Risk of Skin Cancer in Workers Exposed to Diesel Exhaust: A Systematic Review and Meta-Analysis of Cohort Studies

Marika D'Agostini[1], Giulia Collatuzzo[1], Federica Teglia[1], Paolo Boffetta[1,2,*]

[1]Department of Medical and Surgical Sciences, University of Bologna, Bologna, Italy
[2]Stony Brook Cancer Center, Stony Brook University, Stony Brook, NY, USA

Abstract

Background: *Our objective was to study the association between occupational exposure to diesel exhaust (DE) and skin cancer.* **Methods:** *A systematic review following STROBE guidelines and PECOS criteria was conducted to identify cohort studies describing the association between occupational DE exposure and the risk of skin cancer. We extracted 12 independent risk estimates for melanoma skin cancer (MSC), 8 for non-melanoma skin cancer (NMSC), and 3 for skin cancer not otherwise specified (SC-NOS). Random effects meta-analyses were performed, site-specific and stratified by geographic region and quality score. 95% confidence intervals (CI) were reported. Between-study heterogeneity and potential publication bias were investigated.* **Results:** *There was no overall evidence of an increased risk of MSC [RR=0.90, 95% CI: 0.73-1.11; I²=92.86%, 95% CI: 82.83-97.03%], NMSC [RR=1.04, 95% CI: 0.88-1.23; I²=60.79%, 95% CI: 0-87.34%] or SC-NOS [RR=0.72, 95% CI: 0.54-0.97; I²=26.60%, 95% CI: 0-94.87%] in workers exposed to DE. No difference between low-quality and high-quality studies was found. A stratified analysis by geographical region did not reveal any significant differences. There was no evidence of publication bias.* **Conclusions:** *No evidence of an association between skin cancer and occupational DE exposure was found. Residual confounding and other sources of bias cannot be ruled out.*

1. Introduction

Diesel engines have many industrial applications, including on- and off-road equipment used in railroad, mining, construction, agriculture, transportation, and manufacturing operations [1]. The exhaust from diesel engines contains a mixture of gases, vapors, aerosols, and particulate matter that can create a health hazard when not properly controlled. Short-term exposure to high concentrations of diesel exhaust (DE) can cause eye, nose, throat, and lung irritation, headache, dizziness, coughing, phlegm, and nausea. In contrast, prolonged exposure can increase the risk of cardiovascular diseases, respiratory infections, and lung cancer.

In 2012, the International Agency for Research on Cancer (IARC) classified DE as a Group 1 carcinogen based on sufficient evidence in epidemiological studies that occupational exposure is associated with increased risk for lung cancer [2]. DE is also suspected to be linked to other cancers, including cancers of the bladder, larynx, hematolymphopoietic system, stomach, and ovary [3-6]. However, its carcinogenicity in humans has not yet been fully

investigated since DE knowledge is relatively recent and based primarily on lung cancer studies [2].

Occupational risk factors for skin cancer include exposure to chemical carcinogens such as polycyclic aromatic hydrocarbons (PAH) and arsenic [7]. While there is also evidence in the scientific literature of an association between occupational exposure to ionizing and solar radiation and risk of skin cancer [8-10], it is not yet clear if DE exposure can also be considered an occupational risk factor for skin cancer.

This systematic review and meta-analysis aimed to investigate the association between occupational exposure to DE and the risk of all types of skin cancer (SC), including melanoma skin cancer (MSC) and non-melanoma skin cancer (NMSC).

2. Methods

2.1 Identification and Selection of Studies

We carried out a systematic review and reported it herein following the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [11]. The study protocol was registered in the PROSPERO database (Registration No. 352729). To be included in the systematic review, studies had to meet the criteria based on the elements of the review questions PECOS (Population, Exposure, Comparators, Outcomes, Study Design) [12].

The review was restricted to industrial cohort studies. We included all the publications cited in the most recent IARC Monograph on DE [1]. Two authors also independently searched the PubMed database to include all studies reporting results on occupational exposure to DE and risk of any type of cancer other than lung cancer, reported after IARC publication, for which a causal association with DE exposure has already been established. The search query used the string "(diesel OR miner OR garage OR railway OR ((truck OR bus) AND driver) OR (heavy equipment OR docker)) AND (cancer OR neoplasm)" to identify industry-based studies on cancer among workers exposed to DE. Reports found in the reference lists of the articles identified in the aforementioned steps were also used to

complement the search. When several studies based on the same population were published, we only included the most insightful one (typically, the one that provided the largest number of cases or fatalities), and studies with modest overlap (i.e., less than 10%) were considered independent. Finally, we excluded research that did not mention DE exposure, had non-occupational exposure, lacked information on cancers other than lung cancer, and had a different design than cohort or case-control nested in the cohort.

