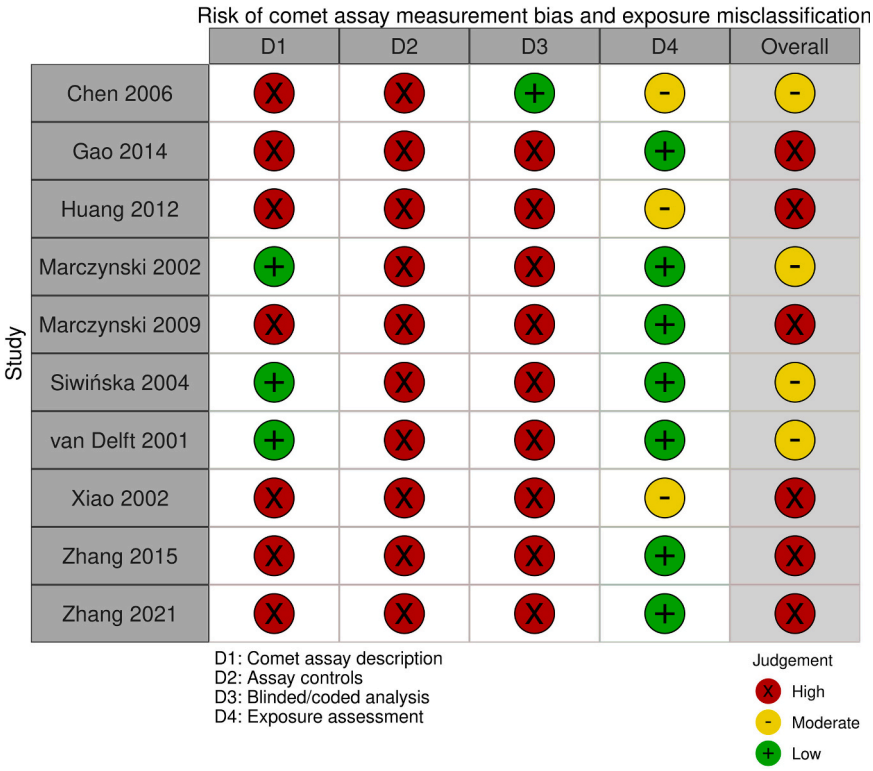

Fig. 7. Risk of comet assay measurement bias and exposure misclassification (traffic light plot) for studies on coke oven emission.

4.1. Generalizability

There are too few studies to assess the generalizability of the overall results in the individual exposure groups because most studies have provided sufficient information on group statistics to be included in the meta-analysis. Of the total number of studies in the review (n = 52, with 53 datasets), there are 12 studies with insufficient information for inclusion in the meta-analyses. However, the combined dataset on emission from traffic-related sources, biomass combustion and coke ovens does not indicate a difference in statistically significant effects between studies in the meta-analysis (68 %, 28 out of 41 studies) and other studies (75 %, 9 out of 12 studies, Z-value = 0.82, $P > 0.05$, Supplementary Table S7).

4.2. Subgroup analyses

The datasets on emission from traffic-related sources, biomass combustion and coke ovens indicate that studies on populations from high-income countries have lower effect sizes than middle-income countries (Table 2). There are substantial differences between studies from high- and middle-income countries in all three groups of emissions, namely 0.32 vs 1.11 (traffic), 0.34 vs 3.21 (biomass), and 0.29 vs 1.18 (coke oven). A pooled analysis of all studies indicates a higher effect size in middle-income countries (SMD: 1.60, 95 % CI: 1.13, 2.07) as compared to high-income countries (SMD: 0.33, 95 % CI: 0.09, 0.57) (Supplementary Figure S7 shows the Forest plot). The corresponding Funnel plot suggests a difference in the relationship between effect size and precision, where studies from high-income countries have a relatively symmetrical distribution and studies from middle-income countries have a distribution that predominantly spreads from low effect/high precision toward high effect/low precision (Supplementary Figure S8). Based on this difference in the Funnel plot, publication bias cannot be ruled out as a factor for the difference in effect between studies from high- and middle-income countries (Egger's test for high-income countries (z = -1.19, P = 0.24) and middle-income countries (z = 3.68, $P < 0.001$)). In addition, inter-study heterogeneity may also occur by combining results from different countries within each group of the high- and middle-income country. Even within each country, there can be differences in socioeconomic status and exposures across regions, and probably more so in large countries. However, the difference in effect sizes might also be due to stricter regulation on emissions and/or on the use of personal protective equipment in high-income countries as compared to at least some middle-income countries. It can also be speculated that effect modification is important because populations in high-income countries have better health status as e.g. documented by longer life-time expectancy (i.e. 80 vs 70 years in high-income vs middle-income countries, respectively) (World Bank; (https://data.worldbank.org/). Populations in middle-income countries may have non-optimal nutritional status due to lower access to healthy food, associated with low-grade inflammation and oxidative stress that increase susceptibility to DNA damage by environmental/occupational exposures. In addition, differences in DNA damage effects between middle- and high-income countries may also be due to comparisons of populations with different genetic polymorphism in metabolism and DNA repair.

4.3. Sensitivity analyses

There is a disproportion of studies from high- and middle-income countries regarding the overall risk of measurement bias and exposure misclassification. The proportion of studies from high-income countries gradually declines from the group of low risk (92 % studies from high-income countries; 11 out of 12 studies), through the group of moderate risk (44 %, 7 out of 16 studies), to the group of high risk of bias (25 %, 3 out to 12 studies, $\chi^2 = 11.5$, $P < 0.01$, Supplementary Table S8). This difference seems to be mainly driven by a high number of studies with low risk of comet assay measurement bias (74 %, 20 out of 27 studies) compared to studies with moderate/high risk of bias (8 %, 1 out of 13 studies; $\chi^2 = 13.4$, $P < 0.01$). Information on assay controls, blinded/coded analysis, and exposure assessment, are not different to

the extent that distributions become statistically significant (Supplementary Table S8).

Table 5 suggests a relationship between the risk of comet assay measurement bias and effect size, although the group sizes are relatively small. Therefore, we have pooled some of the groups to obtain a more equal number of studies in each group (Supplementary Table S9). Combining all categories indicates a difference in effect sizes between groups of low (0.30, 95 % CI: −0.02, 0.62), moderate (0.71, 95 % CI: 0.41, 1.01) and high (1.75, 95 % CI: 1.03, 2.47) risk of measure bias and exposure misclassification. This difference is mainly attributed to variabilities in comet assay measurement bias (low risk: 0.48, 95 % CI: 0.24, 0.72; moderate/high risk: 1.81, 95 % CI: 1.18, 2.45), inclusion of assay controls (low/moderate risk: 0.43, 95 % CI: 0.07, 0.78; high risk: 1.16, 0.78, 1.54) and blinding/coding of samples (low risk: 0.55, 95 % CI: 0.29, 0.82; high risk: 1.16, 95 % CI: 0.72, 1.61). There is not a clear difference between the risk of exposure misclassification and effect size (Supplementary Table S9).

