RESEARCH COMMUNICATION

Urinary Bladder Cancer Risk Among Motor Vehicle Drivers: A Meta-analysis of the Evidence, 1977-2008

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Abstract

Background: The aim of the study was to summarize bladder cancer risk in motor vehicle drivers and railroad workers using meta-analysis techniques. Methods: We retrieved all published results (3 cohort studies and 27 case-control studies) during 1977-2008. We assessed the heterogeneity of the results assuming a fixed-effect model. For cohort studies, the observed and the expected number of cases were added, respectively, to yield pooled observed/expected ratio. For case-control studies, we calculated pooled odds ratio (OR) and corresponding 95% confidence interval (CI) as a weighted average of the ORs in each study, by giving a weight proportional to the inverse of the variance of the ORs. Results: No overall meta-analysis was performed because of heterogeneity in results. The overall pooled risk among motor vehicle and railroad workers based on all cohort studies was 1.08 (95%: 1.00-1.17). The overall pooled risk among truck drivers was 1.18 (95% CI: 1.09-1.28 based on 18 case-control studies). The stratified analysis by year of publication indicated that pooled risk among truck drivers was 1.20 (95% CI: 1.00-1.40) for the period 1998-2008. The corresponding risk for the period 1977-1987 was 1.30 (95%: 1.16-1.46). The overall pooled risk among bus drivers was 1.23 (95% CI: 1.06-1.44 based on 10 case-control studies). The pooled risk among bus drivers was 1.21 (95% CI: 0.72-2.01) for the period 1998-2008 and the corresponding risk for the period 1977-1987 was 1.30 (95%CI: 1.10-1.53). The pooled risk among railroad workers was 1.20 (95% CI: 1.02-1.41 based on 15 case-control studies). Stratified analysis by year of publication was not statistically significant among railroad workers. Conclusion: The pooled analysis suggested an increased bladder cancer risk among motor vehicle drivers and railroad workers. However, the risk among these workers is reduced in recent publications compared to the earlier publications.

Key Words: Urinary bladder cancer - motor vehicle drivers - occupation - meta-analysis

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Introduction

Bladder cancer forms in tissues of the urinary bladder (the organ that stores urine). It is the most common malignant tumor of the urinary system. Currently, it is the seventh most common cancer world wide, with 273,000 new cases and more than 108,000 deaths estimated to have occurred in the year 2002. Internationally, the incidence rate of bladder cancer varies about 10-fold. The disease is reported most often in Europe and North America and least often in several areas of Asia, particularly in India. In Europe and United States, it accounts for 5 to 10% of all malignant tumors in men (Ferlay et al., 2004).

The established risk factor for bladder cancer is smoking and it accounts for about 50% of cases in developed countries. Other risk factors mainly include workers exposed to some aromatic amines, drinking water containing arsenic, less fluid intake and consumption of fruits and vegetables, urinary tract diseases, exposure to certain drugs like cyclophosphamide used in chemotherapy and heavy consumption of phenacetin-containing analgesics (Jankovic and Radosavljevic 2007; Anderson and Naish 2008).

It has been estimated that 5-10% of bladder cancers in industrialized countries were due to exposures of occupational origin (Jankovic and Radosavljevic 2007). Several observational studies have been estimated on the potential association between motor vehicle drivers and bladder cancer in the past three decades (Decoufle et al., 1977; Howe et al., 1980; Silverman et al., 1983; 1986; Schenker et al., 1984; Wynder et al., 1985; Iscovich et al., 1987; Risch et al., 1988; Gallagher et al., 1989; Burns et al., 1991; Dolin et al., 1992; Cordier et al., 1993; Siemiatycki et al., 1994; Pukkala 1995; Porru et al., 1996; Soll-Johanning et al., 1998; Pesch et al., 2000; Zheng et al., 2002; Kogevinas et al., 2003; Colt et al., 2004; Reulen et al., 2007; Dryson et al., 2008). Motor vehicle drivers may spend all working hours close to the sources of air pollution. Several air pollutants, such as polycyclic aromatic hydrocarbons have been reported to confer small to moderate increased bladder cancer risk, particularly among non-smokers (Castano-Vinyals et al., 2008). Secondly, motor vehicle drivers may be exposed to diesel engine exhausts. In a meta-analysis published in 2001, it is reported that exposure to diesel exhaust may increase the occurrence of bladder cancer (Boffetta and Silverman

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2001). An effect on the urinary bladder is plausible with diesel exposure because metabolites of polycyclic and nitro-polycyclic aromatic hydrocarbons present in diesel exhaust are concentrated in the urine and may interact with the urothelium of the bladder (Silverman et al., 1986).