2.2 Data Extraction

Data was collected and organized into predefined forms. The studies yielded the following information: (i) sociodemographic factors; (ii) occupation and industry type; (iii) person-years of observation; (iv) type of cancer – including ICD code with version; (v) measure of association – odds ratio (OR), risk ratio, rate ratio, standardized mortality ratio (SMR), or standardized incidence ratio (SIR), henceforth referred to as relative risk (RR), and 95% Confidence Intervals (CI); (vi) factors adjusted for in the analysis; (vii) characteristics of the study population (e.g., number of subjects included, number of cases). The dataset was then categorized based on the type of cohort study (historical or prospective), the duration of follow-up, geographic region, and the outcome (incidence or mortality). If available, we also gathered data on dose-response analysis for various indicators of DE exposure. However, there was insufficient information for the skin cancer meta-analysis to provide results related to dose-response or specific details regarding the type of DE exposure in the workplace.

2.3 Statistical Analysis

The quality assessment of the studies included in the meta-analysis was done independently by two authors (GC e FT) based on the CASP checklist. [13] The CASP assessment was based on 11 items for 14 points, and the final score was given by the mean of the results obtained by the two authors. A dichotomous variable for CASP assessment was then generated, considering studies that scored less

than 10 as "low quality" and those that scored 10 or more as "high quality".

A series of meta-analyses of non-overlapping studies were conducted to calculate pooled estimates with 95% CI for SC-NOS, MSC, and NMSC. Stratified meta-analyses by geographical region and quality score have also been performed. Further stratified analysis by outcome (incidence and mortality), sex, and industry type could not be conducted due to the small number of studies involved. The random-effects model described by Sidik and Jonkman was used for analysis. [14] RRs were reported with 95% CI, and p-value <0.05 was considered statistically significant. Additionally, we perform sensitivity analyses using multiple leave-one-out meta-analyses. Study heterogeneity was assessed using the inconsistency index (I^2 statistic and relative 95% CI [15]) with values of 0-30%, 31%-60%, 61%-75%, and 76%-100%, indicating low, moderate, substantial, and considerable heterogeneity, respectively [16]. Cochran's Q_b statistic for a test of group differences was used in the stratified analyses [17]. Finally, we assessed publication bias by performing the Egger test and by visually inspecting the funnel plots [18] and the Galbraith plots [19].

All the statistical analyses were performed on STATA, version 17.0 (Stata Corp., College Station, TX, US) [20]. Meta-analyses were reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [11]. PRISMA checklist is available in Table S1.

3. RESULTS

3.1 Study Search and Study Characteristics

First, the systematic review comprised 19 papers that were included in the IARC monograph [2]. 2062 articles resulted from the PubMed literature search to include studies published after the IARC monograph's release. 1982 articles were excluded based on the publications' titles and abstracts, and 78 were excluded after reviewing the entire text. As a result, 9 non-overlapping reports found in the reference lists of the papers found in the previous steps were added to the review along with 2 new studies.

A final number of 30 articles underwent full review, and 11 of them were included in the final analysis regarding skin cancer. Of those, 8 studies provided data on MSC (12 risk estimates), 5 for NMSC (8 risk estimates) and 3 for SC-NOS (3 risk estimates) (Figure 1). Six studies were performed in the United States, 3 in Sweden, and 1 each in Nordic countries combined, Canada, Denmark, and Finland. Further selected characteristics of the studies included in the review and meta-analysis are presented in Table 1.

3.2 Melanoma Skin Cancer

This meta-analysis included 7 studies, corresponding to 12 incidence risk estimates. The forest plot is shown in Figure 2. Overall, the risk of MSC was 0.90 (95% CI: 0.73-1.11). The leave-one-out meta-analysis revealed that no study had a larger influence on the estimation of the overall effect size than the others (Figure S1). The reported inconsistency index I^2 was 92.86% (95% CI: 82.83-97.03), indicating considerable heterogeneity [16]. The between-study variance τ^2 is estimated to be 0.08. The Egger test for publication bias was not significant (p=0.72). The corresponding funnel plot and Galbraith plot are reported in Figures S2 and Figure S3. Table 2 shows the results of the stratified analyses. No significant difference was detected between studies with a quality score greater or equal to 10 and those with a quality score less than 10 (Q_b=1.43; p=0.23). Stratified analysis by geographical region did not reveal any significant difference (Q_b=0.02; p=0.84).

