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Occupational Exposure to Diesel and Gasoline Engine Exhausts and the Risk of Kidney Cancer in Canadian Men

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Abstract

Introduction: Kidney cancer is the fifth most common incident cancer in Canadian men. Diesel and gasoline exhausts are common workplace exposures that have been examined as risk factors for non-lung cancer sites, including the kidney, but limitations in exposure assessment methods have contributed to inconsistent findings. The objective of this study was to assess the relationship between occupational gasoline and diesel engine exhausts and the risk of kidney cancer in men.

Methods: The National Enhanced Cancer Surveillance System (NECSS) is a Canadian population-based case–control study conducted in 1994–1997. Incident kidney cancer cases were identified using provincial registries, while the control series was identified through random-digit dialing, or provincial administrative databases. Self-reported questionnaires were used to obtain information on lifetime occupational history and cancer risk factors. Two hygienists, blinded to case status, coded occupational histories for diesel and gasoline exhaust exposures using concentration, frequency, duration, and reliability. Logistic regression was used to estimate odds ratios (ORs) and 95% confidence intervals (CIs) separately by exhaust type. The separate and combined impacts of both engine exhausts were also examined. ORs were adjusted for age, province, body mass index, occupational secondhand smoke exposure, and education.

Results: Of the kidney cancer cases (n = 712), 372 (52%) had exposure to both exhausts at some point, and 984 (40%) of the controls (n = 2457) were ever exposed. Workers who had ever been exposed to engine exhausts were more likely to have kidney cancer than those who were never exposed (OR diesel = 1.23, 95% CI = 0.99–1.53; OR gasoline = 1.51, 95% CI = 1.23–1.86). Exposure to gasoline exhaust was consistently associated with kidney cancer in a dose–response manner (P value for trends in highest attained and cumulative exposure both <0.0001). Those men with high cumulative exposure to both gasoline and diesel exhaust had a 76% increased odds of kidney cancer (95% CI = 1.27–2.43).
Conclusions: This study provides evidence that occupational gasoline, and to a lesser extent, diesel exhaust exposure may increase the risk of kidney cancer.

Keywords: case–control study; diesel exhaust; engine exhausts; gasoline exhaust; kidney cancer; men; occupation; occupational cancer

Introduction

Kidney cancer is the fifth most commonly diagnosed cancer among Canadian men (2017), and it occurs at double the incidence in men compared to women (22.3 versus 11.3 cases per 100 000 per year) (Canadian Cancer Society, 2017). There are few known risk factors for kidney cancer; these include cystic kidney disease, features of the metabolic syndrome (including obesity and hypertension), and cigarette smoking (Kabaria *et al.*, 2016). The male-to-female incident ratio has contributed to a longstanding interest in identifying occupational causes of kidney cancer, but to date, the only established workplace risk factor is trichloroethylene [International Agency for Research on Cancer (IARC), 2012].

Diesel and gasoline exhausts are ubiquitous exposures that are found in both occupational settings and, at lower levels, the ambient air. Engine emissions are produced through the combustion of diesel or gasoline fuel and are a complex mixture of gases and particulates. Particulate matter may contain elemental carbon, organic compounds such as polycyclic aromatic hydrocarbons, metals, and other trace compounds. Almost all of the particulate matter emitted by diesel and gasoline engines is respirable as the size of most of the particles is <10 microns, and many are <1 micron (Harris and Maricq, 2001). These ultrafine particles are small enough that they can enter the bloodstream via the lungs and translocate to other organs. An estimated 897 000 Canadian workers are exposed to diesel exhaust, and this accounts for nearly 5% of the working population (CAREX Canada, 2015). Workers in underground mining and quarrying occupations, as well as those in forestry and logging, are exposed to higher concentrations of diesel exhaust. Additionally, large groups of transportation workers (e.g. truck drivers) are exposed, although at lower levels (CAREX Canada, 2015).

The IARC has classified diesel exhaust as a Group 1, known human carcinogen, with sufficient evidence for lung carcinogenicity (IARC, 2014). Gasoline exhaust is related to diesel exhaust broadly in mode of production and exposure, but the health effects are less well understood. This is in part because gasoline and diesel exhausts occur together for many exposed populations (IARC, 2014). Relatively, few studies have been published on the relationship between gasoline exhaust and cancer, especially for sites other than the lung (Kachuri *et al.*, 2016). Gasoline contains recognized carcinogens such as benzene and ethylene dibromide; however, the mutagenicity of gasoline exhaust is broadly considered to be less than that of diesel (Seagrave *et al.*, 2002). One study was published noting a positive association between increasing cumulative exposure to gasoline exhaust and lung cancer risk (Guo *et al.*, 2004b). The IARC has classified gasoline exhaust as a possible human carcinogen (Group 2B) based on sufficient evidence in animals, but inadequate evidence in humans (IARC, 2014). The major limitation noted by IARC is the lack of attention paid to gasoline exposure as an effect separate from diesel engine exhaust in studies of lung cancer risk.