We here conducted a meta-analysis of case-control and cohort studies that provided information on bladder cancer risk in motor vehicle drivers and railroad workers during the past three decades.

Materials and Methods

The studies included in the quantitative review were cohort and case-control studies published during the period 1977 and 2008. They were identified through searches on the MEDLINE database, using keywords 'bladder cancer risk' and 'drivers' and/or 'occupation'. Papers were also searched among those quoted as references in the retrieved studies. We also identified previously published quantitative reviews to compare the present results. Smoking unadjusted case-control studies were excluded. Also excluded from the present review, if the observed and expected number of cases were unavailable in cohort studies.

A description of the main characteristics such as the authors, year of publication, country, type of motor vehicle drivers, the observed and expected number of cases or deaths, with the corresponding standardized incidence ratios (SIRs) or standardized mortality ratios (SMR) (for cohort studies), and the number of exposed cases and controls (if available), with the corresponding odds ratios (OR) and the 95% confidence intervals (CI) (for case-control studies) according to the various type of drivers were obtained. We used the risk estimates, which were adjusted for age, smoking and other confounding factors. If the risk was expressed in more than one-way, the estimate with greatest degree of controlling for confounders was used.

For case-control studies, we calculated summary OR (ORsum and corresponding 95% CI) as a weighted average of the ORs (ORi), by giving a weight proportional to its precision (i.e., to the inverse of the variance of the ORi) [i.e. ORsum=sum(weighti x ln ORi)/ sum(weighti)]. To assess the consistency of findings among studies, we calculated test for heterogeneity using general variance-based method. i.e. Q= sum [(weighti x(ln ORsum–ln ORi)^2]. Q is referred to the chi-square distribution with degrees of freedom equal to the number of studies minus 1. When the chi-square p-value is less than 0.1, we excluded studies with a high value of (weighti x (ln ORsum– ln ORi)^2 and then calculated ORsum and the corresponding 95% CI assuming a fixed-effect model (Petiti 2000).

For cohort studies, the observed (O) and the expected (E) number of cases were added, respectively, to yield observed/ expected pooled ratios (PR). Observed and expected deaths were used to calculate pooled PR if incident cases were not available. Approximate 95% CI for the PR was estimated using the formulae; Lower limit of 95% CI= (O/E)* [1-1/(9*O)–1.96/(3*$\sqrt{O}$)]^3 and Upper limit of 95% CI=[(O+1)/E] *{1-1/[9*(O+1)] + 1.96/[3*($\sqrt{O+1}$)]}^{3} (Rothman and Boice 1979). Test for heterogeneity between studies was calculated using the general variance-based method (Petiti 2000). The summary risks were estimated using Microsoft Excel.

Stratified analysis was performed by dividing the total 30 years of publications into 3 groups such as 1977-1987, 1988-1997 and 1998-2008 and estimated the pooled risk in each group. To assess publication bias, funnel plot was constructed by taking natural logarithm of the risk on one axis and inverse standard error on the other axis. Funnel plot was drawn in Excel. The results of the meta-analysis along with the individual studies were presented graphically (forest plot), plotting OR and the corresponding 95% CI using the graph pad software.

Results

During 1977-2008, a total of 30 studies (3 cohort studies and 27 case-control studies) that provided bladder cancer adjusted risk (adjusted for age, smoking and other confounders) among motor vehicle drivers and/or railroad workers. Of the 3 cohort studies that reported bladder cancer risk among drivers (n= 633), 2 (Soll-Johanning et al., 1998; Guo et al., 2004) were based on incident cases and one (Schenker et al., 1984) on deaths. No overall meta-analysis was performed based on all the case-control studies because of heterogeneity in results. The overall pooled risk among motor vehicle and railroad workers based on all cohort studies was 1.08 (95%: 1.00-1.17).

