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## Short Communication

# Motor vehicle exposure and risk of oesophageal adenocarcinoma

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## ABSTRACT

**Objective:** The introduction of motor vehicles in industrialised countries during the mid 20th century seems to fit with the increasing incidence and the strong male predominance of oesophageal adenocarcinoma. The aim of the study was to test this new hypothesis in a large case-control study.

**Methods:** A nationwide, Swedish, population-based case-control study included 189 and 262 cases of oesophageal and cardia adenocarcinoma, respectively, 167 cases of oesophageal squamous-cell carcinoma and 820 frequency-matched controls during 1995–1997. Tumours were uniformly classified. Exposure data were collected at face-to-face interviews. Odds ratios (ORs), with 95% confidence intervals (CIs), were estimated and adjusted for confounding in multivariable logistic regression models.

**Results:** There were no associations between regular contact with cars or airplanes regarding duration, frequency and age of contact and risk of oesophageal adenocarcinoma. The adjusted ORs for oesophageal adenocarcinoma, cardia adenocarcinoma and oesophageal squamous-cell carcinoma among persons spending at least two hours per day in cars were 1.3 (95%CI 0.7–2.3), 1.2 (95%CI 0.7–1.8), and 0.7 (95%CI 0.4–1.3), respectively. The corresponding ORs among frequent airplane passengers were 0.8 (95%CI 0.2–2.3), 1.1 (95%CI 0.5–2.2), and 0.9 (95%CI 0.3–2.5), respectively.

**Conclusion:** This large, population based case-control study does not support the hypothesis that frequent contact with motor vehicles has contributed to the increasing incidence or the male predominance of oesophageal adenocarcinoma.

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## 1. Introduction

The epidemiologic pattern of oesophageal adenocarcinoma is characterised by a rapidly increasing incidence in Western populations and a strong (7:1) male predominance.<sup>1</sup> The main

risk factors are gastro-oesophageal reflux and obesity, but reasons for the increasing incidence and the male predominance are not entirely understood.<sup>2</sup> The suddenness of the increase, starting in the mid 1970s, is likely due to an environmental exposure introduced in industrialised countries about a decade

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or two before the increase was initiated.<sup>3</sup> Such an exposure should be particularly prevalent among men. An exposure that fit with these criteria is the introduction of motor vehicles in Western populations during the 1950s and 1960s. The reported delay of 17 years in the female incidence of oesophageal adenocarcinoma<sup>4</sup> might be associated with an earlier or higher exposure to motor vehicles, e.g. regarding car maintenance. After brainstorming meetings held long before the data collection was initiated, we hypothesised that frequent contact with motor vehicles, due to potentially carcinogenic exposure to e.g. fuel exhaust, cleaning agents, engine oils and engine lubricants is associated with oesophageal adenocarcinoma and contributes to its increasing incidence and male predominance.

## 2. Materials and methods

The design of this large population-based nationwide Swedish case-control study has been described in detail previously.<sup>5</sup> In brief, during 1995–1997, all patients in Sweden diagnosed with adenocarcinoma of the oesophagus and cardia and half of the cases of oesophageal squamous-cell carcinoma, were eligible as cases. The squamous-cell carcinoma cases were primarily included to evaluate recall bias. Uniform and thorough documentation of all tumours was introduced at the 195 participating hospital departments throughout Sweden, and finally one pathologist reviewed all histological slides. Control participants were randomly selected from the computerised Swedish register of the Total Population,