Relatively, few studies have considered the effects of diesel and gasoline exhaust exposure on kidney cancer. Some have reported small but significant increases in kidney cancer risk with occupational exposure to engine emissions (Siemiatycki *et al.*, 1988; Soll-Johanning *et al.*, 1998; Boffetta *et al.*, 2001; Guo *et al.*, 2004a), while others found no increased risk with exposure to either diesel or gasoline engine emissions (Siemiatycki *et al.*, 1988; Nokso-Koivisto and Pukkala, 1994; Boffetta *et al.*, 2001; Guo *et al.*, 2004a). Most of these studies were limited in that they lacked information on specific occupational exposures and tobacco smoking history, including exposure to secondhand smoke. Of the two studies that used a more comprehensive exposure assessment, one reported a slightly elevated risk of kidney cancer among men exposed to diesel emissions (Boffetta *et al.*, 2001), but the other (Attfield *et al.*, 2012) reported an elevated standardized mortality ratio that was not significant. More recently, a large study of particulate air pollution (which, in many areas, consists largely of the combustion products from diesel and gasoline engines) found a statistically significant increased risk of kidney cancer with increasing exposure to PM2.5 (Turner *et al.*, 2017). If particles generated at least partially from traffic-related air pollution can be linked to kidney cancer risk in large environmental cohorts, then it is important to investigate the higher exposure levels experienced by workers in more frequent and direct contact with combustion products.

Possible explanations for the lack of consistent findings across the studies mentioned include insufficient power due to a limited number of cases, and co-existing exposure to both diesel and gasoline exhausts that could not be accounted for in the analyses. Therefore, additional and sufficiently powered studies are needed to determine if these associations are causal. Therefore, the aim of this study was to evaluate the relationship between multiple metrics of occupational exposure to diesel and gasoline exhausts and the risk of kidney cancer in Canadian men.

Methods

Study population

The dataset used for this study was the National Enhanced Cancer Surveillance System (NECSS), which was a population-based case–control study conducted between 1994 and 1997 in eight Canadian provinces. Previous papers on this study have provided detailed background (Johnson *et al.*, 1998; Villeneuve et al., 1999, 2012) but the NECSS will be briefly described here. The NECSS was designed to investigate the environmental and occupational causes of cancer (Johnson *et al.*, 1998). We restricted our analyses to men as they were more likely to be exposed to engine exhausts during the time frame of the study. Histologically confirmed kidney cancer cases were identified through cancer registries in each participating province. Population-based controls were recruited using health insurance plans in five provinces (Prince Edward Island, Nova Scotia, Manitoba, Saskatchewan, and British Columbia) and random-digit dialing in Newfoundland and Alberta. Ontario used a stratified random sample selected from Ministry of Finance data (Villeneuve *et al.*, 1999). Controls were age-matched (±5 years) to the overall case distribution for all of the 19 cancer sites included in the NECSS. Response rates for male kidney cancer cases and controls were 73 and 63%, respectively. Analyses were restricted to men aged ≥40 years to account for the long latencies generally required for cancer induction, resulting in the exclusion of 23 kidney cancer cases.

Information on individual risk factors was collected using a self-administered questionnaire. Questions included socio-demographic information, body size measurements, dietary information, active smoking and secondhand smoke exposure, and physical activity levels.

Several potential confounders (based on previous analyses of this dataset) (Hu and Ugnat, 2005; Hu et al., 2008a,b) were considered in the present analysis. These included whether the subject had a proxy respondent, smoking history (categories: never smokers, <10, 10–25, 25–40, and 40+ pack-years), secondhand smoke exposure at home and work (categories: never exposed, then quartiles of smoker-years among the controls), body mass index [BMI: categories of underweight (<18.5), normal (18.5–<25 kg/m^2), overweight (25–<30), and obese (≥30)—WHO, 1995], income adequacy (low, lower middle, upper middle, and high income), recreational physical activity (categories based on hours per month of moderate or strenuous activity: 0, <10, 10–<30, and ≥30), attained education, alcohol consumption (categories of non-drinkers, then tertiles of drinks per week, 2 years earlier among the controls), and meat consumption (in quartiles among the controls) 2 years earlier.

