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Occupational asphalt is not associated with head and neck cancer

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Background	Epidemiologic studies that evaluate the relationship between occupational asphalt exposure and head and neck cancer have had a limited ability to control for known risk factors such as smoking, alcohol and human papillomavirus (HPV).
Aims	To better elucidate this relationship by including known risk factors in a large case–control study of head and neck squamous cell carcinoma (HNSCC) from the greater Boston area.
Methods	We analysed the relationship between occupational asphalt exposure and HNSCC among men in the Greater Boston area of Massachusetts. Analyses were conducted using unconditional multivariable logistic regression, performed with adjustments for age, race, education, smoking, alcohol consumption and HPV serology.
Results	There were 753 cases and 913 controls. No associations between HNSCC and occupational asphalt exposure (neither among ever-exposed nor by occupational duration) were observed for exposures in any occupation or those restricted to the construction industry. We also observed no associations in subgroup analyses of never-smokers and ever-smokers. Adjusting for known risk factors further reduced the estimated effect of asphalt exposure on HNSCC risk.
Conclusions	We found no evidence for an association between occupational asphalt exposure and HNSCC. The null findings from this well-controlled analysis could suggest that the risk estimates stemming from occupational cohort studies may be overestimated due to uncontrolled confounding and enhance the literature available for weighing cancer risk from occupational exposure to bitumen.
Key words	Bitumen; construction; epidemiology; fumes; head and neck cancer.

Introduction

Head and neck cancer is a major global concern, accounting for an estimated 549 000 cancer diagnoses annually [1]. These cancers are predominately of squamous histology [head and neck squamous cell carcinoma (HNSCC)] and have been causally linked to tobacco use, alcohol consumption and human papillomavirus 16 (HPV16). Asphalt (or bitumen) is produced from the distillation of crude petroleum and used in road surfacing, roofing and waterproofing applications. When heated during application, asphalt emits a mixture of fumes, vapours and solid particulates, including carcinogens such as polycyclic aromatic hydrocarbons (PAHs), which come in direct contact with the epithelium of the upper aerodigestive tract upon inhalation [2]. Dermal exposure has also been found to be a major route of exposure to PAHs among paving and roofing workers [3,4].

Chronic asphalt exposure could potentially result in elevated risk for upper aerodigestive tract cancers. There

are presently no case–control studies reporting on this relationship. There is limited evidence of an association from occupational cohort studies [5–9], although these studies offer poor control for important, potentially confounding factors, such as smoking, alcohol consumption and HPV infection. Thus, the objective of this study was to examine the relationship between occupational asphalt exposure and HNSCC among men enrolled in a large, well-controlled, population-based case–control study of head and neck cancer from the greater Boston area.

Methods

The study population has been previously described [10] and included male cases and controls who provided occupational asphalt exposure data. Epidemiologic data were collected from each participant via self-administered questionnaires while trained study personnel reviewed their responses. Participants provided detailed information about socio-demographics and personal characteristics, alcohol consumption, tobacco use and occupational history. Specifically, with regard to occupational data, subjects were asked to provide detailed information for each past job and occupation held, including industry, job, duration, location, employer and self-reported exposure to selected occupational hazards, including dusts (wood, concrete, metal, leather, soot), fumes (tar/asphalt, automotive exhaust, diesel fumes, plastic fumes, paint fumes, natural gas or wood smoke), solvents, formaldehyde, asbestos, insecticides/pesticides or ionizing radiation. History of HPV16 exposure was determined through serum antibody tests to the L1 capsid protein [10].

Unconditional multivariable logistic regression was performed on men to estimate odds ratios and 95% confidence intervals to assess the relationship between occupational exposure to asphalt and HNSCC. Asphalt exposure was modelled dichotomously as *ever/never* and continuously by duration at the exposed occupation(s). Models were adjusted for age, race (*White/non-White*), cigarette smoking (binary *ever/never* smoking term, and continuously as pack-years, considered additively), alcohol consumption (*non-drinker*, *≤14 drinks/week* and *>14 drinks/week*), highest level of education (*high school or less/greater than high school*) and HPV16 L1 serology (*negative/positive*). Multiple imputation by chained equations was used to account for missing covariate data (2 missing race data, 1 missing education, 5 missing alcohol data and 213 missing HPV16 L1 serology) by regressing on all model covariates (except asphalt and case status), with 20 iterations. Analyses were performed using SAS version 9.4 (SAS institute Inc., Cary, NC) and Stata SE 13.1 (StataCorp LP, College Station, TX). All statistical tests were two-sided and were considered significant when $P \geq 0.05$.

