



Occupational
Cancer
Research
Centre

Bladder cancer and occupational exposure to diesel and gasoline engine emissions among Canadian men

Lidija Latifovic*, Paul J. Villeneuve, Marie-Élise Parent, Kenneth C. Johnson, Linda Kachuri, the Canadian Cancer Registries Epidemiology Group, and Shelley A. Harris

Towards a cancer-free workplace

Diesel and gasoline engine emissions

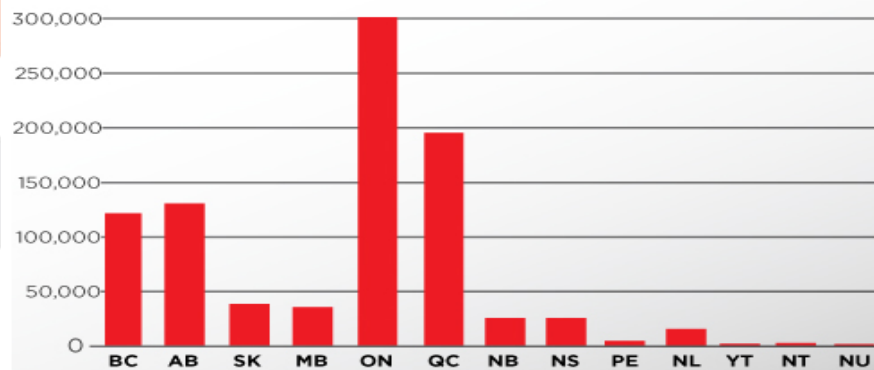
- Ubiquitous exposures in ambient air and occupational settings
- Complex mixture of respirable gases and particulates
 - Including black carbon and polycyclic aromatic hydrocarbons (PAHs)
- **Diesel engine emissions (DEE)**
 - IARC 1988: probable lung carcinogen
 - IARC 2012: definite lung carcinogen
- **Gasoline engine emissions (GEE)**
 - IARC 1988 & 2012: possible carcinogen



Source: U.S. EPA

WORKERS EXPOSED TO DIESEL ENGINE EXHAUST BY REGION

* = <50 WORKERS



897,000
WORKERS (EST.)



DIESEL ENGINE EXHAUST
EXPOSURE **IN CANADA**

FIVE LARGEST EXPOSURE GROUPS BY INDUSTRY

PROPORTION OF INDUSTRY EXPOSED

Truck transportation	206,000	75%
Transit and ground passenger transportation	110,000	76%
Public administration (local)	42,000	15%
Specialty trade contractors (construction)	39,000	7%
Heavy and civil engineering construction	34,000	30%

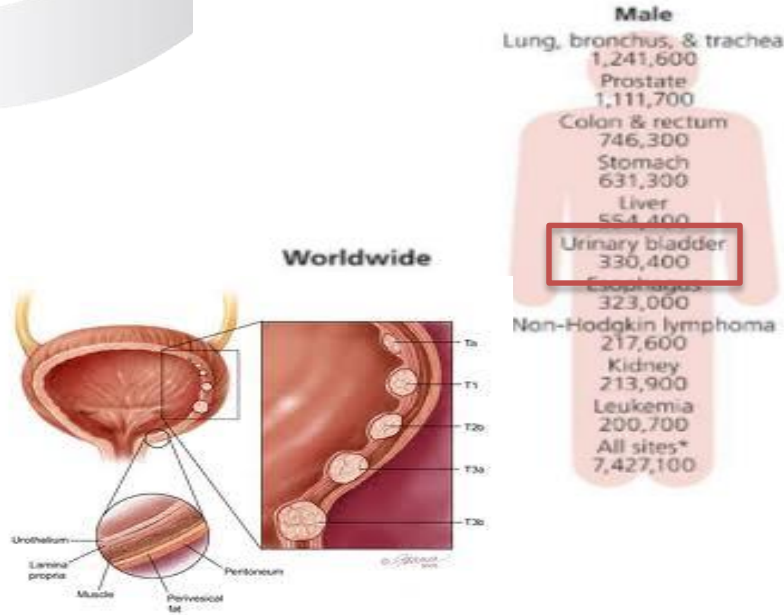
Source: Peters CE, Ge CB, Hall AL, et al. *Occup Environ Med.* doi:10.1136/oemed-2014-102286