Truck drivers

Of the 18 case-control studies that investigated the association between truck drivers and bladder cancer risk after adjusted for age, smoking and other confounding factors, 4 studies reported a significant increased risk (OR ranged from 1.29 to 2.40) (Jensen et al., 1987; Kunze et al., 1992; Silverman et al., 1983; Colt et al., 2004), 4 studies reported increased risk with borderline significance (OR ranged from 1.23 to 1.67) (Decoufle et al., 1977;

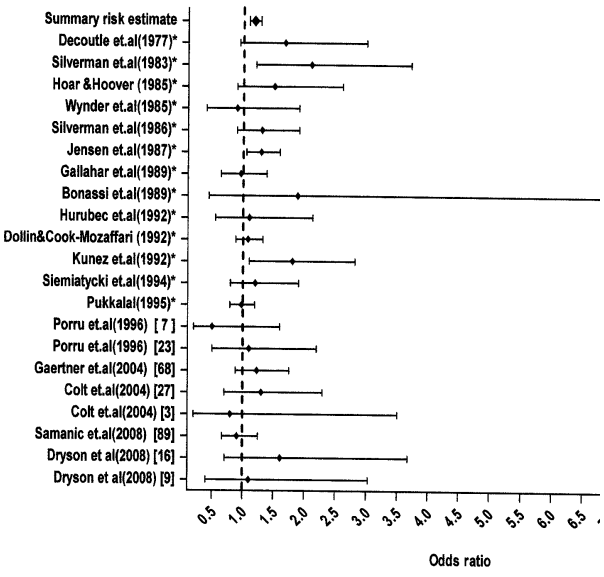


Figure 1. Results of Published Case-control Studies on theAssociation between Truck Driving and Bladder Cancer Risk. *size unavailable

Table 1. Urinary Bladder Cancer Risk Estimates in Motor Vehicle Drivers: Case-control Studies

Author & Year	Country	Occupation	Cases	Controls	OR	95% C I
Truck drivers						
Dryson et al., (2008)	New Zealand	Light truck or van driver	9	9	1.10	0.40-3.03
Dryson et al., (2008)	New Zealand	Heavy truck drivers	16	13	1.61	0.71-3.67
Samanic et al., (2008)	Spain	Truck drivers	89	110	0.91	0.67-1.25
Colt et al., (2004)*	USA	Truck drivers, tractor- trailor	47	25	2.40	1.40-4.10$
Colt et al., (2004)	USA	Truck drivers, heavy	3	4	0.80	0.20-3.5
Colt et al., (2004)	USA	Truck drivers, light	27	25	1.30	0.70-2.30
Gaertner et al., (2004)	Canada	Trucker	68	133	1.23	0.88-1.75
Porru et al., (1996)	Italy	Lorry and van driver - long	23	19	1.10	0.50-2.20
Porru et al., (1996)	Italy	Lorry and van driver -local	7	11	0.50	0.20-1.60
Pukkala (1995)	Finland	Truck drivers	--	--	0.98	0.79-1.19
Siemiatycki et al., (1994)	Canada	Truck drivers	--	--	1.20	0.80-1.90
Kunez et al., (1992)	Germany	Truck drivers	--	--	1.80	1.10-2.80$
Dolin (1992)	UK	Truck drivers	--	--	1.08	0.88-1.32
Hrubec et al., (1992)	USA	Truck drivers	--	--	1.10	0.55-2.13
Bonassi et al., (1989)	Italy	Truck drivers	--	--	1.88	0.44-8.00
Gallahar et al., (1989)	Canada	Truck drivers	--	--	0.96	0.64-1.38
Jensen et al., (1987)	Denmark	Truck, bus drivers	--	--	1.29	1.05-1.59$
Silverman et al., (1986)	USA	Truck drivers	--	--	1.30	0.90-1.90
Wynder et al., (1985)	USA	Truck, bus drivers	--	--	0.90	0.40-1.90
Hoar & Hoover, (1985)	USA	Truck drivers	--	--	1.50	0.90-2.60
Silverman et al., (1983)	USA	Truck drivers	--	--	2.10	1.20-3.70$
Decoutle et al., (1977)	USA	Truck drivers	--	--	1.67	0.94-2.98
(Heterogeneity p-value = 0.09)		Summary risk estimate of truck drivers			1.20	1.11-1.30$
Heterogeneity p-value = 0.25 (*excluded)		Summary risk estimate of rail road workers (*)			1.18	1.09-1.28$
Bus-drivers						
Dryson et al., (2008)	New Zealand	Bus drivers	5	7	1.21	0.35-4.14
Samanic et.al., (2008)	Spain	Bus drivers	11	16	0.75	0.32-1.73
Colt et al., (2004)7	USA	Bus drivers	5	10	0.50	0.20-1.60
Gaertner et al., (2004)*	Canada	Bus/taxi driver	12	48	0.50	0.25-1.00
Dolin & Cook (1992)	UK	Bus drivers	--	--	0.81	0.44-1.36
Hrubec et al., (1992)	USA	Bus drivers	--	--	3.10	1.21-8.12$
Gallahar et al., (1989)	Canada	Bus drivers	--	--	1.40	0.78-2.32
Jensen et al., (1987)	Denmark	Truck, bus drivers	--	--	1.29	1.05-1.59$
Silverman et al., (1986)	USA	Bus drivers	--	--	1.30	1.10-1.40$
Wynder et al., (1985)	USA	Truck, bus drivers	--	--	0.90	0.40-1.90
Silverman et al., (1983)	USA	Bus drivers	--	--	1.50	0.40-5.30
Decoutle et al., (1977)	USA	Bus drivers	--	--	2.89	0.86-9.73
Heterogeneity p-value = 0.05		Summary risk estimate of bus drivers			1.19	1.02-1.38$
Heterogeneity p-value = 0.19 (* excluded)		Summary risk estimate of bus drivers (*)			1.23	1.06-1.44$