3.3 Non-Melanoma Skin Cancer

This meta-analysis included 5 studies, corresponding to 8 incidence risk estimates. The forest plot is shown in Figure 2. Overall, the risk of NMSC was 1.04 (95% CI: 0.88-1.23). The leave-one-out meta-analysis revealed that no study had a larger influence on the estimation of the overall effect size compared with the others (Figure S4). The reported inconsistency index I^2 was 60.79% (95% CI: 0-87.34), indicating a moderate heterogeneity [16]. The between-study variance τ^2 is estimated to
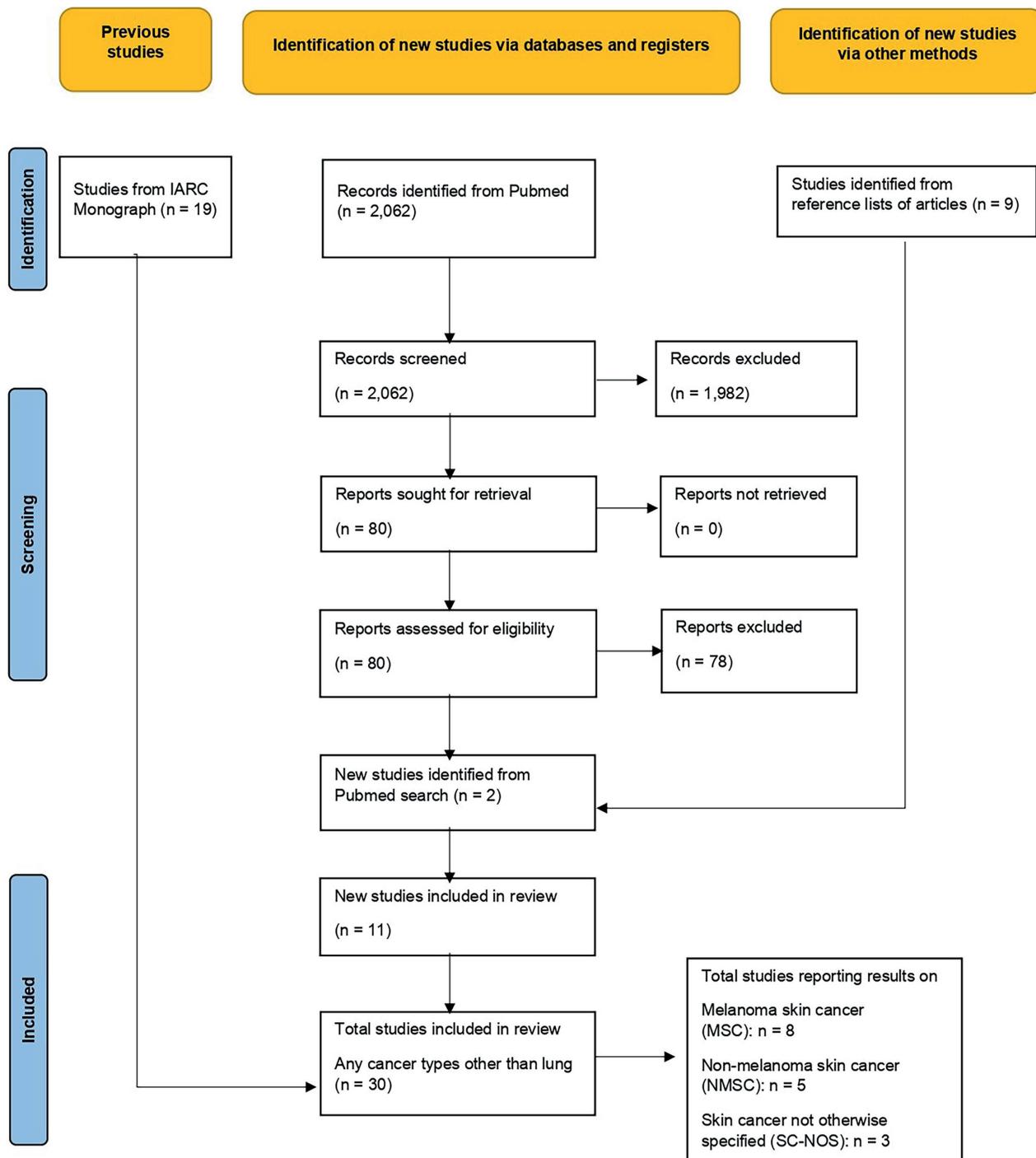
Figure 1. Flow diagram of the study selection process.

be 0.02. The Egger test for publication bias was not significant (p=0.65). The corresponding funnel plot and Galbraith plot are reported in Figures S5 and S6. Stratified analyses by geographical region could not be performed since all studies were conducted in Europe, while stratified analysis by quality score did not reveal any significant difference (Q_b=1.64; p=0.20).

Table 1. Selected characteristics of the studies included in the review and meta-analysis.