CAREX Canada. Diesel Engine Exhaust. Occupational Estimate. www.carexcanada.ca

Bladder Cancer

Estimated new cases¹

- Is 4th most common cancer among men worldwide
- Established risk factors for bladder cancer include:
 - older age, male gender, smoking, occupational exposure to aromatic amines, as well as chronic parasitic infections (*Schistosoma hematobium*)²
- Work related exposures likely account for 4-7% of bladder cancer³



¹ Torre et al. Global Cancer Statistics 2012. *Ca Cancer J Clin.* 2015; 65:87-108

² Pelucchi C, Bosetti C, Negri E, et al. *Nat Rev Urol.* 2006; 3:327-340

³ Kogevinas M, 't Mannetje A, Cordier S, et al. *Cancer Causes Control.* 2003; 14(10):907-914

Objective

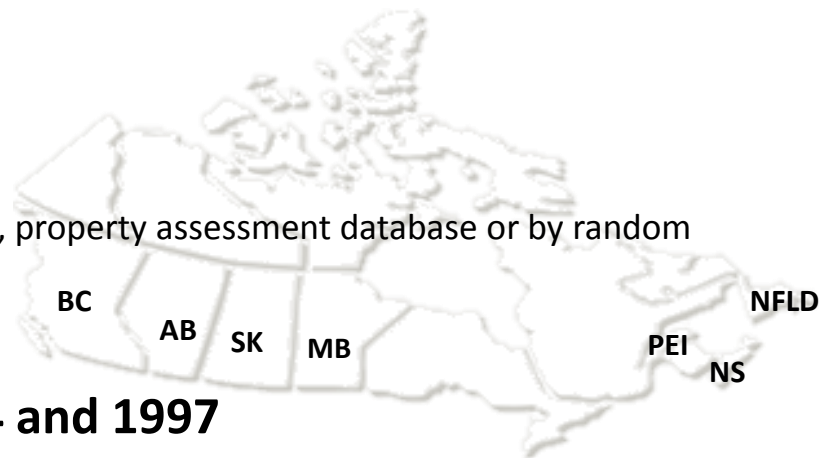


- To investigate the association between **occupational exposure to diesel and gasoline engine emissions** and the **risk of bladder cancer** in Canadian men

Study Population



- National Enhanced Cancer Surveillance System (NECSS):
 - a **population-based, incident case-control study** conducted across Canada
 - **658 male bladder cancer cases**
 - recruited from provincial cancer registries
 - **1 360 age-frequency matched controls**
 - sampled from province health insurance records, property assessment database or by random digit dialing
- Data collection:
 - **Mailed questionnaires between 1994 and 1997**
 - Complete lifetime occupational histories
 - Detailed information on a large number of possible cancer risk factors



Occupational Exposure Assessment



- Based on self-reported lifetime occupational histories
 - a job exposure matrix (JEM) coupled with expert review

- **Concentration of exposure**

	DEE	GEE
Low	Truck driver	Taxi drivers (city)
Medium	Heavy equipment operators	Automobile repair shop workers
High	Underground mining and quarrying	Forestry workers (chainsaws)

- **Frequency of exposure (% work time exposed)**

- < 5%, 5 – 30%, > 30%

- **Reliability of exposure**

- Possible, probable, definite
- Possible exposure was classified as unexposed

Statistical Analyses



- Logistic regression was used to calculate odds ratios (OR) and corresponding 95% confidence intervals (CI) and to test for trend (p_{trend})
 - Adjusted for
 - Proxy respondent
 - Province of residence
 - Age at interview
 - Cigarette pack-years
 - Cumulative asbestos exposure
 - Cumulative silica exposure

Results: Select characteristics



	Cases (N=658)		Controls (N=1360)		OR	95% CI ¹
	Mean	SD	Mean	SD		
Age (years)	63.7	8.3	63.3	8.9		
	N	%	N	%		
Proxy respondent	253	38.5	458	33.7	1.30	1.07, 1.59
Former smoker	366	61.7	754	57.6	1.87	1.41, 2.48
Current smoker	151	25.5	254	19.4	2.46	1.78, 3.40
Added fat:						
Q2 vs Q1	169	25.7	318	23.4	1.49	1.13, 1.95
Q3 vs Q1	169	25.7	334	24.6	1.44	1.10, 1.90
Q4 vs Q1	177	26.9	314	23.1	1.67	1.27, 2.20
Tap water intake:						
Q2 vs Q1	164	19.6	333	24.5	1.48	1.12, 1.96
Q3 vs Q1	178	27.1	333	24.5	1.53	1.16, 2.02
Q4 vs Q1	187	28.4	308	22.7	1.73	1.31, 2.28

¹ Adjusted for age, province of residence, and proxy respondent.