Collectively, the sensitivity analysis indicates a linkage between middle-income countries, a high risk of comet assay measurement bias and a high effect size. The difference in effect sizes between high-income and middle-income countries might be due to bias in comet assay experiments in as much as insufficient description of procedures and lack of assay controls correspond to flawed laboratory work. Still, it must be stressed that the grouping (traffic lights) is not necessarily an indicator of poorly conducted research. It is possible that clarity in reporting comet assay procedures has been a larger issue among researchers in high-income countries, especially Europe, than elsewhere. This is to some extent documented by recent initiatives to unite recommendations on comet assay procedures as well as reporting comet assay procedures and results [2,15,75,76]. European laboratories have also been at the forefront of validating the comet assay in biomonitoring studies, including ring-trials by the European Comet Assay Validation Group [77–83] and hCOMET [84–88]. However, the sensitivity analysis leaves concern about reporting/publication bias if studies with clear (high) effects are easier to publish without proper description and/or control of experimental conditions.

4.4. Limitations

There are several limitations pertaining to biomonitoring studies using the comet assay and meta-analyses of comet assay results from studies in different laboratories. The limitations can be compiled in challenges as follows:

(i) The studies in the meta-analyses have used different comet assay protocols. While all studies have used the same general and widely accepted protocol (so-called alkaline version of the comet assay), the differences in specific steps of the protocol makes it impossible to use primary comet descriptors directly in meta-analyses. The meta-analysis, using SMD, is the procedure of choice for results in different metrics or results obtained by different methods. It is based on assumption that different laboratories will obtain the same effect size, although the mean and variability in DNA migration values cannot be compared between studies. The assumption has been assessed in certain ring studies, where samples have been produced in one laboratory and distributed to other laboratories. These ring studies have shown a variation in effect sizes, even though the samples had the same level of DNA strand breaks [78,80].

(ii) The studies have used different comet descriptors, and the values of these descriptors cannot be compared. To the best of our knowledge, previous systematic reviews have either restricted the meta-analysis to specific comet descriptors (e.g. tail intensity) or done separate meta-analyses on different comet descriptors. We have sought to avoid these limitations by combining comet descriptors into an overall standardized comet descriptor. This does not alleviate a hypothetical issue related to the selection of statistically significant associations for specific comet descriptors. For instance, it can be speculated that researchers have selected the best comet descriptor (i.e. statistically significant association) in articles with only one comet descriptor. This type of reporting bias would give rise to publication bias with an asymmetrical Funnel plot as seen in the studies on air pollution exposures.

(iii) There is heterogeneity in ways the studies have controlled for confounding factors. Controlled exposure studies are not affected by confounders such as age and sex because subjects are their own control. Cross-sectional studies typically control for confounders by matching or excluding subjects. It is likely that the difference in controlling for confounding causes heterogeneity between studies in the meta-analyses. However, it should also be emphasized that the literature does not indicate that confounding factors are consistently associated with an increased level of DNA damage measured by the comet assay, including age, sex, BMI, smoking status and alcohol consumption, which are important confounders in many epidemiological studies [74,89].

(iv) There are inter-study differences in the exposure assessment of air pollution. This pertains to exposure categories without actual assessment of air pollutants (e.g. occupational exposure vs controls), study design that ensures an exposure gradient (controlled exposure studies), measurements of air pollutants (e.g. particle number concentration measurement, without firm knowledge on whether the subjects were present in the exposure environment or used personal protective equipment), personal dosimeters, and biomarkers of exposure (internal dose of presumed reactive species such as PAHs). For this reason, it is not possible to obtain a general measure of the level of air pollution. Treating air pollution as a binary variable across studies has uncertainties because of differences in background levels of air pollutants in the control groups and exposure gradient. For instance, the controlled exposure studies from Copenhagen (Denmark) have been designed to remove air pollution exposure (i.e. subjects are exposed to normal air pollution levels vs filtered air), whereas other studies have compared subjects with presumably low background exposure to a high-exposure group.

(v) It is still uncertain whether high levels of DNA strand breaks, measured by the comet assay, can predict higher risk of diseases. Several cross-sectional studies have shown that patients with non-communicable or high-prevalence diseases have higher levels of DNA strand breaks than disease-free controls [90,91]. However, such observations may be related to reverse causality as the disease is associated with high levels of DNA strand breaks rather than high levels of DNA strand breaks being an underlying cause of disease. Currently, only one prospective study has shown a positive association between high levels of DNA strand breaks and increased risk of mortality [92]. Considering the paucity of prospective cohort studies, it is challenging to convert comet assay results from occupational and environmental monitoring programs to public health interventions.

(vi) The SMD is the most used outcome measure for continuous and different measures in meta-analyses. However, it is difficult to interpret because it quantifies the magnitude of a difference between two group means in standard deviation units. In addition, the effect size depends on the SD. Therefore, it reflects both technical and biological variability. It is vulnerable to the correctness of reported measure of variability. Especially, studies that erroneously report SEMs and SDs will give rise to high SMDs. Such studies tend skew the Funnel plot in right-hand direction. The Ratio of Means (RoM) is an alternative outcome that is independent of SD, and it has a more familiar outcome (i.e. as a ratio it is interpreted in the same way as odds ratio and relative risk). It is easy to understand that a certain exposure is associated with e.g. a two-fold higher level of DNA strand breaks. The

limitation of the RoM analysis is that it can only be used on data with the same sign, and the effect size depends on the baseline level of DNA strand breaks. To the best of our knowledge, there are no studies that have compared the consistency of meta-analyses on RoM and SMD outcomes on the same comet descriptors or a pooled descriptor as used in the present review. However, considering the inter-study heterogeneity in effect sizes, it is worthwhile to investigate alternative methods to the SMD in future meta-analyses.

4.5. Mechanisms of action and evidence of carcinogenicity

Evaluation of the scientific evidence has led the International Agency for Research on Cancer (IARC) to categorize outdoor air pollution, including traffic-related combustion sources, as carcinogenic to humans (Group 1) [93]. Indoor emission from household combustion of biomass/wood is evaluated as probably carcinogenic to humans (Group 2 A), whereas coal combustion has higher evidence of carcinogenicity (Group 1) [94]. The scientific evidence is also sufficiently strong to consider exposure during coke production as carcinogenic to humans (Group 1) [95]. These monographs follow a former preamble, where mechanistic considerations could either upgrade or downgrade classifications, based on epidemiological studies or long-term animal studies with tumour endpoints. The new preamble from 2019 integrates findings from epidemiology, animal models and mechanistic considerations in the final evaluation. Specifically, the 2019 preamble includes genotoxicity as a key characteristic for carcinogens, and consistent and coherent effects in exposed humans is considered strong mechanistic evidence [96,97]. For outdoor air pollution, biomass smoke and coal oven emissions, IARC highlights PAHs in emissions and a genotoxic mechanism of action as key characteristics of the exposures. The outdoor air pollution monograph highlights the mechanistic evidence including bulky DNA adducts (sometimes called PAH-DNA adducts), DNA strand breaks (mainly results on the comet assay), oxidatively damaged DNA bases, chromosome damage and mutations [93]. The monographs on wood/biomass emissions and coke production are not as elaborate as the outdoor air pollution monograph, focussing mainly on PAH-DNA adducts [94,95]. However, recent results from human biomonitoring studies support the notion that various chronic diseases, including cancer, are associated with increased levels of DNA strand breaks in leukocytes [91]. In addition, results from a prospective cohort study have demonstrated that a high level of DNA strand breaks is associated with an increased risk of mortality [92,98]. These findings support the notion that the generation of DNA strand breaks is relevant as a predictor of hard outcomes.