** study includes both men and women; $statistically significant at 5% level

Silverman et al., 1986; Hoar et al., 1985; Gaertner et al., 2004) and 6 studies reported increased risks but non-significant (OR ranged from 1.08 to 1.88) (Gallagher et al., 1989; Dolin et al., 1992; Hrubec et al., 1992; Siemiatycki et al., 1994; Porru et al., 1996; Dryson et al., 2008) and the remaining 4 studies reported no association (Wynder et al., 1985; Gallagher et al., 1989; Pukkala 1995; Samanic et al., 2008). Of the 5 studies that reported dose-response relationship between the increased duration of employment and bladder cancer risk, significant association was observed in 4 studies (Silverman et al., 1983; 1986; Hoar et al., 1985; Colt et al., 2004). After excluding the study by Colt et al (2004) which reported risk among truck drivers and tractor-trailers together, there was no evidence of heterogeneity between the studies (p=0.25) and hence we performed meta analysis after this exclusion. The pooled risk estimate was then 1.18 (95% CI: 1.09-1.28) among truck drivers (Table 1 and Figure 1).

Of the 3 cohort studies, only one study provided information on bladder cancer risk among truck drivers and the same was not significant (Guo et al., 2004). The stratified analysis by year of publication indicated that pooled risk among truck drivers was 1.20 (95% CI: 1.00-1.40) for the period 1998-2008. The corresponding risk for the period 1977-1987 was 1.30 (95% CI: 1.16-1.46).

Bus drivers

Of the 10 case-control studies that investigated the association between bus drivers and bladder cancer risk after adjusting for age, smoking and other confounding factors, 3 studies reported significant increased risk (OR ranged from 1.29 to 3.10) (Silverman et al., 1986; Jensen et al., 1987; Hrubec et al., 1992), 4 studies reported increased risk but non-significant (OR ranged from 1.21 to 2.89) (Decoufle et al., 1977; Silverman et al., 1983; Gallagher et al., 1989; Dryson et al., 2008) and the remaining 3 studies reported no association (Wynder et al., 1985; Dolin et al., 1992; Gaertner et al., 2004). Only one study reported bladder cancer risk with duration of

Table 1 (cont). Urinary Bladder Cancer Risk Estimates in Motor Vehicle Drivers: Case-control Studies