Exposure assessment

All subjects in the NECSS provided information for each job held for at least 1 year since the age of 18. Job-related information included job title, main tasks performed, sector, and employment dates. The assignment of the dimensions of occupational exposure to diesel and gasoline engine exhausts used the expert approach—a methodology applied in previous analyses of the NECSS (Villeneuve *et al.*, 2012; Kachuri *et al.*, 2014; Latifovic *et al.*, 2015). Jobs were coded by hygienists trained in the same lab. Coding was in two phases; firstly, standard occupation (Canadian Classification and Dictionary of Occupations) and industry codes (Standard Industrial Codes) were assigned by a hygienist with several years of experience in these coding systems.

Secondly, hygienists coded three separate dimensions of exposure, each on a three-point scale, and separately for diesel and gasoline exhausts. These included relative intensity of exposure (low, medium, and high), frequency of exposure in a normal work week (<5%, 5–30%, and >30% of the time), and degree of confidence that the exposure had occurred (possible, probable, and definite) (Parent *et al.*, 2007).

Next, we constructed three metrics to characterize occupational exposure to diesel and gasoline exhaust, separately: (i) ever/never exposed; (ii) highest attained intensity of exposure (high, medium, low, where low is above general environmental background levels); and (iii) a cumulative measure of exposure. The latter metric was defined as the sum across all jobs of intensity multiplied by frequency and duration, as follows:

$$CE = \sum_{i=1}^{k} C_i \times F_i \times D_i$$

Where CE = cumulative exposure; i represents the ith job held, k = total number of jobs held, C = intensity of exposure (1 = low, 2 = medium, 3 = high), F = frequency of exposure (1 = <5%, 2 = 6–<30%, 3 = ≥30%), and D = duration of employment in years.

To address the gap in the literature that engine exhausts have not often been evaluated separately, we assessed the separate and combined impact of the two exhausts on the odds of kidney cancer by creating a composite variable with four categories: not exposed to either diesel or gasoline exhaust, exposed to diesel but not gasoline exhaust, exposed to gasoline but not diesel exhaust, and exposed to both exhausts. We examined the impact of cumulative exposure to both exhausts as well by creating a variable with the following categories: no exposure to either exhaust; no exposure to diesel, low cumulative exposure to gasoline; no exposure to diesel, medium exposure to gasoline; no exposure to diesel, high exposure to gasoline; no exposure to gasoline, low exposure to diesel; no exposure to gasoline, medium exposure to diesel; no exposure to gasoline, high exposure to diesel; any combination of exposure to both exhausts, except for both high exposures; and high cumulative exposure to both exhausts.

Statistical and sensitivity analyses

The odds ratios (ORs) and corresponding 95% confidence intervals (CIs) between all exposure metrics for exhaust exposures and kidney cancer were modeled using unconditional logistic regression. Fully adjusted models (separately for diesel and gasoline exhausts) included age and province, as well as potential confounders, defined as variables associated with both the exposures of interest and kidney cancer. Candidate confounders were entered into each model and covariates that produced an appreciable change in the regression coefficients (>10%) were retained. Two further models were constructed in a similar manner to the ones already described to examine the separate and combined exposure categories for both gasoline and diesel engine exhausts. Tests for trend in the ORs were also performed by modeling the categorical variables as continuous.

We undertook several sensitivity analyses. First, we evaluated how the risk estimates changed when restricting exposures to those classified as probable or definite. Additionally, we investigated whether risk estimates varied according to histological subtype of kidney cancer (renal cell carcinoma compared with any other subtype). We also examined using a squared intensity variable (i.e. such that 1 = low, 4 = medium, 9 = high) as a sensitivity analysis.

The Carleton University Research Ethics Board provided ethics approval for this study, and all subjects provided informed consent for the original NECSS study (ethics approvals were obtained by each provincial PI from their respective ethics review boards).

Results

There were 727 cases and 2547 controls in the initial dataset; after excluding individuals with no employment histories or missing birthdate information, a total of 712 cases (98%) and 2457 controls (96%) were available for analysis in the NECSS dataset. Selected characteristics of the cases and controls are shown in Table 1, cross-tabulated by several of the potential confounding variables.