Study	Cancer Type	Country	Cohort Type	Follow-Up	Population	Person-years	Industry	Number of cases	Adjustments	CASP Assessment
[3]	MSC NMSC	Denmark	Retrospective Prospective	1943-92	16 023 men 1967 women	386 395	Bus drivers and tramway employers	MSC (Female): 11 MSC (Male): 255 NMSC (Female): 9 NMSC (Male): 219	-	9.5 – Low Quality
[21]	SC-NOS	Canada	Prospective	1965-77	43 826	290 186	Railroad	SC-NOS: 25	-	9 – Low Quality
[22]	SC-NOS	USA	Prospective	1964-78	34 156	372 525.6	Construction equipment operators	SC-NOS: 16	Age, calendar time	7.5 – Low Quality
[23]	MSC	USA	Prospective	1982-1987	461 981	939817	Railroad workers	MSC: 11	Sex, SES, smoking, BMI	10 – High Quality
[24]	MSC NMSC	Sweden	Prospective	1952-86 (mortality) 1958-84 (incidence)	695	21317.5 (mortality) 16695 (incidence)	Bus garage workers	MSC: 5 NMSC: 2	Occupational activity	9.75 – Low Quality
[25]	MSC	USA	Retrospective	1964-88	160 230	-	People of the KPMCP with self-reported exposure, no job or industry titles	MSC: 252	-	12 – High Quality
[26]	MSC NMSC	Finland	Retrospective	1953-91	212 800	8391	Locomotive drivers	MSC: 17 NMSC: 32	-	9 – Low Quality
[27]	MSC	Sweden	Prospective	1971-89	Employed Swedish adult population	Over 7640000 (exposed men) Over 240000 (exposed women)	Different job and industry titles (farmers excluded)	MSC (Female): 37 MSC (Male): 1272	-	11 – High Quality
[28]	MSC NMSC	Sweden	Prospective	1971-95	14364 Heavy construction equipment operators 6364 Truck drivers	-	(1) Heavy construction equipment operators (2) Truck drivers	MSC (1): 31 MSC (2): 14 NMSC (1): 28 NMSC (2): 19	Smoking	11.25 – High Quality
[29]	MSC NMSC	Denmark Finland Iceland Norway Sweden	Prospective	1961-2005	15 million (NOCCA cohort)	385 million	Engine operators	MSC (Female): 20 MSC (Male): 789 NMSC (Female): 16 NMSC (Male): 969	Age	12.75 – High Quality
[30]	SC-NOS	USA	Prospective	1989-2004	156 241	-	Truck drivers	SC-NOS: 30	Smoking	9.25 – Low Quality

SC-NOS: skin cancer not otherwise specified; MSC: melanoma skin cancer; NMSC: non-melanoma skin cancer; NEC: not elsewhere classified; SES: socio-economic status; BMI: body mass index; NOCCA: Nordic Occupational Cancer; KPMCP: Kaiser Permanente Medical Care Program.
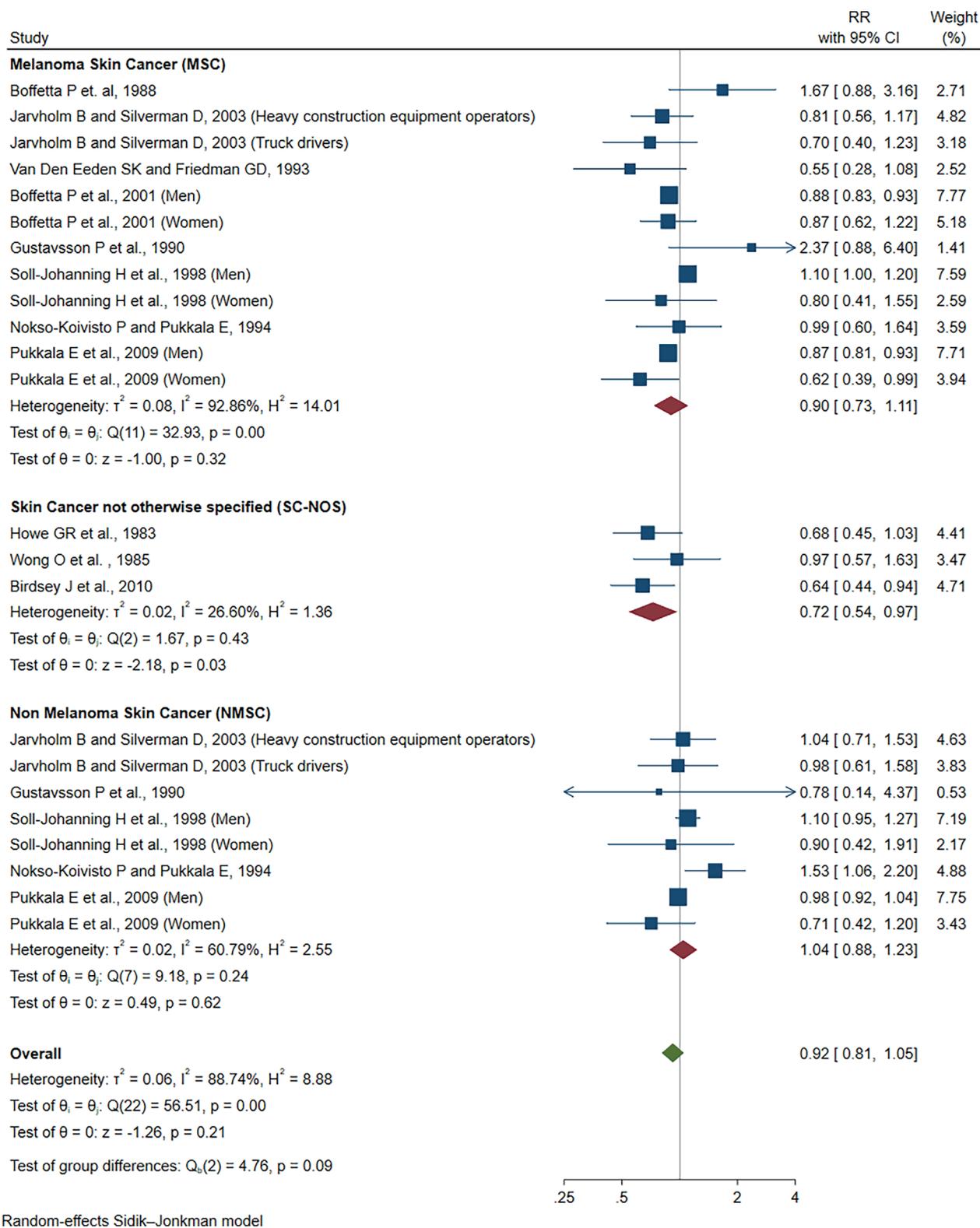
Figure 2. Forest plot of a meta-analysis of cohort studies on occupational exposure to diesel exhaust and skin cancer.

