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Associations between several sites of cancer and ten types of exhaust and combustion products

Results from a case-referent study in Montreal

by Jack Siemiatycki, PhD,^{1,2} Michel Gérin, PhD,³ Pamela Stewart, BSc,¹ Louise Nadon, PhD,¹ Ron Dewar, MSc,¹ Lesley Richardson, MSc¹

SIEMIATYCKI J, GÉRIN M, STEWART P, NADON L, DEWAR R, RICHARDSON L. Associations between several sites of cancer and ten types of exhaust and combustion products: Results from a case-referent study in Montreal. *Scand J Work Environ Health* 14 (1988) 79–90. A population-based case-referent study provided information on the associations between several types of cancer and 10 types of exhaust and combustion products. All site-exposure combinations were investigated. An increased lung cancer risk, in particular squamous-cell cancers, due to exposure to gasoline and diesel exhausts was found. Among the associations that have not been subject to previous attention, the most promising leads for further investigation are the possible relations between gasoline and diesel exhaust and colorectal cancers, gasoline exhaust and kidney cancer, coal combustion products and pancreatic cancer (and possibly non-adenocarcinoma lung cancer), combustion products of heating oil and prostatic cancer, and natural-gas combustion products and bladder cancer.

Key terms: carcinogenesis, diesel, gasoline, lung neoplasms, neoplasms, occupational diseases.

A large population-based case-referent monitoring study was carried out in Montreal. It focused on occupational exposures as potential risk factors (31, 33). About 20 sites of cancer were included in the study. For each patient, information was obtained concerning past exposure to about 300 substances. The overall analytic strategy was to analyze subsets of substances at a time to determine whether there seemed to be any remarkable cancer-exposure associations.

This report examines the associations between the cancers in our study and 10 types of exhaust and combustion products. These 10 “exposures” fit into two classes. Four are exhaust products of internal combustion engines, with the distinction among them depending on the engine fuel used, i.e., gasoline, diesel, jet fuel, or propane. The other six are products derived from the “nonengine” combustion of the following substances: coal, coke, wood, liquid fuel (including without distinction heating oil, kerosene, naphtha, lamp oil), natural gas, and propane. (Note that the profile of products of the direct combustion of propane is considered separately from that which derives from a propane-burning engine).

Subjects and methods

A full description of the fieldwork and analytical methods can be found elsewhere (33). A brief outline follows.

Interviews were carried out for 3 726 cancer patients (response rate 82 %) diagnosed in any of the 19 participating Montreal-area hospitals. These patients were men aged 35 to 70 years, and their cancers were distributed among many sites. Each type of cancer constituted a case series which was investigated in relation to each of the 10 exposures under study. For each case series, a reference group was selected from among the other cancer patients interviewed. Thus each subject could serve as a case in one analysis and as a “referent” in others. The criteria for selecting “referents” among the other cancers have been discussed elsewhere (33). The numbers of cases and referents thereby selected for each type of cancer analyzed separately are shown in table 1.

The in-depth interview elicited a detailed job history of the subjects and information on potentially confounding covariables. A team of chemists and hygienists examined each completed questionnaire and translated each job into a list of potential exposures (15). They did this on a checklist which explicitly listed some 300 of the most common occupational exposures in Montreal. For each product thought to be present in each job, the chemists noted their confidence that the exposure actually occurred (possible, probable, definite), frequency of exposure during a normal workweek (<5, 5–30, and >30 %), and level of concentration of the agent in the work environment (low, medium, high).

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Table 1. Types of cancer analyzed as case series, sites excluded from the reference series, and numbers of cases and referents.