There was no difference between cases and controls in whether or not they had received assistance from a friend or family member to fill out their questionnaire. Active smoking did not show a consistent relationship with kidney cancer, but secondhand exposure to smoke at work was associated with increased odds of kidney cancer. Cases were more likely to be overweight or obese, and ate more meat than controls. Cases were also less likely to be in the most educated group.

The number and proportion of jobs with exposure to gasoline and diesel exhaust are presented in Table 2, with the most common exposure coding for each of the three dimensions of exposure (frequency, intensity, and probability of exposure). Participants in the study held 11 814 jobs in total over their working lives. Of these, 1638 (14%), and 2247 (19%) occupations were determined to have probable or definite exposure to diesel and gasoline engine exhaust, respectively. A further 1440 jobs involved possible exposure to diesel, and 1045 possible exposure to gasoline. All of these jobs flagged as at least possibly exposed are listed in Table 2, along with the percentage of jobs within each code that were flagged as exposed. The most frequent jobs with gasoline exhaust exposure were transportation workers, farmers and farm workers, and service station attendants (Table 2). The most frequent jobs with diesel exhaust exposure were construction workers, transportation workers, and farmers and farm workers. There was a wide range in the proportion of jobs classified as exposed by category; most jobs had

Table 1. Selected characteristics of male incident kidney cancer cases and controls from the National Enhanced Cancer Surveillance System, 1994–1997.

Covariates	Cases, *n* (%)	Controls, *n* (%)	Minimally adjusted ORs[a] (95% CI)
Age at interview, mean (SD)	59.0 (10.2)	57.8 (14.5)	
Assistance with questionnaire			
No	464 (65)	1679 (68)	1.00
Yes	248 (35)	779 (32)	0.85 (0.71–1.02)
Pack-years smoking			
None	164 (24)	637 (26)	1.00
>0–<10	129 (19)	494 (21)	0.99 (0.75–1.29)
10–<25	192 (28)	613 (25)	1.12 (0.87–1.43)
25–<40	114 (16)	353 (15)	1.07 (0.80–1.42)
≥40	96 (14)	313 (13)	1.26 (0.93–1.71)
Occupational secondhand smoke exposure[b], smoker-years			
None	130 (18)	612 (25)	1.00
>0–<48	110 (15)	450 (18)	1.28 (0.95–1.73)
48–<101	162 (23)	469 (19)	1.48 (1.13–1.95)
101–<185	160 (22)	458 (19)	1.32 (1.01–1.73)
≥185	150 (21)	464 (19)	1.46 (1.11–1.93)
Alcohol consumption, servings per week			
None	211 (30)	674 (27)	1.00
>0–<3	151 (21)	498 (20)	0.96 (0.75–1.23)
3–<8.5	182 (26)	655 (27)	0.82 (0.65–1.04)
≥8.5	168 (24)	631 (26)	0.76 (0.59–0.96)
BMI, kg m^{-2}			
<18.5 (underweight)	6 (1)	42 (2)	0.89 (0.36–2.22)
18.5–<25 (normal weight)	159 (22)	925 (38)	1.00
25–<30 (overweight)	363 (51)	1127 (46)	1.82 (1.47–2.26)
≥30 (obese)	184 (26)	364 (15)	2.85 (2.21–3.68)
Moderate to high leisure time physical activity, hours per week			
None	295 (41)	964 (39)	1.00
>0–<10	141 (20)	491 (20)	1.11 (0.66–1.89)
10–<30	145 (20)	598 (24)	0.89 (0.52–1.50)
≥30	131 (18)	405 (16)	1.20 (0.70–2.04)
Educational level			
Less than high school	327 (47)	1025 (42)	1.00
High school complete	134 (19)	423 (18)	0.91 (0.71–1.16)
At least some college	96 (14)	313 (13)	0.97 (0.73–1.29)
At least some university	145 (21)	661 (27)	0.60 (0.48–0.77)
Income adequacy[c]			
Low	88 (12)	374 (15)	1.00
Lower middle	130 (18)	432 (18)	1.23 (0.90–1.67)
Upper middle	209 (29)	663 (27)	1.09 (0.82–1.46)
High	142 (20)	440 (18)	1.04 (0.76–1.42)
Prefers not to answer	143 (20)	549 (22)	1.00 (0.74–1.37)
Meat intake, servings per week[d]			
Low (<5)	161 (23)	681 (28)	1.00
Low–medium (5–<9)	152 (21)	553 (23)	1.20 (0.93–1.55)
Medium–high (9–<12)	174 (24)	568 (23)	1.26 (0.98–1.62)
High (≥12)	225 (32)	656 (27)	1.51 (1.19–1.92)