4.6. Overall summary

The present systematic review on DNA strand breaks in leukocytes in human biomonitoring studies shows that exposure to traffic-related exhausts, biomass combustion and coke oven emissions is associated with statistically significant effects in 37 (71 %) of 52 studies. The studies from middle-income countries have higher effect sizes than studies from high-income countries. This difference might be due to technical issues as studies from middle-income countries tend to have a higher risk of comet assay measurement bias than studies from high-income countries. However, it may also be related to higher exposure levels in middle-income countries (i.e. due to higher emissions and/or less use of personal protective equipment in occupational settings) and individual susceptibility to combustion-derived air pollutants (i.e. lifestyle and health differences between middle- and high-income countries).

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.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.mrrev.2025.108583.

Data availability

Data will be made available on request.

References

[1] C. Ladeira, P. Møller, L. Giovannell, G. Gajski, A. Haveric, E.E. Bankoglu, A. Azqueta, M. Geric, H. Stopper, J. Cabeda, F.S. Tonin, A. Collins, The comet assay as a tool in human biomonitoring studies of environmental and occupational exposure to chemicals - a systematic scoping review, Toxics 12 (2024) 270.

[2] A. Collins, P. Møller, G. Gajski, S. Vodenkova, A. Abdulwahed, D. Anderson, E. E. Bankoglu, S. Bonassi, E. Boutet-Robinet, G. Brunborg, C. Chao, M.S. Cooke, C. Costa, S. Costa, A. Dhawan, J. de Lapuente, C. Del Bo', J. Dubus, M. Dusinska, S. J. Duthie, N.E. Yamani, B. Engelward, I. Gaivao, L. Giovannelli, R. Godschalk, S. Guilherme, K.B. Gutzkow, K. Habas, A. Hernandez, O. Herrero, M. Isidori, A. N. Jha, S. Knasmuller, I.M. Kooter, G. Koppen, M. Kruszewski, C. Ladeira, B. Laffon, M. Larramendy, L.L. Hegarat, A. Lewies, A. Lewinska, G.E. Liwszyc, A.L. de Cerain, M. Manjanatha, R. Marcos, M. Milic, V.M. de Andrade, M. Moretti, D. Muruzabal, M. Novak, R. Oliveira, A.K. Olsen, N. Owiti, M. Pacheco, A.K. Pandey, S. Pfuhler, B. Pourrut, K. Reisinger, E. Rojas, E. Runden-Pran, J. Sanz-Serrano, S. Shaposhnikov, V. Sipinen, K. Smeets, H. Stopper, J.P. Teixeira, V. Valdiglesias, M. Valverde, F. van Acker, F.J. van Schooten, M. Vasquez, J.F. Wentzel, M. Wnuk, A. Wouters, B. Zegura, T. Zikmund, S.A.S. Langie, A. Azqueta, Measuring DNA modifications with the comet assay: a compendium of protocols, Nat. Protoc. 18 (2023) 929–989.

[3] B. Bincova, J. Lewtas, I. Miskova, P. Rössner, M. Cerná, G. Mráckova, K. Peterková, J. Mumford, S. Meyer, R. Sram, Biomarker studies in Northern Bohemia, Environ. Health Perspect. 4 (.3) (1996) 591–597.

[4] M. Valverde, A.D.L. Lopez, I. Lopez, I. Sanchez, T.I. Fortoul, P. Ostrosky-Wegman, E. Rojas, DNA damage in leukocytes and buccal and nasal epithelial cells of individuals exposed to air pullution in Mexico city, Environ. Mol. Mutagen 30 (1997) 147–152.

[5] L. Kazensky, K. Matkovic, M. Geric, B. Zegura, G. Pehnec, G. Gajski, Impact of indoor air pollution on DNA damage and chromosome stability: a systematic review, Arch. Toxicol. 98 (2024) 2817–2841.

[6] WHO (2021) WHO global air quality guidelines. Particulate matter (PM2.5 and PM10), ozone, nitrogen dioxide, sulfor dioxide and carbon monoxide. World Health Organization. https://www.who. int/publications/i/item/9789240034228, Geneva.

[7] P.J. Landrigan, R. Fuller, N.J.R. Acosta, O. Adeyi, R. Arnold, N.N. Basu, A.B. Balde, R. Bertollini, S. Bose-O'Reilly, J.I. Boufford, P.N. Breysse, T. Chiles, C. Mahidol, A. M. Coll-Seck, M.L. Cropper, J. Fobil, V. Fuster, M. Greenstone, A. Haines, D. Hanrahan, D. Hunter, M. Khare, A. Krupnick, B. Lanphear, B. Lohani, K. Martin, K.V. Mathiasen, M.A. McTeer, C.J.L. Murray, J.D. Ndahimananjara, F. Perera, J. Potocnik, A.S. Preker, J. Ramesh, J. Rockstrom, C. Salinas, L.D. Samson, K. Sandilya, P.D. Sly, K.R. Smith, A. Steiner, R.B. Stewart, W.A. Suk, O.C.P. van Schayck, G.N. Yadama, K. Yumkella, M. Zhong, The Lancet Commission on pollution and health, Lancet 391 (2018) 462–512.

[8] J. Lelieveld, A. Haines, R. Burnett, C. Tonne, K. Klingmuller, T. Munzel, A. Pozzer, Air pollution deaths attributable to fossil fuels: observational and modelling study, BMJ 383 (2023) e077784.

[9] V. Stone, M.R. Miller, M.J.D. Clift, A. Elder, N.L. Mills, P. Møller, R.P.F. Schins, U. Vogel, W.G. Kreyling, J.K. Alstrup, T.A.J. Kuhlbusch, P.E. Schwarze, P. Hoet, A. Pietroiusti, A. De Vizcaya-Ruiz, A. Baeza-Squiban, J.P. Teixeira, C.L. Tran, F. R. Cassee, Nanomaterials Versus Ambient Ultrafine Particles: An Opportunity to Exchange Toxicology Knowledge, Environ. Health Perspect. 125 (2017) 106002.

[10] P. Møller, P.H. Danielsen, D.G. Karottki, K. Jantzen, M. Roursgaard, H. Klingberg, D.M. Jensen, D.V. Christophersen, J.G. Hemmingsen, Y. Cao, S. Loft, Oxidative stress and inflammation generated DNA damage by exposure to air pollution particles, Mutat. Res. 762 (2014) 133–166.

[11] P. Møller, J.G. Hemmingsen, D.M. Jensen, P.H. Danielsen, D.G. Karottki, K. Jantzen, M. Roursgaard, Y. Cao, A. Kermanizadeh, H. Klingberg, D.