Cancer case series	Type(s) of cancer excluded ^a from the reference series	Number of cases	Number of referents
Esophageal	Lung, stomach	107	2 514
Stomach	Lung, esophagus	250	2 514
Colon	Lung, other colorectal	364	2 081
Rectosigmoid	Lung, other colorectal	233	2 081
Rectal	Lung, other colorectal	190	1 315
Pancreatic	Lung	117	2 741
Lung			
Oat cell	Other lung	159	1 523
Squamous cell	Other lung	359	1 523
Adenocarcinoma	Other lung	162	1 523
Other cell types ^b	Other lung	177	1 523
Prostatic	Lung	452	1 733
Bladder	Lung, kidney	486	2 196
Kidney	Lung, bladder	181	2 196
Melanoma of the skin	Lung	121	2 737
Non-Hodgkin's lymphoma	Lung, Hodgkin's lymphoma	206	2 599

^a For each case series, all cancer patients interviewed served as referents with the exceptions listed in this column. Furthermore, for rectum, lung and prostate, only those subjects interviewed during the same ascertainment periods as the three respective site series were used as referents.

^b This is a heterogeneous grouping which includes large cell, spindle cell, adenosquamous, and "carcinoma, not otherwise specified."

For each subject, the data set comprised semi-quantitative information on the degree of exposure and the number of years of exposure to each of several hundred occupational substances. For the purpose of the analyses, two indices of exposure to each substance were computed: one comprising the concentration, frequency, and confidence measures cumulated over the working lifetime (cumulative exposure) and another dividing the cumulative exposure by duration to derive an average level of exposure.

The analysis was carried out in stages. First a screening analysis based on the Mantel-Haenszel (19) approach estimated the odds ratio (OR) between each exhaust or combustion product and each type of cancer, stratifying on age, ethnic group, socioeconomic status, smoking habits, and an index of the overall dirtiness of the subject's jobs (ie, blue collar/white collar). This screening analysis was repeated twice, once with the exposed status defined as any versus none and then as substantial versus none. Substantial exposure was defined as exposure levels above the median of the continuous cumulative exposure variable. Any association that appeared to have an elevated odds ratio in either of the two screening runs was earmarked for in-depth analysis.

In-depth logistic regression analyses

First, each association thus selected underwent an analysis to determine which of the hundreds of available covariables might be confounders, and then another analysis was performed to estimate the odds ratio with the confounders taken into account. The search for confounders was based on the empirical principle of finding those covariates which, when included as stratification variables, changed the estimate of the disease-exposure odds ratio by more than 10 %. Some established risk factors were included as confounders whether or not they satisfied this criterion. Thus, asbestos, nickel, and chromium were included for any association involving lung cancer.

Using logistic regression methods (2) and including the potential confounders identified, we estimated the disease-exposure odds ratio associated with any level or duration of exposure to the substance, the odds ratios associated with different levels of exposure to the substance, and the odds ratios in subgroups which received their exposure to the substance in selected occupations.

Characterizing the exhausts and combustion products

The substances selected for analysis in this report derive from the combustion of commonly used fuels. They have certain chemical and physical properties in common, and there is some overlap in their use patterns. They are all gaseous with varying proportions of particulates. Each "substance" is a complex mixture whose composition has varied according to such factors as the geographic source of the raw material for combustion, the process used to extract, refine or transport the raw material, and the specific circumstances of the combustion process.

Engines can run on a variety of fuels, each producing a distinct profile of environmental exhaust fumes. We have distinguished four types. We refer, somewhat loosely, to gasoline exhaust as the mixture of exhausts found in the environment of automobiles. Since gasoline is not the only fuel used on our roadways, exposure to "gasoline exhaust" in our usage inevitably included a small amount of diesel exhaust. Gasoline exhaust may contain, among other things, carbon monoxide, nitrogen oxides, sulfur dioxide, and various hydrocarbons and lead compounds. Diesel exhaust per se was coded when exposure to it was thought to occur at higher than background roadway levels. In contrast with gasoline exhaust, diesel exhaust usually contains much greater concentrations of carbonaceous particulate matter, more nitrogen oxides, and less carbon monoxide (10). The preceding description concerns today's conditions; it is not clear whether it reflects the situation before 1970. Relatively high exposures to diesel exhaust were attributed to persons who worked in close proximity to diesel engines in con-

financed spaces (eg, in mining, tunneling, locomotive maintenance, etc).

Jet fuels can be roughly divided into two types, "wide cut" and kerosene. The kerosene type has been used in most civil aviation and in some military aviation applications. Most of the subjects in our study with exposure to jet fuel exhaust worked in civil aviation. Jet fuel exhaust contains some of the same constituents as gasoline exhaust, although the concentrations of these substances have been reported to be lower in jet fuel exhaust (42). However the volume of exhaust produced by an airplane greatly exceeds that produced by an automobile.