Table 2. Results of the metanalyses on the different skin cancers by geographic region and quality score.

Characteristic	Number of risk estimates	RR [95% CI]	Test of group Differences Q_b
MELANOMA SKIN CANCER (MSC)			
Geographic region			
North America	2	0.96 [0.34; 2.73]	0.02 (p = 0.84)
Europe	10	0.89 [0.74; 1.06]	
Quality score			
< 10	4	1.10 [0.73; 1.65]	1.43 (p = 0.23)
≥ 10	8	0.83 [0.67; 1.03]	
NON-MELANOMA SKIN CANCER (NMSC)			
Geographic region			
North America	-	-	-
Europe	8	1.04 [0.88; 1.23]	
Quality score			
< 10	4	1.18 [0.90; 1.54]	1.64 (p = 0.20)
≥ 10	4	0.96 [0.82; 1.13]	
SKIN CANCER – NOT OTHERWISE SPECIFIED (SC-NOS)			
Geographic region			
North America	3	**0.72 [0.54; 0.97]**	-
Europe	-	-	
Quality score			
< 10	3	**0.72 [0.54; 0.97]**	-
≥ 10	-	-	

3.4 Skin Cancer Not Otherwise Specified

This meta-analysis included 3 studies where the type of skin cancer was not specified, corresponding to 3 incidence risk estimates. The forest plot is shown in Figure 2. Overall, the risk of SC-NOS was 0.72 (95% CI: 0.54-0.97). The leave-one-out meta-analysis revealed that omitting the Howe GR et al. 1983 study [21] or the Birdsey J et al. 2010 study [30] causes the risk estimate to be no more significant (Figure S7). The reported inconsistency index I^2 was 26.60% (95% CI: 0-94.87). Even though the I^2 point estimate suggests low heterogeneity across the studies [16], the wide 95% confidence interval indicates substantial uncertainty around this estimate, suggesting that the true level of heterogeneity could potentially range from minimal to considerable. The between-study variance τ^2 is estimated to be 0.02.

The Egger test for publication bias was not significant (p=0.20). The corresponding funnel plot and Galbraith plot are reported in Figures S8 and S9. Stratified analyses by geographical region and quality score could not be performed since all studies were conducted in North America and had a quality score lower than 10.

4. Discussion

This systematic review and meta-analysis of cohort studies investigated occupational exposure to DE and skin cancer risk. DE contains a complex mixture of chemicals, including PAHs and other potentially carcinogenic substances such as nitroarenes, benzene and formaldehyde, some of which have been linked to hyperkeratosis and dermatitis in humans [31-33], and to skin cancer in animal studies [34, 35].

Individuals with prolonged occupational exposure to DE, such as workers in industries like transportation or mining, may experience higher levels of skin contact with such substances. This prolonged and direct exposure could contribute to an increased risk of skin cancer since if carcinogens penetrate the skin barrier, they could potentially induce DNA damage or other cancer-promoting effects [36, 37]. Higher levels of PAH biomarkers have been detected in non-smoking workers exposed to DE and lubricating oil, suggesting the role of skin absorption in DE toxicology [38].

While we found no overall association between occupational DE exposure and skin cancer, an inverse relationship between occupational DE exposure and SC-NOS was suggested in site-specific analyses.