V. Christophersen, L. Hersoug, Ss Loft, Applications of the comet assay in particle toxicology: air pollution and engineered nanomaterials exposure, Mutagenesis 30 (2015) 67–83.
[12] M.H.G. Andersen, A.T. Saber, M. Frederiksen, P.A. Clausen, C.S. Sejbaek, C. H. Hemmingsen, N.E. Ebbehoj, J. Catalan, K. Aimonen, J. Koivisto, S. Loft, P. Møller, U. Vogel, Occupational exposure and markers of genetic damage, systemic inflammation and lung function: a Danish cross-sectional study among air force personnel, Sci. Rep. 11 (2021) 17998.
[13] K.R. Laursen, N.V. Christensen, F.A. Mulder, J. Schullehner, H.J. Hoffmann, A. Jensen, P. Møller, S. Loft, A.C. Olin, B.B. Rasmussen, B. Rosati, B. Strandberg, M. Glasius, M. Bilde, T. Sigsgaard, G. Climate Chamber, Airway and systemic biomarkers of health effects after short-term exposure to indoor ultrafine particles from cooking and candles - A randomized controlled double-blind crossover study among mild asthmatic subjects, Part Fibre Toxicol. 20 (2023) 26.
[14] P. Møller, S. Loft, Oxidative damage to DNA and lipids as biomarkers of exposure to air pollution, Environ. Health Perspect. 118 (2010) 1126–1136.
[15] P. Møller, A. Azqueta, E. Boutet-Robinet, G. Koppen, S. Bonassi, M. Milic, G. Gajski, S. Costa, J.P. Teixeira, P.C. Costa, M. Dusinska, R. Godschalk, G. Brunborg, K. B. Gutzkow, L. Giovannelli, M.S. Cooke, E. Richling, B. Laffon, V. Valdiglesias, N. Basaran, C. Del Bo', B. Zegura, M. Novak, H. Stopper, P. Vodicka, S. Vodenkova, V.M. de Andrade, M. Sramkova, A. Gabelova, A. Collins, S.A.S. Langie, Minimum Information for Reporting on the Comet Assay (MIRCA): recommendations for describing comet assay procedures and results, Nat. Protoc. 15 (2020) 3817–3826.
[16] M.H.G. Andersen, M. Frederiksen, A.T. Saber, R.S. Wils, A.S. Fonseca, I. K. Koponen, S. Johannesson, M. Roursgaard, S. Loft, P. Møller, U. Vogel, Health effects of exposure to diesel exhaust in diesel-powered trains, Part Fibre Toxicol. 16 (2019) 21.
[17] P.H. Avogbe, L. Ayi-Fanou, H. Autrup, S. Loft, B. Fayomi, A. Sanni, P. Vinzents, P. Møller, Ultrafine particulate matter and high-level benzene urban air pollution in relation to oxidative DNA damage, Carcinogenesis 26 (2005) 613–620.
[18] Y. Bagryantseva, B. Novotna, P., Jr Rossner, I. Chvatalova, A. Milcova, V. Svecova, Z. Lnenickova, I. Solansky, R.J. Sram, Oxidative damage to biological macromolecules in Prague bus drivers and garagemen: impact of air pollution and genetic polymorphisms, Toxicol. Lett. 199 (2010) 60–68.
[19] A. Barth, N. Brucker, A.M. Moro, S. Nascimento, G. Goethel, C. Souto, R. Fracasso, E. Sauer, L. Altknecht, B. da Costa, M. Duarte, C.B. Menezes, T. Tasca, M.D. Arbo, S. C. Garcia, Association between inflammation processes, DNA damage, and exposure to environmental pollutants, Environ. Sci. Pollut. Res Int 24 (2017) 353–362.
[20] E.V. Bräuner, L. Forchhammer, P. Møller, J. Simonsen, M. Glasius, P. Wåhlin, O. Raaschou-Nielsen, S. Loft, Exposure to ultrafine particles from ambient air and oxidative stress-induced DNA damage, Environ. Health Perspect. 115 (2007) 1177–1182.
[21] A. Carere, C. Andreoli, R. Galati, P. Leopardi, F. Marcon, M.V. Rosati, S. Rossi, F. Tomei, A. Verdena, A. Zijno, R. Crebelli, Biomonitoring of exposure to urban pollutants: analysis of sister chromatid exchanges and DNA lesions in peripheral lymphocytes of traffic policemen, Mutat. Res 518 (2002) 215–224.
[22] A. Cebulska-Wasilewska, A. Wiechec, A. Panek, B. Binkova, R.J. Sram, P.B. Farmer, Influence of environmental exposure to PAHs on the susceptibility of lymphocytes to DNA-damage induction and on their repair capacity, Mutat. Res. 588 (2005) 73–81.
[23] A. Cebulska-Wasilewska, I. Pawlyk, A. Panek, A. Wiechec, I. Kalina, T. Popov, T. Georgieva, P.B. Farmer, Exposure to environmental polycyclic aromatic hydrocarbons: influences on cellular susceptibility to DNA damage (sampling Kosice and Sofia), Mutat. Res. 620 (2007) 145–154.
[24] M. Chu, C. Sun, W. Chen, G. Jin, J. Gong, M. Zhu, J. Yuan, J. Dai, M. Wang, Y. Pan, Y. Song, X. Ding, X. Guo, M. Du, Y. Xia, H. Kan, Z. Zhang, Z. Hu, T. Wu, H. Shen, Personal exposure to PM2.5, genetic variants and DNA damage: a multi-center population-based study in Chinese, Toxicol. Lett. 235 (2015) 172–178.
[25] H. Duan, X. Jia, Q. Zhai, L. Ma, S. Wang, C. Huang, H. Wang, Y. Niu, X. Li, Y. Dai, S. Yu, W. Gao, W. Chen, Y. Zheng, Long-term exposure to diesel engine exhaust induces primary DNA damage: a population-based study, Occup. Environ. Med. 73 (2016) 83–90.
[26] G. Goethel, N. Brucker, A.M. Moro, M.F. Charao, R. Fracasso, A. Barth, G. Bubols, J. Durgante, S. Nascimento, M. Baierle, P.H. Saldiva, S.C. Garcia, Evaluation of genotoxicity in workers exposed to benzene and atmospheric pollutants, Mutat. Res Genet Toxicol. Environ. Mutagen 770 (2014) 61–65.
[27] J.G. Hemmingsen, K. Jantzen, P. Møller, S. Loft, No oxidative stress or DNA damage in peripheral blood mononuclear cells after exposure to particles from urban street air in overweight elderly, Mutagenesis 30 (2015) 635–642.
[28] J.G. Hemmingsen, P. Møller, K. Jantzen, B.A. Jonsson, M. Albin, A. Wierzbicka, A. Gudmundsson, S. Loft, J. Rissler, Controlled exposure to diesel exhaust and traffic noise - effects on oxidative stress and activation in mononuclear blood cells, Mutat. Res. 775 (2015) 66–71.
[29] M. Kianmehr, J. Hajavi, J. Gazeri, Assessment of DNA damage in blood lymphocytes of bakery workers by comet assay, Toxicol. Ind. Health 33 (2017) 726–735.
[30] G. Leon-Mejia, I. Luna-Rodriguez, C. Trindade, L. Oliveros-Ortiz, M. Anaya-Romero, J. Luna-Carrascal, N. Navarro-Ojeda, M. Ruiz-Benitez, K. Franco-Valencia, J. Da Silva, J.A.P. Henriques, A. Munoz-Acevedo, M. Quintana-Sosa, Cytotoxic and genotoxic effects in mechanics occupationally exposed to diesel engine exhaust, Ecotoxicol. Environ. Saf. 171 (2019) 264–273.