Propane fueled engines have been used mainly in fork-lift trucks and similar vehicles. Emissions from propane engines have been found to be lower in carbon monoxide, nitrogen oxides, and hydrocarbons than gasoline engine emissions (12).

The natural gas which has been widely available in Montreal since 1957 emits substantial amounts of nitrogen oxides upon combustion, but little carbon monoxide. Propane combustion may produce similar emissions. Cooks comprised one of the main occupation groups exposed to both natural gas combustion and propane combustion, but the highest exposures to natural gas combustion occurred among forgers and blacksmiths, while jewelers and pipe fitters were the workers most highly exposed to the combustion products of propane.

The composition of liquid fuel combustion products depends on the type and grade of fuel (eg, distillate or residual fuel oils, kerosene), the equipment, and the method of firing. The main emissions include carbon monoxide, nitrogen oxides, sulfur dioxide, and particulates (10). Many construction workers were exposed to these mixtures in the long Montreal winter since makeshift furnaces that burn oil were often installed to heat buildings under construction. However the highest exposures were attributed to certain foundry workers and ship engine-room workers.

Wood combustion mainly produces carbon monoxide and particulate carbonaceous matter, with less

amounts of hydrocarbons and nitrogen oxides. These emissions have been reported to be modest when compared to those of fossil fuels (36). There may also be small amounts of aliphatic aldehydes. Among our study subjects the smoking of food among farmers and fire fighting were the most common sources of exposure to wood combustion; however the highest exposure levels were thought to occur among certain cooks and bakers.

Coal combustion has been widespread in certain industries, and was also widespread in domestic uses until the 1950s. Combustion products include variable amounts of particulates such as carbon, silica, alumina, and iron oxides, as well as gases such as aldehydes, carbon monoxide, nitrogen oxides, hydrocarbons, and sulfur oxides (10). Since coke is nearly pure carbon, with little volatile matter, its combustion produces fewer substances than that of coal.

Results

Table 2 describes the exposure patterns of our entire study population (3 726 subjects) to each of the 10 exhausts and combustion products. Gasoline exhaust was by far the most common exposure; 42.6 % of all subjects were considered to have had potential exposure to gasoline exhaust in at least one of their jobs. Most of these persons were considered definitely exposed (39.3 % of the entire sample), and 25.5 % of the entire sample had been exposed at high frequency (ie, more than 30 % of the day). However only 2.6 % was exposed at a high concentration level (on a relative scale). A large percentage, 20.5 %, had over 20 years' exposure to gasoline exhaust at one level or another of frequency, concentration, and confidence. In contrast, exposure to combustion products of coke was the least common, with a lifetime work prevalence of 0.8 % for any level or length of exposure.

Table 3 shows the main occupation groups in which exposure to each substance occurred in our population. Most of these substances also occurred in many

Table 2. Percentage of all 3 726 subjects exposed to each of 10 engine exhausts and combustion products according to degree of exposure.

Substance	Any exposure ^a (%)	High confidence (%)	High frequency (%)	High concentration ^b (%)	> 20 years of exposure (%)
Gasoline exhaust	42.6	39.3	25.5	2.6	20.5
Diesel exhaust	17.5	9.9	6.7	1.6	8.1
Jet fuel exhaust	0.9	0.5	0.3	0.2	0.3
Propane exhaust ^c	2.6	2.0	1.3	0.2	1.1
Propane combustion ^c	3.6	2.1	1.0	0.5	1.6
Natural gas combustion	3.3	2.1	1.8	0.1	1.4
Liquid fuels combustion	6.7	4.8	3.0	0.2	2.1
Wood combustion	4.4	2.9	1.2	1.0	1.4
Coal combustion	4.8	3.6	2.1	0.4	1.2
Coke combustion	0.8	0.5	0.5	0.4	0.1

^a Exposure attributed with any degree of confidence and at any frequency, concentration, and duration.