Author & Year	Country	Occupation	Cases	Controls	OR	95% C I
Other motor vehicle drivers						
Dryson et al., (2008)	New Zealand	Taxi driver	2	10	0.32	0.07-1.53
Dryson et al., (2008)	New Zealand	Car, taxi, light van operators	11	18	0.75	0.33-1.72
Dryson et al., (2008)	New Zealand	Motor vehicle drivers	22	31	0.88	0.47-1.66
Dryson et al., (2008)	New Zealand	Mobile machinery operators	36	52	0.85	0.50-1.43
Samanic et al., (2008)	Spain	Taxicab drivers /chauffers	37	35	1.14	0.69-1.90
Reulen et al., (2007)**	Belgium	Motor vehicle drivers	11	10	0.90	0.40-2.50
Reulen et al., (2007)**	Belgium	Drivers mobile plant operators	16	18	0.80	0.40-1.80
Colt et al., (2004)	USA	Taxicab drivers and chauffers	8	10	0.80	0.30-2.30
Gaertner et al., (2004)	Canada	Bus/taxi driver	12	48	0.50	0.25-1.00
Kogevinas et al., (2003)	West Europe	Motor vehicle drivers	302	636	1.14	0.97-1.33
Zheng et.al., (2002)	Iowa	Drivers	78	79	1.30	0.90-1.80
Pesch et al., (2000)	Germany	Motor vehicle drivers	43	43	1.00	0.70-1.40
Porru et al., (1996)	Italy	Motor vehicle drivers	33	37	0.90	0.50-1.70
Burns et al., (1991)	USA	Drivers	48	87	0.70	0.50-1.00
Silverman et al., (1986)*	USA	Taxicab drivers and chauffers	77	92	1.60	1.20-2.20$
Heterogeneity (p-value) = 0.02		Summary risk estimate of other drivers			1.06	0.96-1.17
Heterogeneity p-value = 0.11 (* excluded)		Summary risk estimate of other drivers (* excluded)			1.11	0.99-1.23
Rail-road workers						
Samanic et al., (2008)	Spain	Rail transportation	11	8	1.04	0.40-2.69
Gaertner et al., (2004)	Canada	Rail road worker	26	57	0.94	0.56-1.58
Kogevinas et al., (2003)	West Europe	Railway drivers and firemen	34	53	1.41	0.87-2.28
Kogevinas et al., (2003)	West Europe	Railway brakemen, signalmen	18	35	1.43	0.77-2.63
Zheng et al., (2002)	Iowa	Railroad transportation	33	33	1.40	0.80-2.30
Pukkala, (1995)	Finland	Railroad workers	--	--	1.35	0.85-2.05
Cordier et al., (1993)	France	Railroad workers	--	--	0.80	0.49-1.30
Kunez et al., (1992)	Germany	Railroad workers	--	--	3.00	1.00-8.80$
Dolin & Cook (1992)	UK	Railroad workers	--	--	1.61	0.85-2.75
Burns et.al., (1991)	USA	Railroad workers	5	8	0.70	0.20-2.40
Gallahar et al., (1989)	Canada	Railroad workers	--	--	0.69	0.33-1.28
Risch et al., (1988)	Canada	Railroad workers	--	--	1.07	0.71-1.61
Iscovich et al., (1987)*	Argentina	Railroad workers, drivers	--	--	4.16	1.82-9.53$
Wynder et al., (1985)	USA	Railroad workers	--	--	2.00	0.30-11.6
Howe et al., (1980)	Canada	Rail road workers	--	--	9.00	1.20-39.5$
Decoutle et al., (1977)	USA	Rail road workers	--	--	1.63	0.66-4.04
Heterogeneity p-value = 0.06		Summary risk estimate of rail road workers			1.25	1.07-1.47$
Heterogeneity p-value = 0.31 (*excluded)		Summary risk estimate of rail road workers (*)			1.20	1.02-1.41$

** study includes both men and women; $statistically significant at 5% level

employment and the same was non-significant (Silverman et al., 1986). Two studies (Jensen et al., 1987; Wynder et al., 1985) reported bladder cancer risk including truck and bus drivers together and one study reported bladder cancer risk among bus and taxi drivers together (Gaertner et.al., 2004). Hence these studies were included in the estimation of pooled risk among bus drivers. There was no evidence of heterogeneity among the remaining studies (p=0.20). The pooled risk was 1.23 (95% CI: 1.06-1.44) among bus drivers (Table 1 and Figure 2).