[31] B. Novotna, J. Topinka, I. Solansky, I. Chvatalova, Z. Lnenickova, R.J. Sram, Impact of air pollution and genotype variability on DNA damage in Prague policemen, Toxicol. Lett. 172 (2007) 37–47.
[32] E. Oh, H. Im, H.S. Kang, W. Jung, N.H. Won, E. Lee, D. Sul, Comparison of immunnological and genotoxicological parameters in automobile emission inspectors exposed to polycyclic aromatic hydrocarbons, Environ. Toxicol. Pharm. 21 (2006) 108–117.
[33] S.M. Piperakis, E. Petrakou, S. Tsilimigaki, Effects of air pollution and smoking on DNA damage of human lymphocytes, Environ. Mol. Mutagen 36 (2000) 243–249.
[34] R. Harnung Scholten, Y.J. Essig, M. Roursgaard, A. Jensen, A.M. Krais, L. Gren, K. Dierschke, A. Gudmundsson, A. Wierzbicka, Ps Møller, Inhalation of hydrogenated vegetable oil combustion exhaust and genotoxicity responses in humans, Arch. Toxicol. 95 (2021) 3407–3416.
[35] M. Shen, P. Bin, H. Li, X. Zhang, X. Sun, H. Duan, Y. Niu, T. Meng, Y. Dai, W. Gao, S. Yu, G. Gu, Y. Zheng, Increased levels of etheno-DNA adducts and genotoxicity biomarkers of long-term exposure to pure diesel engine exhaust, Sci. Total Environ. 543 (2016) 267–273.
[36] P. Vinzents, P. Møller, M. Sørensen, L.E. Knudsen, O. Hertel, F. Palmgren, B. Schibye, S. Loft, Personal exposure to ultrafine particles and oxidative DNA damage, Environ. Health Perspect. 113 (2005) 1485–1490.
[37] T. Cetkovic, A. Haveric, S. Behmen, M. Hadzic Omanovic, L. Caluk Klacar, A. Dzaferspahic, I. Durmisevic, M. Mehanovic, S. Haveric, A pilot biomonitoring study of air pollution in the urban area of Sarajevo, Bosnia and Herzegovina: genotoxicity assessment in buccal cells, Mutagenesis 38 (2023) 33–42.
[38] M. Geric, G. Pehnec, K. Matkovic, J. Rinkovec, I. Jakovljevic, R. Godec, S. Zuzul, I. Beslic, A. Cvitkovic, L. Delic, P. Wild, I. Guseva Canu, N.B. Hopf, G. Gajski, Air Pollution and Primary DNA Damage among Zagreb (Croatia) Residents: A Cross-Sectional Study, J. Xenobiot. 14 (2024) 368–379.
[39] P.T.L. Scheepers, D. Coggon, L.E. Knudsen, R. Anzion, H. Autrup, S. Bogovski, R. P. Bos, D. Dahmann, P. Farmer, E.A. Martin, V. Micka, V. Muzyka, H.G. Neumann, J. Poole, A. Schmidt-Ott, F. Seiler, J. Volf, I. Zwirner-Baier, BIOMarkers for occupational diesel exhaust exposure monitoring (BIOMODEM) - a study in underground mining, Toxicol. Lett. 134 (2002) 305–317.
[40] M. Sørensen, H. Autrup, O. Hertel, H. Wallin, L.E. Knudsen, S. Loft, Personal exposure to $PM_{2.5}$ and biomarkers of DNA damage, Cancer Epidemiol. Biomark. Prev. 12 (2003) 191–196.
[41] H. Tovalin, M. Valverde, M.T. Morandi, S. Blanco, L. Whitehead, E. Rojas, DNA damage in outdoor workers occupationally exposed to environmental air pollutants, Occup. Environ. Med 63 (2006) 230–236.
[42] I. Ullah, M. Zahid, M. Jawad, A. Arsh, Assessment of DNA damage and oxidative stress among traffic conductors and coal miners, Pak. J. Med Sci. 37 (2021) 499–502.
[43] P. Møller, L.E. Knudsen, G. Frentz, M. Dybdahl, H. Wallin, B.A. Nexø, Seasonal variation of DNA damage and repair in patients with non-melanoma skin cancer and referents with and without psoriasis, Mutat. Res 407 (1998) 25–34.
[44] P. Møller, H. Wallin, E. Holst, L.E. Knudsen, Sunlight induced DNA damage in human mononuclear cells, FASEB J. 16 (2002) 45–53.
[45] A. Abreu, C. Costa, P.E. Silva, S. Morais, P.M. do Carmo, A. Fernandes, D.A. V. Moraes, J.P. Teixeira, S. Costa, Wood smoke exposure of Portuguese wildland firefighters: DNA and oxidative damage evaluation. J Toxicol Environ Health A, In press, 2017.
[46] M.H.G. Andersen, A.T. Saber, P.A. Clausen, J.E. Pedersen, M. Løhr, A. Kermanizadeh, S. Loft, N. Ebbehøj, A.M. Hansen, P.B. Pedersen, I.K. Koponen, E. C. Nørskov, P. Møller, U. Vogel, Association between polycyclic aromatic hydrocarbon exposure and peripheral blood mononuclear cel DNA damage in human volunteers during fire extinction exercises, Mutagenesis 33 (2018) 105–115.
[47] P.H. Danielsen, E.V. Bräuner, L. Barregard, G. Sallsten, M. Wallin, R. Olinski, R. Rozalski, P. Møller, S. Loft, Oxidatively damaged DNA and its repair after experimental exposure to wood smoke in healthy humans, Mutat. Res 642 (2008) 37–42.
[48] L. Forchhammer, P. Møller, I.S. Riddervold, J. Bonlokke, A. Massling, T. Sigsgaard, S. Loft, Controlled human wood smoke exposure: oxidative stress, inflammation and microvascular function, Part Fibre Toxicol. 9 (2012) 7.
[49] A. Jensen, D.G. Karottki, J.M. Christensen, J.H. Bønløkke, T. Sigsgaard, M. Glasius, S. Loft, P. Møller, Biomarkers of oxidative stress and inflammation after wood smoke exposure in a reconstructed Viking Age house, Environ. Mol. Mutagen 55 (2014) 652–661.
[50] K. Miglani, S. Kumar, A. Yadav, N. Aggarwal, I. Ahmad, R. Gupta, A multibiomarker approach to evaluate the effect of polyaromatic hydrocarbon exposure on oxidative and genotoxic damage in tandoor workers, Toxicol. Ind. Health 35 (2019) 486–496.
[51] N.K. Mondal, B. Mukherjee, D. Das, M.R. Ray, Micronucleus formation, DNA damage and repair in premenopausal women chronically exposed to high level of indoor air pollution from biomass fuel use in rural India, Mutat. Res 697 (2010) 47–54.
[52] A.K. Pandey, M. Bajpayee, D. Parmar, S.K. Rastogi, N. Mathur, P.K. Seth, A. Dhawan, DNA damage in lymphocytes of rural Indian women exposed to biomass fuel smoke as assessed by the Comet assay, Environ. Mol. Mutagen 45 (2005) 435–441.
[53] A. Torres-Dosal, I.N. Perez-Maldonado, Y. Jasso-Pineda, R.I. Martinez Salinas, J. A. Alegria-Torres, F. Diaz-Barriga, Indoor air pollution in a Mexican indigenous community: evaluation of risk reduction program using biomarkers of exposure and effect, Sci. Total Environ. 390 (2008) 362–368.
[54] J. Panumasvivat, R. Sapbamrer, N. Sittitoon, S. Khacha-Ananda, W. Kiratipaisarl, W. Sirikul, W. Insian, P. Assavanopakun, Exploring the adverse effect of fine particulate matter (PM(2.5)) on wildland firefighters' pulmonary function and DNA damage, Sci. Rep. 14 (2024) 7932.