^b Concentration is on a relative scale which is not comparable between substances.

^c The term "exhaust" has been used to signify the products of combustion in an internal combustion engine. The term "combustion" signifies other forms of combustion.

Table 3. Main occupations for which exposure to each substance was attributed in the entire study group of 3 726 subjects.^a

Substance	N ^b	Main occupations for which exposure to the substance was coded ^c
Gasoline exhaust	1 589	Motor transport operating (28.6 %), sales occupations, commodities (15.7 %), mechanics and repairmen except electrical (7.2 %)
Diesel exhaust	651	Motor transport operation (30.6 %), mechanics and repairmen except electrical (13.2 %), excavating, grading, paving (9.1 %), mining and quarrying (8.6 %)
Jet fuel exhaust	33	Air transport operation (27.3 %), aircraft mechanics and repairmen (24.2 %)
Propane exhaust	98	Materials handling (42.9 %), shipping and receiving clerks (9.2 %), stock clerks (8.2 %)
Propane combustion	135	Food and beverage preparation (35.6 %), construction trades (25.9 %), metal shaping and forming except machining (8.9 %)
Natural-gas combustion	122	Food and beverage preparation (36.9 %), metal shaping and forming (9.8 %), food and beverage processing (9.0 %), stationary engine and utilities equipment operation (7.4 %)
Liquid-fuel combustion	251	Construction trades (38.2 %), stationary engine and utilities equipment operation (12.7 %), metal processing (7.6 %)
Wood combustion	163	Farming (25.8 %), firefighters (20.2 %), chefs and cooks (12.9 %), construction trades (10.4 %)
Coal combustion	177	Railway transport operation (14.2 %), construction trades (12.5 %), stationary engine and utilities equipment operation and maintenance (12.5 %), chefs and cooks (6.2 %)
Coke combustion	29	Metal processing (37.9 %), mineral ore treating (20.7 %), materials handling (10.3 %)

^a Note that the ordering of occupations does not necessarily reflect the degree of exposure in various occupations. For instance, while the largest occupational category exposed to wood combustion was "farming" the exposure level was much lower among farmers than among chefs and cooks.

^b This is the number of persons exposed at any level; N is the denominator for each percentage corresponding to the substance in question.

^c Percentage of subjects in the occupation in question in parentheses.

other job classes than those shown in the table. In addition the indication that a substance was attributed to some workers bearing a given job title does not imply that all workers with that job title were attributed that exposure. For instance, while many of those exposed to coke combustion products were "metal processors" only a fraction of "metal processors" were considered to have been exposed to coke combustion products.

Screening results

Tables 4 and 5 show the odds ratio screening results for the 10 substances by the 15 cancer types which had over 100 cases and thus reasonable statistical power. These tables are based on any exposure versus no exposure. Although not shown, the same analysis was carried out with exposure dichotomized as "substantial" versus none. A subject was considered substantially exposed if his cumulative exposure index exceeded the median of all nonzero values of this parameter.

For in-depth analysis any association was selected which showed a suggestively elevated odds ratio either in the any/none analysis (tables 4 and 5) or in the corresponding substantial/none analysis. For the most part we used a P-value of less than 0.10, one-sided with a minimum of five exposed cases, as a criterion. For coal combustion it was noted that there were somewhat elevated odds ratios for all types of lung cancer except adenocarcinoma. For this substance, therefore, the in-depth analysis was carried out with the grouping of nonadenocarcinoma lung cancers, rather than for the more specific histological types.

A total of 16 associations were thereby selected, five with various histological types of lung cancer (including one with nonadenocarcinoma lung cancers), three with prostate cancer, and one each with cancers of the following eight sites: esophagus, stomach, colon, rectum, pancreas, bladder, kidney, and melanoma of the skin.

In-depth analyses

Each selected association was analyzed with the purpose of obtaining odds ratio estimates for various exposure subgroups, adjusted for all potential confounders. First a series of analyses was carried out to identify a short list of potential confounders. Then, using logistic regression, we estimated odds ratios in various exposure subgroups. The results for all 16 associations are shown in table 6.