UV radiation is considered a skin carcinogen, which relates to work in the context of outdoor occupations [9]. However, we found evidence of a decreased risk of skin cancer in studies considering any type of SC-NOS. One might speculate that the reduced risk in workers exposed to DE might be related, for example, to the lack of solar exposure. It must be pointed out that we were not able to account for ultraviolet radiation exposure, and we did not have detailed information on the type of work activities of the populations of this meta-analysis, because the included studies did not report such data. Moreover, only 3 incidence risk estimates were available in studies with quality scores less than 10, limiting the power of the analysis. Also, the dispersion of true effect sizes addressed by the PI, which crossed the no-effect threshold, indicates that there are contexts where DE exposure has no effect or even an effect in the opposite direction on SC-NOS [15].

The importance of latency effects and other time-related factors, such as age at exposure, in determining cancer risk has long been acknowledged [39-40]. We restricted the meta-analysis to cohort studies since they provide higher-quality data and less opportunity for bias. This choice also resulted in the analysis of only long-term data, reducing the possibility of missing incident cases in the study populations.

It must also be pointed out that MSC and NMSC differ importantly in their epidemiology and known causes, and it is crucial to acknowledge and interpret the results with consideration to the distinct characteristics and risk factors associated with the two types of skin cancer. While UV exposure is a common risk factor for both types, MSC is often associated with intense, intermittent sun exposure, while NMSCs are linked to cumulative sun exposure [41, 42]. We decided however to combine them in a composite outcome, together with SC-NOS, for several reasons. First of all, pooling data from all three types of skin cancer increases the sample size, enhancing statistical power and the ability to detect significant associations. It also allows for a comprehensive examination of overall skin cancer risk, providing a more global view of the impact of DE. Finally, the focus of our analysis is on general skin cancer prevention and risk factors rather than specific cancer types.

4.1 Strengths and Limitations

This study has several strengths. To our knowledge, this is the first systematic review to investigate the association between occupational DE exposure and the risk of skin cancer. We focused on cohort studies since they provide higher-quality data compared to case-control or cross-sectional studies. Also, we focused on a specific working population that experiences higher levels of DE exposure than other working groups. Moreover, data collection included the working categories more likely to be exposed to DE. Regarding the statistical methods, we used the Random-Effects Sidik–Jonkman model [14] rather than the most popular DerSimonian–Laird method [43] due to the known tendency of the latter to underestimate the between-study variance τ^2 when the number of studies is small [44]. Finally, the meta-analysis was performed following solid methodological guidelines, considering the quality of the involved studies, and testing for possible publication bias.

However, the results should be interpreted cautiously, as some limitations should be acknowledged in addition to those inherent in meta-analyses. Firstly, the studies were heterogeneous in terms of the working population considered exposed, time period, and region of studies, and sample sizes were

variable. The small number of studies available for each meta-analysis also led to imprecise estimates of the heterogeneity, measured using the I^2 index. Further, we could not provide results by certain characteristics such as sex and industry type because data were insufficient, and only two studies adjusted for important confounders such as age. Secondly, differences in the definition of DE exposure and of the worker population involved might introduce misclassification, leading to bias in an unpredictable direction. Also, the lack of available dose-response data implied a limited ability to assess the association between DE exposure and skin cancer. A further important limitation is the lack of adjustment for major confounders, including solar radiation and chemical exposure. Moreover, the lack of studies conducted outside North America or Europe limits the global interpretability of the study results. Finally, as with all meta-analyses, publication bias cannot be ruled out entirely, given the low power of the relevant tests.

5. Conclusion

This study provided no evidence of an increased risk of skin cancer in workers exposed to DE. We did not identify patterns of risk that could be related to occupational DE exposure. The possibility of residual confounding and other sources of bias cannot be ruled out. Thus, additional investigations are required to understand better if an association between DE exposure and skin cancer exists.

Supplementary Materials: The following are available online:

- Table S1: PRISMA checklist
- Figure S1: Forest plot of the leave-one-out meta-analysis of cohort studies on occupational diesel exhaust exposure and risk of melanoma skin cancer (MSC)
- Figure S2: Funnel plot of the analysis on occupational diesel exhaust exposure and risk of melanoma skin cancer (MSC)
- Figure S3: Galbraith plot of the analysis on occupational diesel exhaust exposure and risk of melanoma skin cancer (MSC)
- Figure S4: Forest plot of the leave-one-out meta-analysis of cohort studies on occupational diesel

exhaust exposure and risk of non-melanoma skin cancer (NMSC)
- Figure S5: Funnel plot of the analysis on occupational diesel exhaust exposure and risk of non-melanoma skin cancer (NMSC)
- Figure S6: Galbraith plot of the analysis on occupational diesel exhaust exposure and risk of non-melanoma skin cancer (NMSC)
- Figure S7: Forest plot of the leave-one-out meta-analysis of cohort studies on occupational diesel exhaust exposure and risk of skin cancer not otherwise specified (SC-NOS)
- Figure S8: Funnel plot of the analysis on occupational diesel exhaust exposure and risk of skin cancer not otherwise specified (SC-NOS)
- Figure S9: Galbraith plot of the analysis on occupational diesel exhaust exposure and risk of skin cancer not otherwise specified (SC-NOS)

References

1. Pronk A, Coble J, Stewart PA. Occupational exposure to diesel engine exhaust: a literature review. *J Expo Sci Environ Epidemiol.* 2009;19(5):443-457. Doi: 10.1038/jes.2009.21
2. IARC: diesel engine exhaust carcinogenic. *Cent Eur J Public Health.* 2012;20(2):120, 138.