Results: Select characteristics



	Cases (N=658)		Controls (N=1360)		OR ¹	95% CI
	N	%	N	%		
Occupational exposure to aromatic amines:						
Never	652	99.1	1348	99.1	1.00	
Ever	6	0.9	12	0.9	1.36	0.49, 3.79
Cumulative occupational exposure to asbestos:						
Unexposed	538	82.1	1209	89.1	1.00	
Lowest	43	6.6	47	3.5	1.24	0.91, 1.71
Middle	38	5.8	48	3.5	1.01	0.73, 1.40
Highest	36	5.5	53	3.9	1.33	1.00, 1.78
Cumulative occupational exposure to silica:						
Unexposed	404	62.4	929	69.1	1.00	
Lowest	74	11.4	128	9.5	1.98	1.28, 3.06
Middle	68	10.5	133	9.9	1.70	1.08, 2.66
Highest	102	15.7	155	11.5	1.50	0.96, 2.34

¹ Adjusted for age, province of residence, and proxy respondent

Exposure Metrics



1. Ever exposed
2. Highest attained concentration of exposure
3. Highest attained frequency of exposure
4. Duration of exposure (years of employment):
 - At any concentration
 - At low concentrations
 - At high concentrations
5. Cumulative Exposure (CE)
 - $CE = \sum_{i=1}^k C_i F_i D_i$
 - k=total number of jobs, i=ith job held
 - C=concentration, F=frequency, D=duration

Results: DEE



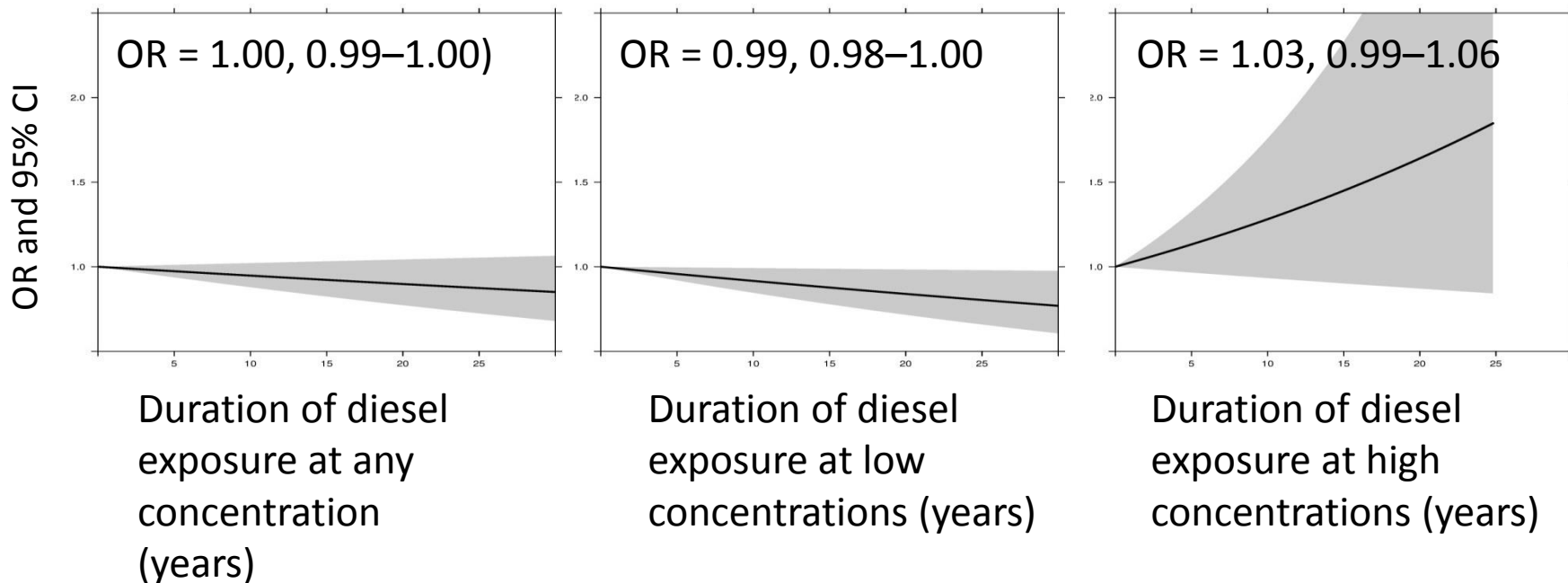
	Cases (N=658)		Controls (N=1360)		OR	95% CI
	N	%	N	%		
Unexposed	402	61.1	869	63.9	1.00	
Ever exposed	256	38.9	491	36.1	1.07	0.88, 1.31
Highest attained concentration:						
Unexposed	402	61.1	869	63.9	1.00	
Low	162	24.6	377	27.7	0.78	0.60, 1.00
Medium	66	10.0	89	6.5	1.19	0.81, 1.75
High	28	4.2	26	1.6	1.64	0.87, 3.08
					P _{trend}	0.49
Duration of exposure at high concentrations (years):						
Unexposed	630	96.0	1335	98.2	1.00	
≤ 10	11	1.7	13	1.0	1.24	0.52, 2.94
> 10	15	2.3	11	0.8	2.45	1.04, 5.74
					P _{trend}	0.07