We estimated risk associated with any level or duration of exposure, as well as with subgroups at different levels and durations of exposure. When an association was based on 20 or more exposed cases, we categorized them into four exposure subgroups based on the duration and level of exposure. The groups are called short-low, short-high, long-low, and long-high. When there were fewer than 20 exposed cases, we categorized them into two exposure subgroups with the use of the median of the cumulative exposure index (which combines level and duration) as the cutpoint. These were called nonsubstantial and substantial.

Concerning the occupation-specific odds ratios, it should be noted that "exposed" was defined as exposed to the substance and in the occupation, "unexposed" was defined as unexposed to the substance regardless of whether the man was in the occupation of interest. For each association, we examined the risk in up to six of the main occupations in which the ex-

Table 4. Odds ratios (OR) between 15 types of cancer^a and exposure^b to gasoline exhaust, diesel exhaust, jet fuel exhaust, propane exhaust, and propane combustion on the basis of Mantel-Haenszel analyses with five stratifying variables.^c (N = number of exposed cases, 90 % CI = 90 % confidence interval)

Cancer category	Gasoline exhaust			Diesel exhaust			Jet fuel exhaust			Propane exhaust			Propane combustion		
	N	OR	90 % CI	N	OR	90 % CI	N	OR	90 % CI	N	OR	90 % CI	N	OR	90 % CI
Esophageal	47	1.0	0.8–1.4	12	0.6	0.4–0.9	2	2.5	0.4–14.8	0	0.0	0.0–1.7	4	1.2	0.5–3.0
Stomach	111	1.1	0.9–1.3	41	0.9	0.7–1.1	2	0.8	0.2–3.5	7	1.2	0.6–2.2	12	1.5	0.9–2.4
Colon	147	1.0	0.9–1.2	68	1.3*	1.1–1.6	4	1.3	0.4–4.2	7	0.9	0.5–1.8	12	1.0	0.6–1.6
Rectosigmoid	102	1.2	1.0–1.4	39	1.1	0.8–1.4	1	0.4	0.0–4.3	7	1.4	0.7–2.8	6	0.7	0.3–1.4
Rectal	89	1.2	1.0–1.5	35	1.1	0.9–1.5	3	1.7	0.4–7.8	3	0.7	0.2–2.4	10	1.1	0.6–1.9
Pancreatic	47	0.9	0.7–1.2	15	0.6	0.4–0.9	2	1.6	0.3–7.7	2	0.7	0.2–2.5	3	0.8	0.3–2.2
Lung															
Oat cell	68	0.9	0.7–1.1	34	1.1	0.8–1.5	1	0.5	0.1–3.6	4	0.8	0.3–1.8	10	1.8	1.0–3.2
Squamous cell	182	1.2*	1.0–1.4	81	1.2	1.0–1.5	1	0.2	0.0–1.9	17	1.6	1.0–2.5	13	0.9	0.6–1.5
Adenocarcinoma	68	0.8	0.6–1.0	28	0.9	0.6–1.2	0	0.0	0.0–1.4	7	1.3	0.7–2.5	5	0.7	0.3–1.5
Other ^d	72	0.8	0.7–1.0	34	1.0	0.8–1.4	1	0.4	0.1–3.7	6	1.0	0.5–2.1	8	1.3	0.7–2.4
Prostatic	197	1.1	0.9–1.2	86	1.2	1.0–1.5	2	0.7	0.1–5.1	13	1.5	0.9–2.7	17	1.3	0.8–2.0
Bladder	208	1.0	0.9–1.1	82	1.0	0.8–1.2	1	0.2	0.0–1.2	9	0.7	0.4–1.2	14	0.8	0.5–1.2
Kidney	80	1.2	0.9–1.4	29	0.9	0.7–1.3	4	1.4	0.5–3.9	3	0.7	0.3–2.1	3	0.4	0.2–1.0
Melanoma	43	0.9	0.7–1.2	17	1.1	0.7–1.7	3	1.8	0.5–6.4	5	3.3*	1.2–9.0	2	0.6	0.2–2.2
Non-Hodgkin's lymphoma	83	0.9	0.8–1.1	29	0.7	0.5–1.0	4	1.7	0.5–5.2	3	0.6	0.2–1.6	6	0.7	0.4–1.4

^a In this table only those site series with over 100 interviewed cases are presented.