3. Soll-Johanning H, Bach E, Olsen JH, Tüchsen F. Cancer incidence in urban bus drivers and tramway employees: a retrospective cohort study. *Occup Environ Med.* 1998;55(9):594-598. Doi: 10.1136/oem.55.9.594

4. Vasama-Neuvonen K, Pukkala E, Paakkulainen H, et al. Ovarian cancer and occupational exposures in Finland. *Am J Ind Med.* 1999;36(1):83-9. Doi: 10.1002/(sici)1097-0274(199907)36:1<83::aid-ajim12>3.0.co;2-q

5. Guo J, Kauppinen T, Kyyrönen P, et al. Risk of esophageal, ovarian, testicular, kidney and bladder cancers and leukemia among finnish workers exposed to diesel or gasoline engine exhaust. *Int J Cancer.* 2004;111(2):286-92. Doi: 10.1002/ijc.20263

6. Andersen A, Barlow L, Engeland A, et al. Work-related cancer in the Nordic countries. *Scand J Work Environ Health.* 1999;25 Suppl 2:1-116.

7. Gawkrodger DJ. Occupational skin cancers. *Occup Med (Lond).* 2004;54(7):458-463. Doi: 10.1093/occmed/kqh098

8. Sena JS, Girão RJ, Carvalho SM, et al. Occupational skin cancer: Systematic review. *Rev Assoc Med Bras (1992).* 2016;62(3):280-286. Doi: 10.1590/1806-9282.62.03.280

9. Diepgen TL. Occupational skin diseases. *J Dtsch Dermatol Ges.* 2012;10(5):297-315. Doi: 10.1111/j.1610-0387.2012.07890.x

10. Karagas MR, Weinstock MA, Nelson HH. Keratinocyte Carcinomas (Basal and Squamous Cell Carcinomas of the Skin) In: Schottenfeld D, Fraumeni JF, editors. Cancer Epidemiology and Prevention. New York (US): Oxford University Press; 2006. p. 1230-50.

11. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ.* 2021;372:n71. Published 2021 Mar 29. Doi: 10.1136/bmj.n71

12. Morgan RL, Whaley P, Thayer KA, Schünemann HJ. Identifying the PECO: A framework for formulating good questions to explore the association of environmental and other exposures with health outcomes. *Environ Int.* 2018;121(Pt 1):1027-1031. Doi: 10.1016/j.envint.2018.07.015

13. Page MJ, Moher D, Bossuyt PM, et al. PRISMA 2020 explanation and elaboration: updated guidance and exemplars for reporting systematic reviews. *BMJ.* 2021;372:n160. Doi: 10.1136/bmj.n160

14. Sidik K, Jonkman JN. A simple confidence interval for meta-analysis. *Stat Med.* 2002;21(21):3153-9. Doi: 10.1002/sim.1262

15. Thorlund K, Imberger G, Johnston BC, et al. Evolution of heterogeneity (I2) estimates and their 95% confidence intervals in large meta-analyses. *PLoS One.* 2012;7(7):e39471. Doi: 10.1371/journal.pone.0039471

16. Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. *Stat Med.* 2002;21(11):1539-58. Doi: 10.1002/sim.1186

17. Cochran, WG. The comparison of percentages in matched samples. *Biometrika.* 1950;37(3-4):256-66.

18. Egger M, Davey Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. *BMJ.* 1997;315(7109):629-34. Doi: 10.1136/bmj.315.7109.629

19. Galbraith RF. A note on graphical presentation of estimated odds ratios from several clinical trials. *Stat Med.* 1988;7(8):889-94. Doi: 10.1002/sim.4780070807

20. StataCorp. 2021. Stata Statistical Software: Release 17. College Station, TX: StataCorp LLC.

21. Howe GR, Fraser D, Lindsay J, Presnal B, Yu SZ. Cancer mortality (1965-77) in relation to diesel fume and coal exposure in a cohort of retired railway workers. *J Natl Cancer Inst.* 1983;70(6):1015-9

22. Wong O, Morgan RW, Kheifets L, et al. Mortality among members of a heavy construction equipment operators union with potential exposure to diesel exhaust emissions. *Br J Ind Med.* 1985;42(7):435-48. Doi: 10.1136/oem.42.7.435

23. Boffetta P, Stellman SD, Garfinkel L. Diesel exhaust exposure and mortality among males in the American Cancer Society prospective study. *Am J Ind Med.* 1988;14(4):403-15. Doi: 10.1002/ajim.4700140405

24. Gustavsson P, Plato N, Lidström EB, Hogstedt C. Lung cancer and exposure to diesel exhaust among bus garage workers. *Scand J Work Environ Health.* 1990;16(5):348-54. Doi: 10.5271/sjweh.1780

25. Van Den Eeden SK, Friedman GD. Exposure to engine exhaust and risk of subsequent cancer. *J Occup Med.* 1993;35(3):307-11.