[55] Y. Chen, Y. Bai, J. Yuan, W. Chen, J. Sun, H. Wang, H. Liang, L. Guo, X. Yang, H. Tan, Y. Su, Q. Wei, T. Wu, Association of polymorphisms in AhR, CYP1A1, GSTM1, and GSTT1 genes with levels of DNA damage in peripheral blood lymphocytes among coke-oven workers, Cancer Epidemiol. Biomark. Prev. 15 (2006) 1703–1707.
[56] J. Cheng, S. Leng, H. Li, C. Huang, Y. Niu, L. Zhang, X. Liang, H. Lin, Y. Zheng, Suboptimal DNA repair capacity predisposes coke-oven workers to accumulate more chromosomal damages in peripheral lymphocytes, Cancer Epidemiol. Biomark. Prev. 18 (2009) 987–993.
[57] M. Gao, Y. Li, A. Zheng, X. Xue, L. Chen, Y. Kong, Lymphocyte oxidative stress/genotoxic effects are related to serum IgG and IgA levels in coke oven workers, ScientificWorldJournal 2014 (2014) 801346.
[58] G. Huang, H. Guo, T. Wu, Genetic variations of CYP2B6 gene were associated with plasma BPDE-Alb adducts and DNA damage levels in coke oven workers, Toxicol. Lett. 211 (2012) 232–238.
[59] S. Leng, J. Cheng, Z. Pan, C. Huang, Y. Niu, Y. Dai, B. Li, F. He, Y. Zheng, Associations between XRCC1 and ERCC2 polymorphisms and DNA damage in peripheral blood lymphocyte among coke oven workers, Biomarkers 9 (2004) 395–406.
[60] B. Marczynski, H.-P. Rihs, B. Rossbach, J. Hölzer, J. Angerer, M. Scherenberg, G. Hoffmann, T. Brüning, M. Wilhelm, Analysis of 8-oxo-7,8-dihydro-2′-deoxyguanosine and DNA strand breaks in white blood cells of occupationally exposed workers: comparison with ambient monitoring, urinary metabolites and enzyme polymorphisms, Carcinogenesis 23 (2002) 273–281.
[61] B. Marczynski, B. Pesch, M. Wilhelm, B. Rossbach, R. Preuss, J.U. Hahn, S. Rabstein, M. Raulf-Heimsoth, A. Seidel, H.P. Rihs, A. Adams, M. Scherenberg, A. Erkes, B. Engelhardt, K. Straif, H.U. Kafferlein, J. Angerer, T. Bruning, Occupational exposure to polycyclic aromatic hydrocarbons and DNA damage by industry: a nationwide study in Germany, Arch. Toxicol. 83 (2009) 947–957.
[62] E. Siwinska, D. Mielzynska, L. Kapka, Association between urinary 1-hydroxypyrene and genotoxic effects in coke oven workers, Occup. Environ. Med. 61 (2004) e10.
[63] J.H.M. van Delft, M.J.S.T. Steenwinkel, J.G. van Asten, N. de Vogel, T.C. D. Bruijntjes-Rozier, T. Schouten, P. Cramers, L. Maas, M.H. van Herwijnen, F. J. van Schooten, P.M.J. Hopmans, Biological monitoring the exposure to polycyclic aromatic hydrocarbons of coke oven workers in relation to smoking and genetic polymorphisms for *GSTM1* and *GSTT1*, Ann. Occup. Hyg. 45 (2001) 395–408.
[64] M. Wilhelm, G. Eberwein, J. Holzer, D. Gladtke, J. Angerer, B. Marczynski, H. Behrendt, J. Ring, D. Sugiri, U. Ranft, Influence of industrial sources on children's health - hot spot studies in North Rhine Westphalia, Germany, Int. J. Hyg. Environ. Health 210 (2007) 591–599.
[65] F. Wang, Y. He, H. Guo, J. Li, Y. Yang, Z. Wu, H. Zheng, T. Wu, Genetic variants of nucleotide excision repair genes are associated with DNA damage in coke oven workers, Cancer Epidemiol. Biomark. Prev. 19 (2010) 211–218.
[66] C. Xiao, S. Chen, J. Li, T. Hai, Q. Lu, E. Sun, R. Wang, R.M. Tanguay, T. Wu, Association of HSP70 and genotoxic damage in lymphocytes of workers exposed to coke-oven emission, Cell Stress Chaperon.. 7 (2002) 396–402.
[67] H. Zhang, X. Li, L. Ge, J. Yang, J. Sun, Q. Niu, Methylation of CpG island of p14 (ARK), p15(INK4b) and p16(INK4a) genes in coke oven workers, Hum. Exp. Toxicol. 34 (2015) 191–197.
[68] Z. Zhang, X. Xing, S. Jiang, C. Qiu, Z. Mo, S. Chen, L. Chen, Q. Wang, Y. Xiao, G. Dong, Y. Zheng, W. Chen, D. Li, Global H3K79 di-methylation mediates DNA damage response to PAH exposure in Chinese coke oven workers, Environ. Pollut. 268 (2021) 115956.
[69] J. Yu, M. Liu, Q. Fang, X. Zhang, Polycyclic aromatic hydrocarbons, long non-coding RNA expression, and DNA damage in coke oven workers, Environ. Sci. Pollut. Res. Int. 29 (2022) 57277–57286.
[70] P. Møller, L.E. Knudsen, S. Loft, H. Wallin, The comet assay as a rapid test in biomonitoring occupational exposure to DNA-damaging agents and effect of confounding factors, Cancer Epidemiol. Biomark. Prev. 9 (2000) 1005–1015.
[71] M. Valverde, E. Rojas, Environmental and occupational biomonitoring using the Comet assay, Mutat. Res 681 (2009) 93–109.
[72] P. Møller, D.M. Jensen, D.V. Christophersen, A. Kermanizadeh, N.R. Jacobsen, J. G. Hemmingsen, P.H. Danielsen, D.G. Karottki, M. Roursgaard, Y. Cao, K. Jantzen, H. Klingberg, L.G. Hersoug, S. Loft, Measurement of oxidative damage to DNA in nanomaterial exposed cells and animals, Environ. Mol. Mutagen 56 (2015) 97–110.
[73] A. Collins, G. Koppen, V. Valdiglesias, M. Dusinska, M. Kruszewski, P. Møller, E. Rojas, A. Dhawan, I. Benzie, E. Coskun, M. Moretti, G. Speit, S. Bonassi, The comet assay as a tool for human biomonitoring studies: The ComNet Project, Mutat. Res. 759 (2014) 27–39.
[74] A. Azqueta, C. Ladeira, L. Giovannelli, E. Boutet-Robinet, S. Bonassi, M. Neri, G. Gajski, S. Duthie, C. Del Bo', P. Riso, G. Koppen, N. Basaran, A. Collins, P. Møller, Application of the comet assay in human biomonitoring: An hCOMET perspective, Mutat. Res. 783 (2020) 108288.
[75] S. Vodenkova, A. Azqueta, A. Collins, M. Dusinska, I. Gaivao, P. Møller, A. Opattova, P. Vodicka, R.W.L. Godschalk, S.A.S. Langie, An optimized comet-based in vitro DNA repair assay to assess base and nucleotide excision repair activity, Nat. Protoc. 15 (2020) 3844–3878.
[76] P. Møller, E.E. Bankoglu, H. Stopper, L. Giovannelli, C. Ladeira, G. Koppen, G. Gajski, A. Collins, V. Valdiglesias, B. Laffon, E. Boutet-Robinet, H. Perdry, C. Del Bo', S.A.S. Langie, M. Dusinska, A. Azqueta, Collection and storage of human white blood cells for analysis of DNA damage and repair activity using the comet assay in molecular epidemiology studies, Mutagenesis 36 (2021) 193–211.
[77] P. Møller, L. Möller, R.W. Godschalk, G.D. Jones, Assessment and reduction of comet assay variation in relation to DNA damage: studies from the European Comet Assay Validation Group, Mutagenesis 25 (2010) 109–111.