Table 1. (Continued)

Covariates	Cases, *n* (%)	Controls, *n* (%)	Minimally adjusted ORs[a] (95% CI)
Province of residence			
British Columbia	148 (21)	450 (18)	
Alberta	112 (16)	326 (13)	
Saskatchewan	43 (6)	139 (6)	
Manitoba	55 (8)	151 (6)	
Ontario	274 (39)	876 (36)	
Nova Scotia	40 (6)	324 (13)	
Prince Edward Island	13 (2)	77 (3)	
Newfoundland	27 (4)	115 (5)	

[a]Presented ORs are adjusted for province and age.
[b]Number of people smoking near the subject at work multiplied by years of exposure, in quartiles among controls.
[c]Low: income <$20 000/year, or income $20 000–29 999 and four or more people living in the home. Lower middle: income $20 000–29 999 and less than four people in the home, or income $30 000–39 999 and four or more people in the home. Upper middle: income $30 000–39 999 and less than four people in the home, or income $40 000–49 999 and four or more people in the home. High: income $50 000–99 999 and less than four people in the home, or income ≥$100 000/year.
[d]Defined as quartiles of average number of meat servings per week among the controls.

low intensity of exposure for both exhaust types, and the frequency of contact with exhausts was most often medium (Table 2). Additionally, 427 kidney cancer cases (60%) and 1262 (51%) controls were exposed to diesel exhaust in their working lives. Gasoline exhaust exposure was more prevalent than diesel exhaust, with 470 (66%) kidney cancer cases and 1285 (52%) controls ever exposed in their careers. Many workers had occupational exposure to both exhausts at some point in their career. For the kidney cancer cases, 372 (52%) had exposure to both exhausts at some point, and for the controls, this number was 984 (40%). We also examined whether there was a difference between cases and controls in terms of the longest job they held (results not shown). Cases were slightly more likely to have been transportation workers in their longest job (7.7% in cases versus 5.9% in controls), but they were also likelier to have held administrative jobs (14.2% for cases versus 12.9% in controls). There were no statistically significant differences in longest job held by case status, however.

Results for the fully adjusted models are presented in Table 3 for diesel exhaust, and Table 4 for gasoline exhaust. In each case, the middle column includes all participants in the study for any level of confidence of exposure to the particular exhaust, and the rightmost column is restricted to participants with probably or definite exposure to the particular exhaust. The only variables which remained significant in the models were age, province, secondhand smoke exposure at work, BMI, and education.

Men who were ever occupationally exposed (for any level of confidence) to diesel exhaust were 30% more likely to be diagnosed with kidney cancer than those who were never exposed to diesel (Table 3, 95% CI = 1.07–1.57). Those with higher attained intensity of exposure diesel had an increased risk of kidney cancer as well, but the categories of low and medium/high were not substantially different from each other. When we examined cumulative exposure to diesel exhaust, all categories of exposure had an elevated odds of kidney cancer, but there was a non-monotonic increase across the increasing exposure categories. When we restricted the analysis to only those men with probable or definite exposure to diesel exhaust, the results were quite similar, although some CIs included the null (likely due to a reduced number of workers included in the analysis) (Table 3, rightmost column).

Workers who were ever exposed to gasoline engine exhaust (for any level of confidence) were 63% more likely to have kidney cancer than those who were never exposed (Table 4). There was a consistent dose–response relationship between increasing intensity of exposure and risk of kidney cancer. Those with peak exposures in the highest intensity category for gasoline exhaust were twice as likely to have kidney cancer as unexposed men. Similarly, cumulative exposure to gasoline engine exhaust was associated with an elevated risk of kidney cancer across all categories, with the largest point estimates observed for the highest level of exposure (OR = 1.64, 95% CI = 1.25–2.14) (Table 4).

When we restricted the analysis to those with only probable or definite occupational exposure to gasoline engine exhaust, the conclusions remained similar. Higher intensity of attained exposure to gasoline engine exhaust and higher cumulative exposure were both significantly associated with kidney cancer (Table 4).

Table 2. Typical jobs with exposure to diesel and/or gasoline engine emissions, and most common exposure coding[a], National Enhanced Cancer Surveillance System, 1994–1997.