Estimates were restricted to reliability > than possible; estimates with reliability ≤ possible were classified as unexposed

Results: DEE



- Exposure-response curves for duration



Results: GEE



	Cases (N=658)		Controls (N=1360)		OR	95% CI
	N	%	N	%		
Unexposed	343	52.1	783	57.6	1.00	
Ever exposed	315	47.9	577	42.4	1.05	0.85, 1.29
Highest attained concentration:						
Unexposed	343	52.1	783	57.6	1.00	
Low	251	38.2	462	34.0	1.05	0.84, 1.30
Medium	46	7.0	71	5.2	1.07	0.68, 1.69
High	18	2.7	44	3.2	1.01	0.56, 1.85
					P _{trend}	0.71
Duration of exposure at high concentrations (years):						
Unexposed	640	52.8	1316	97.1	1.00	
≤ 5	11	1.7	21	1.6	1.21	0.55, 2.66
> 5	7	1.1	18	1.3	0.89	0.36, 2.23
					P _{trend}	0.85

Estimates were restricted to reliability > than possible; estimates with low reliability were classified as unexposed

Results: GEE



- Sensitivity analysis for men exposed to gasoline engine emission who had never been exposed to diesel engine emissions

Highest attained frequency:

Unexposed	273	80.1	644	83.0	1.00	
< 5%	23	6.7	39	5.0	0.86	0.32, 2.30
5 – 30%	20	5.9	53	6.8	1.02	0.72, 1.43
> 30%	25	7.3	40	5.2	1.59	1.04, 2.43
					P _{trend}	0.12

Cumulative exposure:

Unexposed	273	80.1	644	83.0	1.00	
Lower tertile	15	4.4	35	4.5	1.08	0.73, 1.60
Middle tertile	21	6.2	42	5.4	1.06	0.70, 1.60
Higher tertile	32	9.4	55	7.1	1.66	0.98, 2.80
					P _{trend}	0.12

Conclusions



- Weak or null associations were observed for the other exposure metrics:
 - highest attained frequency of exposure, duration at any and low concentrations and cumulative exposure to DEE
- The results do not provide strong support for an association between GEE and bladder cancer
- Occupational exposure to high concentrations of DEE is associated with an increased risk of bladder cancer
 - Long duration of exposure at high concentrations (> 10 years) is particularly important
 - Effect of exposure to DEE was independent of the effect of cigarette smoking on bladder cancer

Acknowledgments



- **Investigators:**
 - Shelley Harris
 - Paul Villeneuve
 - Marie-Élise Parent
 - Ken Jonson
- **Cancer Care Ontario:**
 - Linda Kachuri
- **Institut national de la recherche scientifique:**
 - Louise Nadon
 - Ramzan Lakhani
 - Benoit Latreille
- This work was funded by the **Workplace Safety and Insurance Board (WSIB) Ontario** —WSIB#10011
- We acknowledge the support of the **Occupational Cancer Control Research Center (OCRC)** and **Health Canada**
- Marie-Élise Parent received funds from **Fonds de recherche du Québec-Santé (FRQS)**.
- **Canadian Cancer Registries Epidemiology Research Group:**
 - **Farah McCrate**, Eastern Health, Newfoundland; **Ron Dewar**, Nova Scotia Cancer Registry, **Nancy Krieger**, Cancer Care Ontario; **Donna Turner**, Cancer Care, Manitoba