[78] L. Forchhammer, C. Johansson, S. Loft, L. Möller, R.W. Godschalk, S.A. Langie, G. D. Jones, R.W. Kwok, A.R. Collins, A. Azqueta, D.H. Phillips, O. Sozeri, M. Stepnik, J. Palus, U. Vogel, H. Wallin, M.N. Routledge, C. Handforth, A. Allione, G. Matullo, J.P. Teixeira, S. Costa, P. Riso, M. Porrini, P. Møller, Variation in the measurement of DNA damage by comet assay measured by the ECVAG inter-laboratory validation trial, Mutagenesis 25 (2010) 113–123.
[79] C. Johansson, P. Møller, L. Forchhammer, S. Loft, R.W. Godschalk, S.A. Langie, S. Lumeij, G.D. Jones, R.W. Kwok, A. Azqueta, D.H. Phillips, O. Sozeri, M. N. Routledge, A.J. Charlton, P. Riso, M. Porrini, A. Allione, G. Matullo, J. Palus, M. Stepnik, A.R. Collins, L. Möller, An ECVAG trial on assessment of oxidative damage to DNA measured by the comet assay, Mutagenesis 25 (2010) 125–132.
[80] C. Ersson, P. Møller, L. Forchhammer, S. Loft, A. Azqueta, R.W.L. Godschalk, F. J. van Schooten, G.D.D. Jones, J.A. Higgins, M.S. Cooke, V. Mistry, M. Karbaschi, D.H. Phillips, O. Sozeri, M.N. Routledge, K. Nelson-Smith, P. Riso, M. Porrini, G. Matullo, A. Allione, M. Stepnik, M. Ferlinska, J.P. Teixeira, S. Costa, L. A. Corcuera, A.L. de Cerain, B. Laffon, V. Valdiglesias, A.R. Collins, L. Möller, An ECVAG inter-laboratory validation study of the comet assay: inter- and intra-laboratory variation of DNA strand breaks and FPG-sensitive sites in human mononuclear cells, Mutagenesis 28 (2013) 279–286.
[81] L. Forchhammer, C. Ersson, S. Loft, L. Möller, R.W. Godschalk, F.J. van Schooten, G.D. Jones, J.A. Higgins, M. Cooke, V. Mistry, M. Karbaschi, A.R. Collins, A. Azqueta, D.H. Phillips, O. Sozeri, M.N. Routledge, K. Nelson-Smith, P. Riso, M. Porrini, G. Matullo, A. Allione, M. Steepnik, M. Komorowska, J.P. Teixeira, S. Costa, L.A. Corcuera, A.L. de Cerain, B. Laffon, V. Valdiglesias, P. Møller, Inter-laboratory variation in DNA damage using a standard comet assay protocol, Mutagenesis 27 (2012) 665–672.
[82] R.W. Godschalk, C. Ersson, P. Riso, M. Porrini, S.A. Langie, F.J. van Schooten, A. Azqueta, A.R. Collins, G.D. Jones, R.W. Kwok, D.H. Phillips, O. Sozeri, A. Allione, G. Matullo, L. Möller, L. Forchhammer, S. Loft, P. Møller, DNA-repair measurements by use of the modified comet assay: an inter-laboratory comparison within the European Comet Assay Validation Group (ECVAG), Mutat. Res. 757 (2013) 60–67.
[83] R.W. Godschalk, C. Ersson, M. Stepnik, M. Ferlinska, J. Palus, J.P. Teixeira, S. Costa, G.D. Jones, J.A. Higgins, J. Kain, L. Möller, L. Forchhammer, S. Loft, Y. Lorenzo, A.R. Collins, F.J. van Schooten, B. Laffon, V. Valdiglesias, M. Cooke, V. Mistry, M. Karbaschi, D.H. Phillips, O. Sozeri, M.N. Routledge, K. Nelson-Smith, P. Riso, M. Porrini, C.A. Lopez de, A. Azqueta, G. Matullo, A. Allione, P. Møller, Variation of DNA damage levels in peripheral blood mononuclear cells isolated in different laboratories, Mutagenesis 29 (2014) 241–249.
[84] P. Møller, D. Muruzabal, T. Bakuradze, E. Richling, E.E. Bankoglu, H. Stopper, S.A. S. Langie, A. Azqueta, A. Jensen, F. Scavone, L. Giovannelli, M. Wojewodzka, M. Kruszewski, V. Valdiglesias, B. Laffon, C. Costa, S. Costa, J.P. Teixeira, M. Marino, C. Del Bo', P. Riso, S. Shaposhnikov, A. Collins, Potassium bromate as positive assay control for the Fpg-modified comet assay, Mutagenesis 35 (2020) 341–348.
[85] P. Møller, A. Azqueta, M. Collia, T. Bakuradze, E. Richling, E.E. Bankoglu, H. Stopper, V.C. Bastos, S.A.S. Langie, A. Jensen, S. Ristori, F. Scavone, L. Giovannelli, M. Wojewodzka, M. Kruszewski, V. Valdiglesias, B. Laffon, C. Costa, S. Costa, J.P. Teixeira, M. Marino, C. Del Bo, P. Riso, C. Zhang, S. Shaposhnikov, A. Collins, Inter-laboratory variation in measurement of DNA damage by the alkaline comet assay in the hCOMET ring trial, Mutagenesis 38 (2023) 283–294.
[86] P. Møller, A. Azqueta, A. Rodriguez-Garraus, T. Bakuradze, E. Richling, E. E. Bankoglu, H. Stopper, V.C. Bastos, S.A.S. Langie, A. Jensen, F. Scavone, L. Giovannelli, M. Wojewodzka, M. Kruszewski, V. Valdiglesias, B. Laffon, C. T. Costa, S. Costa, J.P. Teixeira, M. Marino, C. Del Bo, P. Riso, C. Zheng, S. Shaposhnikov, A. Collins, DNA strand break levels in cryopreserved mononuclear blood cell lines measured by the alkaline comet assay: results from the hCOMET ring trial, Mutagenesis 38 (2023) 273–282.
[87] P. Møller, A. Azqueta, J. Sanz-Serrano, T. Bakuradze, E. Richling, E.E. Bankoglu, H. Stopper, V.C. Bastos, S.A.S. Langie, A. Jensen, F. Scavone, L. Giovannelli, M. Wojewodzka, M. Kruszewski, V. Valdiglesias, B. Laffon, C.T. Costa, S. Costa, J. P. Teixeira, M. Marino, C. Del Bo, P. Riso, C. Zheng, S. Shaposhnikov, A. Collins, Visual comet scoring revisited: a guide to scoring comet assay slides and obtaining reliable results, Mutagenesis 38 (2023) 253–263.
[88] P. Møller, A. Azqueta, A. Rodriguez-Garraus, T. Bakuradze, E. Richling, E. E. Bankoglu, H. Stopper, V.C. Bastos, S.A.S. Langie, A. Jensen, S. Ristori, F. Scavone, L. Giovannelli, M. Wojewodzka, M. Kruszewski, V. Valdiglesias, B. Laffon, C. Costa, S. Costa, J.P. Teixeira, M. Marino, C. Del Bo, P. Riso, C. Zhang, S. Shaposhnikov, A. Collins, Long-term cryopreservation of potassium bromate positive assay controls for measutement of oxidatively damaged DNA by the Fpg-modified comet assay, Mutagenesis 38 (2023) 264–272.
[89] P. Møller, G. Gajski, M. Geric, L. Giovannell, A. Azqueta, A. Haveric, H. Stopper, E. E. Bankoglu, A. Collins, C. Ladeira, The comet assay as a tool in human biomonitoring studies: effcets of confounding factors, Mutat. Res Rev. Mutat. Res (2025) 108566.
[90] M. Milic, A. Frustaci, B.A. Del, J. Sanchez-Alarcon, R. Valencia-Quintana, P. Russo, S. Bonassi, DNA damage in non-communicable diseases: A clinical and epidemiological perspective, Mutat. Res 776 (2015) 118–127.
[91] P. Møller, H. Stopper, A.R. Collins, Measurement of DNA damage with the comet assay in high-prevalence diseases: current status and future directions, Mutagenesis 35 (2020) 5–18.
[92] S. Bonassi, M. Ceppi, P. Møller, A. Azqueta, M. Milic, N. Monica, G. Brunborg, R. Godschalk, G. Koppen, S.A.S. Langie, J.P. Teixeira, M. Bruzzone, J. Da Silva, D. Benedetti, D. Cavallo, C.L. Ursini, L. Giovannelli, S. Moretti, P. Riso, C. Del Bo', P. Russo, M. Dobrzynska, I.A. Goroshinskaya, E.I. Surikova, M. Staruchova, M. Barancokova, K. Volkovova, A. Kazimirova, B. Smolkova, B. Laffon,