^b Exposure at any level and for any duration.

^c Stratifying variables: age, socioeconomic status, ethnic group, cigarette smoking, and blue/white-collar job history.

^d Includes other and unknown cell types.

* OR was significantly greater than 1.0 at P = 0.05 (one-sided). Note that a lower limit of 1.0 for the 90 % CI does not necessarily imply a significantly elevated OR. The lower limit may have been rounded to 1.0. In addition the test and the confidence interval computations have been based on separate algorithms (33).

Table 5. Odds ratio (OR) between 15 types of cancer^a and exposure^b to natural gas, liquid fuel, wood, coal, and coke combustion on the basis of Mantel-Haenszel analyses with five stratifying variables.^c (N = number of exposed cases, 90 % CI = 90 % confidence interval)

Cancer category	Natural gas combustion			Liquid fuel combustion			Wood combustion			Coal combustion			Coke combustion		
	N	OR	90 % CI	N	OR	90 % CI	N	OR	90 % CI	N	OR	90 % CI	N	OR	90 % CI
Esophageal	3	0.8	0.3–2.0	5	0.7	0.3–1.4	8	2.2*	1.1–4.1	4	0.9	0.4–1.9	2	2.1	0.5–9.8
Stomach	11	1.3	0.8–2.2	16	0.9	0.6–1.3	17	1.8*	1.2–2.7	14	1.3	0.8–2.0	3	1.5	0.4–5.8
Colon	6	0.5	0.2–0.9	19	0.9	0.6–1.4	17	1.1	0.8–1.7	8	0.5	0.3–0.8	2	0.7	0.1–3.5
Rectosigmoid	10	1.4	0.8–2.4	14	1.0	0.7–1.6	14	1.4	0.9–2.3	8	0.7	0.4–1.2	4	2.0	0.6–6.8
Rectal	5	0.8	0.3–1.8	14	1.1	0.7–1.8	6	0.5	0.2–1.0	7	0.7	0.4–1.3	0	0.0	0.0–1.7
Pancreatic	6	1.5	0.7–3.1	10	1.3	0.8–2.3	8	1.7	0.9–3.1	10	2.3*	1.4–4.0	2	2.2	0.4–10.5
Lung															
Oat cell	8	1.3	0.7–2.4	15	1.1	0.7–1.6	8	1.0	0.6–1.8	10	1.3	0.8–2.2	1	0.5	0.1–4.3
Squamous cell	12	0.9	0.6–1.5	38	1.2	0.9–1.6	20	1.0	0.7–1.5	25	1.3	0.9–1.9	4	0.8	0.3–2.2
Adenocarcinoma	4	0.7	0.3–1.6	8	0.5	0.3–0.9	8	1.1	0.6–2.0	6	0.6	0.3–1.2	0	0.0	0.0–1.3
Other ^d	6	0.9	0.5–1.9	12	0.7	0.5–1.2	5	0.6	0.3–1.2	13	1.6	1.0–2.6	1	0.3	0.0–2.6
Prostatic	9	0.8	0.4–1.4	39	1.6*	1.2–2.1	15	0.8	0.5–1.2	35	1.6*	1.2–2.2	5	1.0	0.3–2.6
Bladder	22	1.6*	1.1–2.3	28	0.9	0.7–1.2	20	0.9	0.6–1.3	16	0.7	0.5–1.0	3	0.7	0.2–2.5
Kidney	5	0.9	0.4–2.0	10	0.8	0.5–1.4	3	0.3	0.1–0.9	8	1.0	0.6–1.8	1	0.6	0.0–7.4
Melanoma	1	0.3	0.0–1.4	8	1.8	0.9–3.4	2	0.5	0.1–2.0	1	0.4	0.1–2.4	0	0.0	0.0–1.9
Non-Hodgkin's lymphoma	5	0.6	0.3–1.3	11	0.8	0.5–1.3	7	0.8	0.4–1.4	7	0.8	0.5–1.5	2	1.4	0.3–7.3

^a In this table only those site series with over 100 interviewed cases are presented.