Of the 2 cohort studies that reported association between bus drivers and bladder cancer risk, one study reported an increased bladder cancer risk (OR=1.29; 95% CI: 1.02-1.62) (Guo et al., 2004) and the other study, which included bus drivers and tramway workers together, also reported an increased risk but borderline significant (OR=1.10; 95% CI: 0.90-1.30) (Soll-Johanning et al., 1998). The stratified analysis by year of publication indicated that pooled risk among bus drivers was 1.21 (95% CI: 0.72-2.01) for the period 1998-2008. The corresponding risk for the period 1977-1987 was 1.30 (95%CI: 1.10-1.53).

Other motor vehicle drivers

These included taxi, taxicab drivers and chauffeurs. Of the 11 case-control studies that investigated the association between motor vehicle drivers (excluded truck and bus drivers) and bladder cancer risk after adjusted for

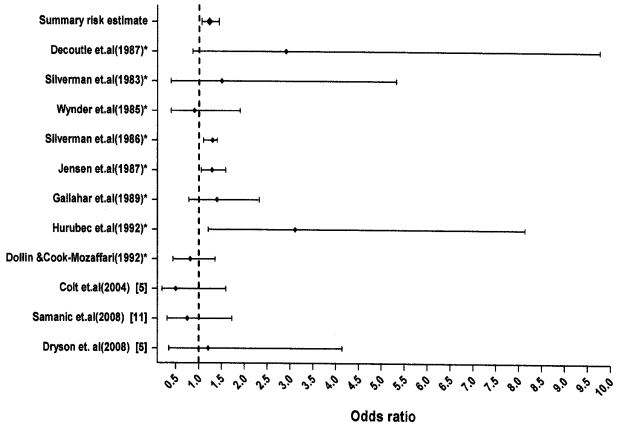


Figure 2. Results of Published Case-control Studies on theAssociation between Bus Driving and Bladder Cancer Risk. *size unavailable

Table 2. Bladder Cancer Risk Estimates in Motor Vehicle Drivers and Railroad Workers: Cohort Studies

Author & Year	Country	Vehicle/Site	Cases	Observed	Expected	SIR /SMR	95% CI
Guo et al., (2004)	Finland	Locomotive	Incidence	22	25.88	0.85	0.53-1.28
Guo et al., (2004)	Finland	Road building vehicles	Incidence	15	14.56	1.03	0.58-1.70
Guo et al., (2004)	Finland	Bus	Incidence	75	58.14	1.29	1.02-1.62$
Guo et al., (2004)	Finland	Taxi	Incidence	55	51.89	1.06	0.80-1.38
Guo et al., (2004)	Finland	Truck	Incidence	144	142.57	1.01	0.85-1.19
Guo et al., (2004)	Finland	Motor vehicle/tram	Incidence	129	114.16	1.13	0.94-1.34
Guo et al., (2004)	Finland	Forklift (pulp/paper)	Incidence	6	8.11	0.74	0.27-1.61
Guo et al., (2004)	Finland	Forklift (NEC)	Incidence	19	17.76	1.07	0.65-1.67
Soll-Johanning et al., (1998)	Denmark	Bus tram	Incidence	165	150.00	1.10	0.90-1.30
Schenker et al., (1984)	USA	Rail road	Mortality	3	4.00	0.76	0.15-2.21
Heterogeneity p-value = 0.85							
Summary risk estimate of motor vehicle drivers and rail road workers						1.08	1.00-1.17$

$statistically significant at 5% level

age, smoking and other confounding factors, one study reported a significant increased risk (OR=1.6; 95%CI: 1.2-2.2) (Silverman et al., 1986), 2 studies reported increased risk with borderline significance (OR ranged from 1.14 to 1.3) (Zheng et al., 2002; Kogevinas et al., 2003), 2 studies reported increased risk but non-significant (OR ranged from 1.0 to 1.14) (Pesch et al., 2000; Samanic et al., 2008) and the remaining 6 studies reported no association (Burns et al., 1991; Porru et al., 1996; Colt et al., 2004; Gaertner et al., 2004; Reulen et al., 2007; Dryson et al., 2008). After excluding the study by Gaertner et al (2004), there was no evidence of heterogeneity between the remaining studies (p=0.11) and hence we performed a pooled analysis based on the remaining studies. The pooled risk estimate was 1.11 (95% CI: 0.99-1.23) among the motor vehicle drivers (excluding truck and bus drivers) (Table 1).