V. Valdiglesias, S. Pastor, R. Marcos, A. Hernandez, G. Gajski, B. Spremo-Potparevic, L. Zivkovic, E. Boutet-Robinet, H. Perdry, P. Lebailly, C.L. Perez, N. Basaran, Z. Nemeth, A. Safar, M. Dusinska, A. Collins, h C.p, DNA damage in circulating leukocytes measured with the comet assay may predict the risk of death, Sci. Rep. 11 (2021) 16793.

[93] IARC (2016) IARC Monographs on the evaluation of carcinogenic risk to humans. Outdoor Air Pollution. Vol 109. IARC, Lyon, France.

[94] IARC (2010) IARC Monographs on the evaluation of carcinogenic risk to humans. Household use of solid fuels and high-temperature frying. Vol 95. IARC, Lyon, France.

[95] IARC (2012) IARC Monographs on the evaluation of carcinogenic risk to humans. Chemical agents and related occupations. Vol 100F. IARC, Lyon, France.

[96] IARC (2019) Monographs on the evaluation of carcinogenic risk to humans. Preamble. Lyon, France.

[97] IARC (2025) Key characteristics-associated end-points for evaluating mechsnistic evidence of carcinogenic hazard. IARC, Lyon, France.

[98] M. Milic, M. Ceppi, M. Bruzzone, A. Azqueta, G. Brunborg, R. Godschalk, G. Koppen, S. Langie, P. Møller, J.P. Teixeira, A.A. Alija, D. Anderson, V. Andrade, C. Andreoli, F. Asllani, E.E. Bangkoglu, M. Barančoková, N. Basaran, E. Boutet-Robinet, A. Buschini, D. Cavallo, C.C. Pereira, C. Costa, S. Costa, J. Da Silva, C. Del Bo', V.D. Srećković, N. Djelić, M. Dobrzyńska, Z. Duračková, M. Dvořáková, G. Gajski, S. Galatiz, O.G. Lima, L. Giovannell, I.A. Goroshinskaya, A. Grindel, K. B. Gutzkowe, A. Hernández, C. Hernández, K.B. Holven, I. Ibero-Baraibar, I. Ottestad, E. Kadioglu, A. Kažimirová, W. Kuznetsova, C. Ladeira, B. Laffon, P. Lamonaca, P. Lebailly, H. Louro, T.M. Cardoso, F. Marcon, R. Marcos, M. Moretti, S. Moretti, M. Najafzadeh, Z. Nemeth, M. Neri, B. Novotna, I. Orlowaw, Z. Paduchova, S.P. Pastor, H. Spremo-Potparevic, B. Ramadhani, D. Riso, P. Rohr, P. Rojas, E. Rossner, P. Safar, A. Sardas, S. Silva, M.J. Sirota, N. Smolkova, B. Staruchova, M. Stetina, R. Stopper, H. Surikova, E.I. Ulven, S.M. Ursini, C. L. Valdiglesia, V. Valverde, M. Vodicka, P. Volkovova, K. Wagner, K.H. Zivković, L. Dušinská, M. Collins, A.R, Ss Bonassi, The hCOMET project: International database comparison of results with the comet assay in human biomonitoring. Baseline frequency of DNA damage and effect of main confounders, Mutat. Res. 787 (2021) 108371.