Occupational group[b]	Gasoline engine exhaust					Diesel engine exhaust				
	n jobs exposed	% exposed in that job	Most common exposure coding			*n* jobs exposed	% exposed in that job	Most common exposure coding		
			Confidence	Intensity	Frequency			Confidence	Intensity	Frequency
Transportation workers	640	77	Certain[c]	Low	Medium	556	67	Certain	Low	Medium
Farmers and farm workers	616	77	Possible[c]	Low	Medium	449	56	Certain	Low	Medium
Traveling sales, service station attendants	437	39	Probable	Low	Medium	129	11	Possible	Low	Low
Firefighters, police, other services	333	32	Probable	Low	Medium	247	24	Possible	Low	Medium
Mechanics, repair, fabrication	394	34	Certain	Medium	High	246	21	Certain	Medium	High
Material handlers	147	62	Possible	Low	Medium	141	59	Possible	Low	Medium
Stock and production clerks, mail carriers	136	21	Possible	Low	High	79	12	Possible	Low	High
Forestry workers	126	78	Certain[c]	High	High	40	25	Probable	Low	Medium
Administrators and managers	107	8	Possible	Low	Medium	115	9	Possible	Low	Medium
Fishermen, hunters	97	96	Probable	Low	High	79	78	Probable	Low	Medium
Construction workers	82	6	Possible	Low	Medium	607	47	Possible	Low	Medium
Scientists, engineers, technicians	74	12	Possible	Low	Low	114	19	Possible	Low	Low
Miners and quarrymen	3	2	Possible	Low	Medium	177	90	Possible	Low	Medium
Other miscellaneous occupations	100	5	Possible	Low	Medium	99	5	Possible	Low	Medium

[a]Defined by highest percentage.
[b]Based on the first two digits of the Canadian Classification and Dictionary of Occupations.
[c]Mixed between the three possible categories of possible, probable, and certain.

Table 3. Adjusted[a] ORs of kidney cancer in relation to occupational diesel engine exhaust exposure, by confidence level of exposure assessment.

Occupational diesel exhaust exposure	Adjusted ORs for any level of confidence of exposure to diesel exhaust (95% CI)	Adjusted ORs for probable or definite exposure to diesel exhaust (95% CI)
Ever exposed		
Unexposed	1.00	1.00
Ever exposed	1.30 (1.07–1.57)	1.23 (0.99–1.53)
Highest attained exposure		
Unexposed	1.00	1.00
Low	1.32 (1.08–1.60)	1.26 (1.00–1.58)
Medium/high	1.22 (0.89–1.67)	1.16 (0.82–1.64)
Cumulative categories of exposure[b]		
Unexposed	1.00	1.00
Low (>0–<10)	1.40 (1.07–1.83)	1.20 (0.82–1.74)
Medium (10–<36)	1.34 (1.05–1.71)	1.30 (0.97–1.75)
High (≥36)	1.15 (0.89–1.50)	1.16 (0.88–1.54)

[a]Adjusted for age, province, BMI, secondhand smoke exposure at work, and education level.
[b]Cumulative exposure = sum of the frequency × intensity × duration of exposure across all jobs.

Table 4. Adjusted[a] ORs of kidney cancer in relation to occupational gasoline engine exhaust exposure, by confidence level of exposure assessment.

Occupational gasoline exhaust exposure	Adjusted ORs for any level of confidence of exposure to gasoline exhaust (95% CI)	Adjusted ORs for probable or definite exposure to gasoline exhaust (95% CI)
Ever exposed		
Unexposed	1.00	1.00
Ever exposed	1.63 (1.34–2.20)	1.51 (1.23–1.86)
Highest attained exposure		
Unexposed	1.0	1.00
Low	1.59 (1.30–1.94)	1.47 (1.18–1.82)
Medium	1.76 (1.24–2.49)	1.65 (1.13–2.41)
High	1.99 (1.20–3.31)	1.79 (1.02–3.13)
Test for trend	$P < 0.0001$	$P < 0.0001$
Cumulative categories of exposure[b]		
Unexposed	1.00	1.00
Low (>0–<10)	1.67 (1.29–2.16)	1.39 (1.03–1.86)
Medium (10–<28)	1.49 (1.16–1.92)	1.45 (1.10–1.92)
High (≥28)	1.72 (1.34–2.22)	1.64 (1.25–2.14)
Test for trend	$P < 0.0001$	$P < 0.0001$

[a]Adjusted for age, province, BMI, secondhand smoke exposure at work, and education level.
[b]Cumulative exposure = sum of the frequency × intensity × duration of exposure across all jobs.