For more information: Lidija.Latifovic@cancercare.on.ca



Towards a cancer-free workplace



Occupational
Cancer
Research
Centre

Supplementary Information

S1. Interaction analysis - cigarette pack-years and highest DEE concentration attained

Pack-years smoking	DEE concentration	Label	Cases		Controls		OR ^a	95% CI
			N	%	N	%		
< 10	Unexposed	OR ₀	98	14.9	374	27.5	1.00	
	Low		35	5.3	139	10.2	0.74	0.46 – 1.19
	Medium/High		21	3.2	36	2.7	1.78	0.94 – 3.36
10 - < 40	Unexposed	OR _D	236	35.9	362	26.6	3.85	2.56 – 5.79
	Low		80	12.2	177	13.0	2.32	1.44 – 3.72
	Medium/High		51	7.8	55	4.0	4.36	2.50 – 7.62
≥ 40	Unexposed	OR _S	68	10.3	133	9.8	2.26	1.47 – 3.47
	Low		47	7.1	61	4.5	3.21	1.92 – 5.35
	Medium/High		22	3.3	23	1.7	2.59	1.26 – 5.32

^a Adjusted for proxy respondent, province of residence, age at interview, cigarette pack-years, cumulative asbestos, and cumulative silica exposure

S2. Stratified analysis - cigarette pack-years and highest DEE concentration attained

DEE concentration	Cigarette smoking (pack-years)								
	< 10			10 - < 40			≥ 40		
	N ^a	OR ^b	95% CI	N ^a	OR ^b	95% CI	N ^a	OR ^b	95% CI
Unexposed	98	1.00		236	1.00		68	1.00	
Low	35	0.80	0.47 – 1.37	80	0.61	0.42 – 0.87	47	1.53	0.88 – 2.68
Medium	17	2.05	0.97 – 4.37	36	1.00	0.59 – 1.69	13	0.79	0.30 – 2.07
High	4	1.54	0.35 – 6.81	15	1.36	0.58 – 3.22	9	2.70	0.64 – 11.42

^a Exposed cases

DEE: Proxy excluded



	Cases (N=405)		Controls (N=902)		OR	95% CI
	N	%	N	%		
Unexposed	270	66.7	608	67.4	1.00	
Ever exposed	135	33.3	294	32.6	0.76	0.56, 1.03
Highest attained concentration:						
Unexposed	270	66.7	608	67.4	1.00	
Low	88	21.7	229	25.4	0.68	0.49, 0.94
Medium	32	7.9	52	5.8	0.96	0.57, 1.62
High	15	3.7	13	1.4	1.76	0.75, 4.14
					P _{trend}	0.49
Duration of exposure at high concentrations (years):						
Unexposed	390	96.3	889	98.7	1.00	
≤ 10	6	1.5	6	0.7	1.63	0.49, 5.42
> 10	9	2.2	6	0.7	2.56	0.83, 8.04
					P _{trend}	0.07

DEE concentration	Ever exposed to silica					
	Never			Ever		
	N ^a	OR ^b	95% CI	N ^a	OR ^b	95% CI
Unexposed	352	1.00		50	1.00	
Low	84	0.69	0.52 – 0.93	78	0.90	0.54 – 1.49
Medium	37	1.16	0.72 – 1.84	29	1.23	0.62 – 2.46
High	19	2.56	1.10 – 5.93	9	1.20	0.43 – 3.38

DEE concentration	Ever exposed to asbestos					
	Never			Ever		
	N ^a	OR ^b	95% CI	N ^a	OR ^b	95% CI
Unexposed	381	1.00		21	1.00	
Low	158	0.80	0.62 – 1.03	4	0.58	0.11 – 3.22
Medium	57	1.23	0.82 – 1.85	9	1.45	0.39 – 5.42
High	23	1.97	0.98 – 3.94	5	1.54	0.23 – 10.28