**Table 1 – Contact with motor vehicles and risk of oesophageal adenocarcinoma.**

Exposure	Cases Number (%)	Controls Number (%)	Odds ratio (95% confidence interval)	
			Basic model <sup>a</sup>	Full model <sup>b</sup>
			Reference	
Age at first contact with cars				
Never	4 (2)	15 (2)		
≥30 years	32 (17)	140 (17)	0.9 (0.3–2.8)	0.7 (0.2–2.7)
10–29 years	130 (69)	537 (66)	0.9 (0.3–2.7)	0.7 (0.2–2.5)
0–9 years	23 (12)	124 (15)	0.7 (0.2–2.4)	0.6 (0.2–2.3)
Time spent in car per day				
<20 min	38 (20)	189 (23)		
20–59 min	31 (16)	184 (23)	0.8 (0.5–1.4)	0.9 (0.5–1.7)
60–119 min	53 (28)	205 (25)	1.2 (0.8–2.0)	1.4 (0.8–2.4)
≥120 min	64 (34)	229 (28)	1.3 (0.8–2.1)	1.3 (0.7–2.3)
Repair of cars				
No car	13 (7)	48 (6)		
No	110 (58)	503 (62)	0.8 (0.4–1.6)	0.7 (0.3–1.6)
Yes	66 (35)	265 (32)	0.9 (0.5–1.8)	0.8 (0.4–1.8)
Driving diesel vehicles				
No	122 (65)	576 (71)		
Yes	67 (35)	240 (29)	1.3 (0.9–1.8)	0.8 (0.5–1.2)
<10 years	20 (11)	82 (10)	1.1 (0.7–2.0)	0.8 (0.4–1.5)
10–29 years	25 (13)	94 (12)	1.2 (0.7–2.0)	0.7 (0.4–1.3)
≥30 years	22 (12)	64 (8)	1.5 (0.9–2.5)	0.9 (0.4–1.9)
Age start flying				
Never	27 (14)	100 (12)		
≥50 years	37 (20)	110 (13)	1.2 (0.7–2.2)	1.8 (0.9–3.5)
20–49 years	88 (47)	463 (57)	0.7 (0.4–1.1)	1.1 (0.6–2.0)
<20 years	35 (19)	136 (17)	1.0 (0.5–1.8)	1.4 (0.7–3.1)
Duration of flying				
Never	27 (14)	100 (12)		
0–14 years	19 (10)	61 (8)	1.1 (0.6–2.2)	1.3 (0.6–3.0)
15–39 years	88 (47)	422 (52)	0.8 (0.5–1.3)	1.2 (0.7–2.3)
≥40 years	53 (28)	226 (28)	0.8 (0.5–1.4)	1.4 (0.7–2.6)
Number of flights in 1970–79				
Never	78 (42)	272 (34)		
<10 times	63 (34)	266 (33)	0.8 (0.6–1.2)	1.0 (0.6–1.6)
10–99 times	40 (21)	224 (28)	0.6 (0.4–1.0)	1.1 (0.6–1.9)
≥100 times	6 (3)	48 (6)	0.4 (0.2–1.0)	0.8 (0.2–2.3)

<sup>a</sup> The basic model included adjustments for age and sex.

<sup>b</sup> The full model included adjustments for age, sex, socio-economic status, reflux, body mass index, tobacco smoking, alcohol use, intake of fruit or vegetables, and infection with *Helicobacter pylori*.

and frequency matched to the age distribution of the cases of oesophageal adenocarcinoma. All study participants underwent comprehensive computer-aided face-to-face interviews by professional interviewers, collecting data on various exposures, including seven items regarding contact with cars, repair of cars (at home or professional mechanic work), airplanes and other motor vehicles, as well as other known or suspected risk factors, i.e. age, sex, socio-economic status, gastro-oesophageal reflux, body mass index (BMI), tobacco smoking, use of alcohol, and dietary intake of fruit and vegetables. Moreover, the occurrence of infection with *Helicobacter pylori* was assessed through collection of blood samples from cases and controls. Confounding by the listed covariates was evaluated in a multivariable logistic regression model, while a basic model included adjustment for age and sex only. Indi-

vidual informed consent was obtained from all study participants and all regional ethics committees in Sweden approved the study.

### 3. Results

The 189, 262 and 167 interviewed cases of oesophageal adenocarcinoma, cardia adenocarcinoma and oesophageal squamous cell carcinoma, represented 87%, 83% and 73% of all eligible cases during the study period, respectively. There were 820 control participants representing 73% of all those who were eligible.

Table 1 shows the results regarding contacts with motor vehicles and risk of oesophageal adenocarcinoma. Age at first contact with cars, time spent in cars per day, repairing cars