Table 5 shows the results of analyses examining the separate and combined effect of gasoline and diesel exhaust exposure. Gasoline exhaust exposure (both alone and in combination with diesel exhaust exposure) is associated with an increased odds of kidney cancer. Diesel exhaust exposure alone does not appear to increase the likelihood of kidney cancer. In addition, the highest odds of kidney cancer observed was among those men with high cumulative exposure to both diesel and gasoline exhaust (OR = 1.76, 95% CI = 1.27–2.43).

Restricting the analysis to renal cell carcinomas (n = 592) did not alter the pattern of the main findings

Table 5. Adjusted ORs of kidney cancer in relation to combinations of occupational gasoline and diesel engine exhaust exposures.

Metrics for combined exposure to gasoline and diesel exhaust	Cases, *n* (%)	Controls, *n* (%)	Fully adjusted ORs[a] (95% CI)
Ever exhaust exposure category			
Never exposed to either	187 (26)	895 (36)	1.00
Exposed to gasoline, but not diesel	98 (14)	301 (12)	1.47 (1.09–1.98)
Exposed to diesel, but not gasoline	55 (8)	278 (11)	0.91 (0.64–1.30)
Exposed to both gasoline and diesel	372 (52)	984 (40)	1.64 (1.31–2.04)
Cumulative exhaust exposure category			
Never exposed to either	187 (27)	895 (37)	1.00
No diesel, low gasoline exhaust	35 (5)	102 (4)	1.48 (0.94–2.55)
No diesel, medium gasoline exhaust	29 (4)	102 (4)	1.29 (0.81–2.06)
No diesel, high gasoline exhaust	29 (4)	88 (4)	1.58 (0.98–2.55)
No gasoline, low diesel exhaust	12 (2)	70 (3)	0.88 (0.44–1.73)
No gasoline, medium diesel exhaust	22 (3)	98 (4)	1.01 (0.61–1.70)
No gasoline, high diesel exhaust	0	0	–
Mixed cumulative exposure to both	286 (41)	809 (34)	1.50 (1.19–1.90)
High cumulative exposure to both	93 (28)	244 (10)	1.76 (1.27–2.43)

[a]Adjusted for age, province, BMI, occupational secondhand smoke exposure, and education level.

of the analysis interpretations. In general, a widening of CIs due to the reduced power with less cases did occur, but all general conclusions remained the same. Results are thus retained for all histological subtypes together. Finally, using a squared value for intensity of exposure in the cumulative models (i.e. intensity score of 1 for low exposure, 4 for medium, and 9 for high exposure) did not alter our interpretations (results not shown).

Discussion

The analyses presented herein support the hypothesis that exposure to diesel engine exhausts increases the risk of kidney cancer. More convincing evidence was found for a relationship between occupational exposure to gasoline engine exhaust and the development of kidney cancer, especially when we consider the highest intensity of exposure attained. These findings add to the fairly limited and mixed body of evidence surrounding engine exhaust exposures and kidney cancer risk.

In particular, we found a 30% increased odds of kidney cancer associated with ever exposure to diesel engine exhaust, and a 60% increased odds associated with ever exposure to gasoline exhaust. Intensity of exposure emerged as an informative exposure metric for gasoline but not diesel exhaust. Men with the highest attained intensity of exposure were at double the odds of kidney cancer than unexposed men, and the increased odds showed a dose–response relationship. Few studies have examined diesel and gasoline exposure using comparable metrics. A study in Montreal in the 1980s found a non-statistically significant increased risk of kidney cancer among those exposed to gasoline (but not diesel) engine exhaust (Siemiatycki *et al.*, 1988). Further, mixed results for exhaust exposures and kidney cancer risk were reported by Guo and colleagues in a large Finnish study (Guo *et al.*, 2004a). Increased risk of kidney cancer was found for those in the lower exposure category for diesel exhaust exposure only, though a similar pattern (not statistically significant) of the lowest two categories of exposure to gasoline exhaust being at increased risk of kidney cancer was also detected. The authors noted that these results were primarily influenced by truck drivers, who were classified as exposed at lower levels, but nonetheless were at increased risk of kidney cancer. It should also be noted that this study used job title as a proxy for exposure, as many previous studies on exhausts exposure and cancer risk have done (Latifovic *et al.*, 2015). For example, in a Swedish study of occupational causes of kidney cancer, increased risks were found among miners and quarry workers, drivers and driving sales workers, transportation workers, and safety and protection workers (for men) (Ji *et al.*, 2005). All of these occupations are likely to be exposed, to some degree, to both diesel and gasoline engine exhaust.