One cohort study by Guo et al (2004) reported an increased bladder cancer risk with borderline significance in motor vehicle/tram drivers (standardized incidence ratio= 1.13; 95%CI: 0.94-1.34). No significant association was observed in the stratified analysis by year of publication.

Railroad workers

Of the 15 case-control studies that investigated the association between railroad workers and bladder cancer risk after adjusted for age, smoking and other confounding factors, 3 studies reported significant increased risk (OR ranged from 3.0 to 9.0) (Howe et al., 1980; Iscovich et al., 1987; Kunze et al., 1992), non-significant increased risks in 8 studies (OR ranged from 1.04 to 2.00) (Decoufle et al., 1977; Wynder et al., 1985; Risch et al., 1988; Pukkala 1995; Dolin et al., 1992; Zheng et al., 2002; Kogevinas et al., 2003;Samanic et al., 2008), and no association in 4 studies (Gallagher et al., 1989; Burns et al., 1991; Cordier et al., 1993; Gaertner et al., 2004). After excluding the study by Iscovich et al (1987), there was no evidence of heterogeneity between the remaining studies (p=0.31) and hence we performed meta analysis based on the remaining studies. The pooled risk estimate was 1.20 (95% CI: 1.02-1.41) among the railroad workers (Table 1 and Figure 3). None of the cohort studies have reported any association between railroad workers and bladder cancer risk (Schenker et al., 1984) (Table 2).

The stratified analysis by year of publication indicated that pooled risk among railroad workers was 1.25 (95% CI: 0.96-1.61) for the period 1998-2008. The corresponding risk for the period 1977-1987 was 1.33 (95%CI: 0.98-1.54).

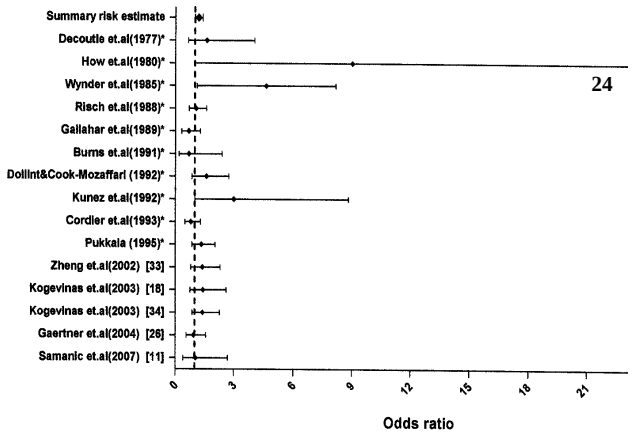


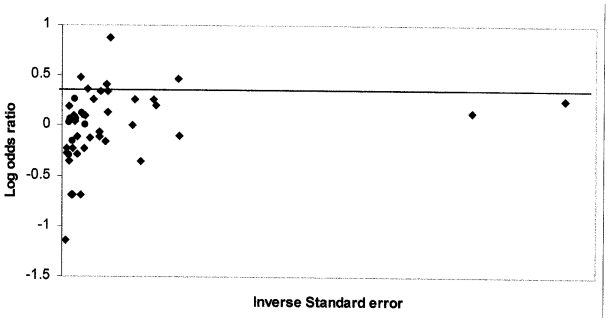
Figure 2. Results of Published Case-control Studies on theAssociation between Railroad Working and Bladder Cancer Risk. *size unavailable

Discussion

Results of the present meta-analysis indicated an overall excess risk of bladder cancer among motor vehicle drivers and railroad workers (OR=1.18; 95% CI: 1.09-1.28 among truck drivers; OR=1.23; 95% CI: 1.06-1.44 among bus drivers and OR=1.20 (95% CI: 1.02-1.41) among the railroad workers). The stratified analysis by year of publication indicated a reduction in risk in recent decade among the motor vehicle workers. The pooled risk among truck drivers was 1.20 (95% CI: 1.00-1.40) for the period 1998-2008 and the corresponding risk for the period 1977-1987 was 1.30 (95% CI: 1.16-1.46). Similarly among the bus drivers, the pooled risk was 1.21 (95%CI: 0.72-2.01) for the period 1998-2008 and the corresponding risk for the period 1977-1987 was 1.30 (95%CI: 1.10-1.53). Also, the present review suggested a small reduction in bladder cancer risk among bus drivers (OR=1.23; 95% CI: 1.06-1.44) as against the previous review by Boffetta and Silverman (2001) (OR=1.33; 95% CI: 1.22-1.45).