Table 1. Description of the study participants in a case–control study of head and neck cancer in men from the greater Boston area by self-reported occupational asphalt exposure and case status

Occupational asphalt exposure	Controls			HNSCC		
	Exposed (n = 136)	Unexposed (n = 777)	$P_{difference}$	Exposed (n = 128)	Unexposed (n = 625)	$P_{difference}$
Age, mean years (σ)	58.7 (10.9)	61.4 (10.5)	<0.01[a]	57.9 (9.5)	59.6 (10.6)	NS[a]
Race, n (%)						
White	120 (88)	714 (92)	NS[b]	114 (89)	563 (90)	NS[b]
Non-White	16 (12)	62 (8)		14 (11)	61 (10)	
Cigarette smoking, n (%)						
Never-smoker	52 (38)	299 (39)	NS[b]	17 (13)	146 (23)	<0.05
Ever-smoker	84 (62)	478 (62)		111 (87)	479 (77)	
Pack-years[c], median (IQR)	33 (14–46)	27 (14–45)	NS[d]	38 (23–59)	35 (16–57)	NS[d]
Alcohol consumption, n (%)						
Non-drinker	7 (5)	72 (9)	<0.001[b]	6 (5)	34 (6)	NS[b]
≤2 drinks per day	68 (50)	488 (63)		48 (38)	253 (41)	
>2 drinks per day	61 (45)	215 (28)		74 (58)	335 (54)	
Highest level of education, n (%)						
High school or less	55 (40)	189 (24)	<0.001[b]	68 (53)	240 (38)	<0.01[b]
Greater than high school	81 (60)	587 (76)		60 (47)	385 (62)	
HPV16 serostatus, n (%)						
Negative	118 (94)	625 (94)	NS[b]	79 (68)	368 (68)	NS[b]
Positive	7 (6)	43 (6)		37 (32)	176 (32)	

IQR, interquartile range; NS, non-significant; σ = standard deviation.
[a]Two-sample t-test.
[b]Fisher's exact test.
[c]Ever-smokers only.
[d]Wilcoxin's rank sum test.

Results

There were a total of 753 male cases and 913 male controls available for inclusion. Analyses were restricted to men due to the low number of women reporting an occupational asphalt exposure (n = 19). Of the 753 cases, 128 (17%) reported occupational exposures to asphalt compared to 136 of the 913 controls (15%). The median duration of employment at an asphalt-exposed job(s) was slightly higher for cases (24 years) than controls (22.5 years). A description of the study population by asphalt exposure and case–control status is presented in Table 1. However, after adjusting for potential confounders, we observed no association between history of asphalt exposure in any occupation or duration at the exposed job and HNSCC (Table 2). Since cigarettes are a substantial source of PAH exposure among smokers, we performed subgroup analyses restricted to never-smokers and ever-smokers, respectively, but still did not observe any significant association. We also examined the relationship between asphalt exposure in the construction industry and HNSCC, and again saw no significant associations, neither overall nor among never-smokers.

Discussion

These results do not support the notion that occupational exposure to asphalt confers a substantial risk for HNSCC. As opposed to the previous occupational cohort studies, the design of our study allows us to

Table 2. HNSCC risk from occupational asphalt exposure among men from the greater Boston area, overall and by smoking status, for any occupation and construction industry occupations, respectively