In the cumulative models of exposure, we noted a strong dose–response relationship for gasoline exhaust exposure and the risk of kidney cancer. Occupational exposure to diesel exhaust also showed some evidence of increased risk of kidney cancer, though the impact was most pronounced in the group with low cumulative exposure compared to the unexposed. This could be due in part to the effects of non-differential misclassification of exposure in models with theoretically continuous exposures, often not normally distributed, and classified into categorical exposure levels (Birkett, 1992).

When we considered separate and combined levels of exposure to gasoline and diesel exhaust, we saw that gasoline exposure alone, as well as in combination with diesel exhaust exposure, conferred a risk of kidney cancer. Diesel exhaust exposure alone did not appear to increase the odds of kidney cancer. Those workers with high cumulative exposure to both gasoline and diesel exhaust had nearly double the odds of kidney cancer as those who were not exposed to either exhaust in their working lives, which was the highest OR we observed in our analyses (OR = 1.76 for high cumulative exposure to both exhausts, compared to 1.58 when looking only at those workers with high gasoline exhaust exposure). For many of the exposed jobs noted in Table 2, there is an overlap in exposure (i.e. firefighters, miners, truck drivers, etc. are likely to be exposed to both diesel and gasoline exhausts), which suggests that the observed results may be primarily attributed to the gasoline engine exhaust. Table 5 also highlights just how prevalent both of these exhausts are in many workplaces (52% of cases and 40% of controls were ever exposed to both exhausts).

Restricting analyses to include only men with probable or definite exposure produced modest changes in the risk estimates. Assuming that a true relationship exists, reducing exposure misclassification by removing observations with uncertain exposure status should improve our ability to detect an association (Teschke *et al.*, 2002). However, the concomitant reduction in sample size may have also reduced our power.

The main limitations of the very few previous studies of diesel and gasoline exhausts and the risk of kidney cancer have been using job title as a proxy and having no detailed assessment of intensity, duration, or frequency of exposure. Additionally, and likely because gasoline exhaust is considered to have less carcinogenic potential, this particular exhaust has not been assessed in a detailed manner in the literature. Our analyses have been able to address gasoline and diesel exhaust exposure in a detailed manner, separately from one another, and over the entire working life. Our results suggest that occupational gasoline exhaust could increase the risk of kidney cancer, and that additional exposure to diesel exhaust (but not diesel on its own) may increase this risk further.

It is important to note a number of key strengths in this study. Firstly, the NECSS contains detailed information on confounding factors and other risk factors for cancer. The risk of recall bias was reduced as compared to some case–control studies, since exposure was not self-reported by the participants but coded by experts who were blinded to case status. The NECSS reports moderate participation rates (at 73% for male kidney cancer cases and 63% among male controls), which may have caused some degree of participation bias in our study. However, we did not find any meaningful differences in income between the cases and controls (and income adequacy is normally a key driver of participation bias), which suggests this bias may not have been strong (if present at all).

Some limitations are also present in this analysis. We were unable to adjust for occupational exposure to trichloroethylene (the only known occupational exposure with a link to kidney cancer), since task information was not sufficiently detailed to assess it, but we expect very low prevalence of exposure in our population (<2%).

The main strength in these analyses was our ability to undertake a detailed exposure assessment approach. The NECSS study relied on self-reported occupational histories, and there is strong evidence in the literature that these are reliable and valid tools for exposure assessment (Teschke *et al.*, 2002). The subsequent expert assessment by hygienists approach is considered the reference approach for retrospective studies such as this one (Bouyer and Hémon, 1993). The high reliability of the expert-based approach has been well documented by the coding team of hygienists and researchers in the previous Montreal-based case–control studies in Canada (Fritschi *et al.*, 1996; Siemiatycki *et al.*, 1997).

Conclusions

We found evidence for an association between occupational exposure to gasoline exhaust and kidney cancer in a large, population-based study of Canadian men. Additionally, we noted that diesel engine exhaust may also be related to a higher risk of kidney cancer, but likely only in combination with gasoline exhaust exposure. The relationship was particularly strong when we considered workers who had higher intensity of gasoline exhaust exposure, and those with higher cumulative exposure. Further studies should be performed in order to confirm this new link, however, since there is still a lack of strong mechanistic data for gasoline engine exhaust and kidney cancer.

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