It is possible that the lower risk observed in the latest decade might be due to better analytical approaches such

Figure 4. Funnel Plot. (36 studies excluded due to the unavailability of case numbers)



as removal of confounding effect used in the data analysis. Further, in the present analysis we considered only smoking adjusted risks and if the risk was expressed in more than one way, the estimate with greatest degree of controlling for confounders was used.

On the other hand, it may be possible that the occupational exposure to diesel exhaust might be changed. For example diesel-locomotive drivers in many countries, the railway traction is almost entirely electrical. The main exposure regarding the occupational driving is exposure to the fuel used. A working group under the International Agency for Research on Cancer in 1989 (IARC 1989) reviewed the evidence for carcinogenicity of engine exhaust fumes based on epidemiologic studies, experimental studies in animals, and other relevant biological data. It found limited evidence for the carcinogenicity of diesel engine exhaust in humans and inadequate evidence for the carcinogenicity of petrol engine exhaust in human.

Even though several case-control studies were reported the association between motor vehicle drivers and bladder cancer risk, the cohort studies that reported the above association during the past three decades were only a few. Only two studies reported the association between truck drivers and only one study reported the association between bus drivers and bladder cancer risk. As cohort studies are in principle, more valid study design among the observational studies, a pooled risk based on more cohort studies may provide better results. In the present analysis, the overall pooled risk based on the three cohort studies indicated only a slightly increased risk (8%) with borderline significance.

Smoking and other confounders such as age, certain occupational exposures, drinking water containing arsenic, less fluid intake and less consumption of fruits and vegetables, urinary tract diseases, exposure to certain drugs like cyclophosphamide used in chemotherapy and heavy consumption of phenacetin-containing analgesics were reported as factors associated with the development of bladder cancer (Jankovic and Radosavljevic 2007; Anderson and Naish 2008). In the present analysis, we included the estimates with greatest degree of controlling for confounders were used. Thus it is assumed that the confounding bias is removed to a great extent in the pooled analysis. However, residual bias due to smoking may exist, since it has been reported that smoking prevalence in drivers was higher than the general population (Lam et al., 2002).

The asymmetric nature of the funnel plot (Figure 4) indicated presence of publication bias, however, several studies were excluded for drawing funnel plot due to the unavailability of sample sizes. Hence it is difficult to conclude the presence of publication bias.

A potential source of bias that might have played a role in the pooled analysis is that the specific occupations studied were compared with other occupational populations in each study. This can over or under estimate the pooled risk. However, this source of bias is applicable in both case-control and cohort studies. Another limitation is that the number of cases and controls were not available in some of the case-control studies and thus the pooled estimate based on case-control studies, the number of cases and controls were unknown.

There can be several arguments in favour of an association between motor vehicle drivers and railroad workers and the occurrence of bladder cancer. An increased risk with reversibility (reduced risk) was observed in the present meta-analysis. Out of the 5 studies that reported dose-response relationship between truck drivers and bladder cancer risk, significant association was observed in 4 (Silverman et al., 1983; 1986; Hoar et al., 1985; Colt et al., 2004). Further a biologic plausibility exists as motor vehicle drivers and railroad workers spend longer time on the roads, several air pollutants, such as polycyclic aromatic hydrocarbons have been reported small to moderate positive association with bladder cancer risk particularly stronger effect among non-smokers (Castano-Vinyals et al., 2008). Secondly, such workers may be exposed to diesel engine exhausts. An effect on the urinary bladder is plausible with diesel exposure because metabolites of polycyclic and nitro-polycyclic aromatic hydrocarbons present in diesel exhaust are concentrated in the urine and may interact with the urothelium of the bladder (Silverman et al., 1986).

In conclusion, the pooled analysis suggested an increased bladder cancer risk among motor vehicle drivers and railroad workers. However, the risk among these workers is reduced in recent publications compared to the earlier publications.

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