**Table 2 – Contact with motor vehicles and risk of cardia adenocarcinoma.**

Exposure	Cases Number (%)	Controls Number (%)	Odds ratio (95% confidence interval)	
			Basic model <sup>a</sup>	Full model <sup>b</sup>
			Reference	
Age at first contact with cars				
Never	3 (1)	15 (2)		
≥30 years	46 (18)	140 (17)	1.8 (0.5–6.6)	1.3 (0.3–5.2)
10–29 years	178 (68)	537 (66)	1.5 (0.4–5.2)	1.0 (0.3–4.0)
0–9 years	35 (13)	124 (15)	1.1 (0.3–4.2)	0.9 (0.2–3.5)
Time spent in car per day				
<20 min	59 (23)	189 (23)		
20–59 min	43 (16)	184 (23)	0.7 (0.5–1.2)	0.8 (0.5–1.3)
60–119 min	65 (25)	205 (25)	1.0 (0.6–1.5)	1.1 (0.7–1.7)
≥120 min	89 (34)	229 (28)	1.2 (0.8–1.8)	1.2 (0.7–1.8)
Repair of car				
No car	16 (6)	48 (6)		
No	154 (59)	503 (62)	0.9 (0.5–1.7)	0.8 (0.4–1.5)
Yes	92 (35)	265 (32)	1.0 (0.5–1.9)	0.8 (0.4–1.6)
Driving diesel vehicles				
No	169 (65)	576 (71)		
Yes	93 (35)	240 (29)	1.3 (0.9–1.7)	1.0 (0.7–1.4)
<10 years	23 (9)	82 (10)	0.9 (0.5–1.5)	0.7 (0.4–1.2)
10–29 years	33 (13)	94 (12)	1.1 (0.7–1.8)	0.9 (0.6–1.5)
≥30 years	37 (14)	64 (8)	2.0 (1.2–3.1)	1.7 (1.0–2.9)
Age start flying				
Never	30 (11)	100 (12)		
≥50 years	34 (13)	110 (13)	1.1 (0.6–1.9)	1.4 (0.8–2.6)
20–49 years	158 (60)	463 (57)	1.0 (0.7–1.6)	1.5 (0.9–2.5)
<20 years	38 (15)	136 (17)	0.7 (0.4–1.3)	1.0 (0.5–1.9)
Duration of flying				
Never	30 (12)	100 (12)		
0–14 years	26 (10)	61 (8)	1.3 (0.7–2.4)	1.6 (0.8–3.1)
15–39 years	139 (53)	422 (52)	1.0 (0.6–1.6)	1.4 (0.8–2.3)
≥40 years	65 (25)	226 (28)	0.9 (0.6–1.5)	1.3 (0.7–2.3)
Number of flights in 1970–79				
Never	102 (39)	272 (34)		
<10 times	88 (34)	266 (33)	0.9 (0.6–1.2)	1.0 (0.7–1.4)
10–99 times	53 (20)	224 (28)	0.6 (0.4–0.9)	0.7 (0.5–1.2)
≥100 times	17 (7)	48 (6)	0.9 (0.5–1.7)	1.1 (0.5–2.2)

<sup>a</sup> The basic model included adjustments for age and sex.

<sup>b</sup> The full model included adjustments for age, sex, socio-economic status, reflux, body mass index, tobacco smoking, alcohol use, intake of fruit or vegetables, and infection with *Helicobacter pylori*.

and driving diesel vehicles were not significantly associated with this tumour. The point estimates were, however, slightly above unity regarding longer duration of contacts with cars per day, and those who spent at least 2 hours per day in a car had an elevated point estimate of 1.3 (95%CI 0.7–2.3). The results regarding regular contact with airplanes show slightly elevated point estimates, but not significant, and there were no dose–response associations regarding age at first contact, duration or frequency of flying (Table 1).

The results regarding cardia adenocarcinoma are presented in Table 2. No significant associations were identified regarding regular contact with cars and risk of this tumour, except for an increased risk among people driving diesel vehicles for at least 30 years (OR 1.7, 95%CI 1.0–2.9). The point estimates regarding exposure to airplanes were increased, but not significantly or in a dose–response pattern regarding age at first contact, duration or frequency of flying (Table 2).

There were no indications of any increased risk of oesophageal squamous-cell carcinoma among persons with regular contact with cars or airplanes (data not shown).

#### 4. Discussion

This study does not provide evidence supporting the hypothesis that frequent contact with cars or airplanes are associated with an increased risk of oesophageal or cardia adenocarcinoma.

Strengths of the study include the population-based design with high participation rates, thorough and complete classification of all tumours, availability of several potential confounding factors and a large sample size. Exposure misclassification is a potential limitation of the study, but as all case patients and control participants were interviewed by professional interviewers this bias should be minimised.

An association between motor car density and lung adenocarcinoma has been reported,<sup>6</sup> but previous studies addressing contact with motor vehicles and risk of oesophageal and cardia adenocarcinoma are rare. We have, however, studied occupational airborne exposures, including diesel exhaust, without finding any such association with these tumours.<sup>7,8</sup> Moreover, although the United States was the first country with large scale car ownership, the incidence of oesophageal adenocarcinoma lagged behind the United Kingdom, which further indicates that introduction of motor vehicles is not involved in the aetiology of this tumour.<sup>9</sup>

In conclusion, this large and population-based case–control study with face-to-face interviews with all participants

and the ability to adjust for confounding by all known risk factors does not provide any evidence in favour of the hypothesis that frequent contact with cars or airplanes would contribute to the increasing incidence or male predominance of oesophageal adenocarcinoma.

#### Conflict of interest statement

None declared.

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