26. Nokso-Koivisto P, Pukkala E. Past exposure to asbestos and combustion products and incidence of cancer among Finnish locomotive drivers. *Occup Environ Med.* 1994;51(5):330-4. Doi: 10.1136/oem.51.5.330

27. Boffetta P, Dosemeci M, Gridley G, et al. Occupational exposure to diesel engine emissions and risk of cancer in Swedish men and women. *Cancer Causes Control.* 2001;12(4):365-74. Doi: 10.1023/a:1011262105972

28. Järvholm B, Silverman D. Lung cancer in heavy equipment operators and truck drivers with diesel exhaust exposure in the construction industry. *Occup Environ Med.* 2003;60(7):516-20. Doi: 10.1136/oem.60.7.516

29. Pukkala E, Martinsen JI, Lynge E, et al. Occupation and cancer − follow-up of 15 million people in five Nordic countries. *Acta Oncol.* 2009;48(5):646-790. Doi: 10.1080/02841860902913546

30. Birdsey J, Alterman T, Li J, et al. Mortality among members of a truck driver trade association. *AAOHN J.* 2010;58(11):473-80. Doi: 10.3928/08910162-20101018-01

31. Risher JF, Rhodes SW. Toxicological Profile for Fuel Oils. Atlanta (GA): Agency for Toxic Substances and Disease Registry (US); 1995 Jun.

32. Li FK, Yip PS, Chan KW, et al. Acute renal failure after immersion in seawater polluted by diesel oil. *Am J Kidney Dis.* 1999;34(6):E26. Doi: 10.1016/s0272-6386(99)70031-4

33. Barrientos A, Ortuño MT, Morales JM, et al. Acute renal failure after use of diesel fuel as shampoo. *Arch Intern Med.* 1977;137(9):1217.

34. Weistenhöfer W, Lutz R, Hiller J, Schmitz-Spanke S, Drexler H. Syncarcinogenesis of natural UV radiation and polycyclic aromatic hydrocarbons in the development of squamous cell carcinomas of the skin? *J Dtsch Dermatol Ges.* 2022;20(9):1179-1186. Doi: 10.1111/ddg.14818

35. National Toxicology Program. 15th Report on Carcinogens [Internet]. Research Triangle Park (NC): National Toxicology Program; 2021 Dec 21. Diesel Exhaust Particulates: CAS No.: none assigned. Available from: https://www.ncbi.nlm.nih.gov/books/NBK590901/

36. Stenehjem JS, Robsahm TE, Bråtveit M et al. Aromatic hydrocarbons and risk of skin cancer by anatomical site in 25000 male offshore petroleum workers. *Am J Ind Med.* 2017;60(8):679-688. Doi: 10.1002/ajim.22741

37. Kurtul S, Güngördü N. Occupational skin carcinogens. *Eur Res J.* 2023. Doi: 10.18621/eurj.1193815

38. IARC Working Group on the Evaluation of Carcinogenic Risks to Humans. Diesel and Gasoline Engine Exhausts and Some Nitroarenes. Lyon (FR): International Agency for Research on Cancer; 2014. (IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, No. 105.) 4. MECHANISTIC AND OTHER RELEVANT DATA. Available from: https://www.ncbi.nlm.nih.gov/books/NBK294271/

39. Solar and ultraviolet radiation. IARC Monogr Eval Carcinog Risks Hum. 1992;55:1-316.

40. Armenian HK. Incubation periods of cancer: old and new. *J Chronic Dis.* 1987;40 Suppl 2:9S-15S. Doi: 10.1016/s0021-9681(87)80004-8

41. Armstrong BK. How sun exposure causes skin cancer: An epidemiological perspective In: Hill D, Elwood JM, English D. Prevention of Skin Cancer. Dordrecht, The Netherlands: Kluwer Academic Publishers; 2004. p. 89-116. Doi: 10.1007/978-94-017-0511-0_6

42. Leiter U, Garbe C. Epidemiology of melanoma and nonmelanoma skin cancer--the role of sunlight. *Adv Exp Med Biol.* 2008;624:89-103. Doi: 10.1007/978-0-387-77574-6_8

43. DerSimonian R, Laird N. Meta-analysis in clinical trials. *Control Clin Trials.* 1986;7(3):177-88. Doi: 10.1016/0197-2456(86)90046-2

44. Veroniki AA, Jackson D, Viechtbauer W, et al. Methods to estimate the between-study variance and its uncertainty in meta-analysis. *Res Synth Methods.* 2016;7(1):55-79. Doi: 10.1002/jrsm.1164