Occupational asphalt exposure	n_{case}	$n_{control}$	All HNSCC					
			Crude			Adjusted[a]		
			OR	LCI	UCI	OR	LCI	UCI
Any occupation								
All subjects								
No asphalt exposure	625	777	Reference			Reference		
Asphalt exposure	128	136	1.17	0.90	1.52	0.91	0.68	1.22
Per decade at exposed occupation[b]			1.05	0.95	1.16	0.98	0.87	1.10
Never-smokers								
No asphalt exposure	146	299	Reference			Reference		
Asphalt exposure	17	52	0.67	0.37	1.20	0.55	0.28	1.07
Per decade at exposed occupation[c]			0.89	0.70	1.12	0.80	0.61	1.06
Ever-smokers								
No asphalt exposure	479	478	Reference			Reference		
Asphalt exposure	111	84	1.32	0.97	1.80	1.06	0.75	1.49
Per decade at exposed occupation[d]			1.08	0.96	1.22	1.02	0.90	1.17
Construction industry only[e]								
All subjects								
No asphalt exposure	683	846	Reference			Reference		
Asphalt exposure	19	22	1.10	0.59	2.05	0.64	0.32	1.31
Per decade at exposed occupation[f]			1.22	0.92	1.63	1.02	0.74	1.41
Never-smokers								
No asphalt exposure	141	282	Reference			Reference		
Asphalt exposure	5	10	1.00	0.34	2.98	0.77	0.23	2.60
Per decade at exposed occupation[g]			1.28	0.83	1.99	1.17	0.71	1.94
Ever-smokers								
No asphalt exposure	433	450	Reference			Reference		
Asphalt exposure	14	12	1.21	0.55	2.65	0.59	0.25	1.40
Per decade at exposed occupation[h]			1.21	0.83	1.76	0.93	0.62	1.39

LCI, lower 95% confidence interval; OR, odds ratio; UCI, upper 95% confidence interval.
[a]Models are adjusted for age, race, education, smoking (except models that include never-smokers only), alcohol consumption and HPV16 serology.
[b]Duration is missing for 26 of the 264 subjects reporting occupational asphalt exposure (14 cases, 12 controls).
[c]Duration is missing for 7 of the 69 never-smokers reporting occupational asphalt exposure (3 cases, 4 controls).
[d]Duration is missing for 19 of the 195 ever-smokers reporting occupational asphalt exposure (8 cases, 11 controls).
[e]Exposed group includes only those with asphalt exposure in a construction industry occupation; unexposed group excludes all study subjects reporting non-construction industry asphalt exposure.
[f]Duration is missing for 4 of the 41 subjects reporting asphalt exposure in a construction industry occupation (3 cases, 1 control).
[g]Duration is missing for 1 of the 15 never-smokers reporting asphalt exposure in a construction industry occupation (1 case).
[h]Duration is missing for 3 of the 26 never-smokers reporting asphalt exposure in a construction industry occupation (2 cases, 1 control).

account for potential confounding factors, most notably smoking and alcohol consumption, making it, to the best of our knowledge, the first study of HNSCC risk among asphalt workers to do so in a well-controlled manner.

However, while we were able to perform subgroup analyses on workers in the construction industry as a whole, we should note that we were not adequately powered to evaluate the association in specific construction occupations, such as among roofers/waterproofers or road pavers. As such, we cannot draw any conclusions regarding the risk in these specific subsets of workers. Other limitations include our use of self-reported data, and potential for recall bias due to the retrospective nature of the data collection, although the latter is not likely, as it would be expected to bias results *away* from the null. Despite the inherent limitations of the case–control study design, a major strength of this study was the ability to adjust for powerful confounding factors; this was not possible in the existing occupational cohort studies and provides an extremely important contrast in the literature when considering occupational cancer risks associated with asphalt workers.

In conclusion, we found no evidence to support an association between occupational asphalt exposure and HNSCC, after adjusting for major risk factors associated with the disease. These observations suggest that the risk estimates for HNSCC among asphalt workers provided by occupational cohort studies may be overstated due to uncontrolled confounding and represent a substantial addition to the literature available for weighing head and neck cancer risk from occupational bitumen exposure.

Key points

- Prior occupational cohort studies have reported an elevated risk for head and neck squamous cell carcinoma among asphalt workers but offered poor control for potential confounding by major head and neck squamous cell carcinoma risk factors.
- We found no evidence to support an association between asphalt exposure and head and neck squamous cell carcinoma risk after adjusting for major risk factors for the disease in a large, population-based case–control study.
- These observations suggest that the risk estimates for head and neck squamous cell carcinoma among asphalt workers provided by occupational cohort studies may be overstated due to uncontrolled confounding.

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Conflicts of interest

None declared.

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