^b Exposure at any level and for any duration.

^c Stratifying variables: age, socioeconomic status, ethnic group, cigarette smoking, and blue/white-collar job history.

^d Includes other and unknown cell types.

* OR was significantly greater than 1.0 at P = 0.05 (one-sided). Note that a lower limit of 1.0 for the 90 % CI does not necessarily imply a significantly elevated OR. The lower limit may have been rounded to 1.0. In addition the test and the confidence interval computations have been based on separate algorithms (33).

posure occurred; in table 6 we present only those occupations in which the risk was particularly high in comparison to that of other occupations.

The data-based potential confounders were divided into the following three categories: nonoccupational covariates (eg, beverage consumption, marital status), other occupational exposures excluding the nine exhausts and combustion substances, and, finally, the nine exhaust and combustion substances themselves. There was a final restriction placed on the covariates that were closely related to the exposure variable of interest and which may have led to overadjustment if

included in the model. For instance, in analyses of gasoline exhaust, we excluded the covariates "gasoline fuel" and "lead compounds" from the model, and in the analyses of diesel exhaust we excluded "diesel fuel." Each regression model was built up gradually in five cumulative steps. First, we estimated the crude odds ratio. Second, we included the same a priori confounders that were included in the Mantel-Haenszel analyses, though the continuous variables among them were included as continuous variables. Then we included in sequence each of the three aforementioned categories of data-based confounders. It was not clear-

Table 6. Detailed analyses of selected associations^a with the substances subdivided according to exposure level^b and according to occupation^c in which the exposure occurred. (N = number of exposed cases, 90 % CI = 90 % confidence interval for OR₂)

Exposure subgroup	N	OR ₁ ^d	OR ₂ ^e	90 % CI	Exposure subgroup	N	OR ₁ ^d	OR ₂ ^e	90 % CI				
<i>Gasoline exhaust-rectal cancer</i>					<i>Propane combustion-oat-cell lung cancer</i>								
Exposure level					Exposure level								
Short-low	17	1.3	1.3	0.8–2.1	Nonsubstantial	4	1.3	1.0	0.4–2.7				
Short-high	9	0.9	1.0	0.5–1.8	Substantial	6	1.8	1.3	0.6–3.0				
Long-low	27	1.0	1.1	0.7–1.6	Both combined	10	1.5	1.2	0.6–2.2				
Long-high	36	1.6	1.6	1.1–2.3	<i>Natural gas combustion-bladder cancer</i>								
All combined	89	1.2	1.3	1.0–1.7	Exposure level								
Occupation					Short-low					2	1.3	1.4	0.4–5.3
Sales including service station	19	1.5	1.5	1.0–2.4	Short-high					6	3.3	3.6	1.5–8.7
Bus, truck, taxi drivers	24	1.4	1.5	1.0–2.2	Long-low					4	0.6	0.7	0.3–1.7
All others	46	1.1	1.2	0.8–1.6	Long-high					10	2.4	2.6	1.4–5.0
<i>Gasoline exhaust-squamous-cell lung cancer</i>					All combined					22	1.6	1.7	1.1–2.6
Exposure level					<i>Liquid fuels combustion-prostatic cancer</i>								
Short-low	21	0.9	0.9	0.6–1.4	Exposure level								
Short-high	20	1.1	1.1	0.7–1.7	Short-low					5	2.6	2.2	0.8–5.9
Long-low	65	1.3	1.3	1.0–1.7	Short-high					6	1.2	1.1	0.5–2.6
Long-high	76	1.4	1.4	1.1–1.8	Long-low					12	1.5	1.4	0.7–2.5
All combined	182	1.2	1.2	1.0–1.5	Long-high					16	2.1	2.2	1.2–3.8
Occupation					All combined					39	1.7	1.7	1.1–2.4
Farmers	12	2.9	2.9	1.5–5.6	Occupation								
Taxi drivers	21	1.5	1.5	0.9–2.5	Water transport					5	8.7	5.4	1.6–18.3
All others	149	1.1	1.2	0.9–1.4	Stationary engineers					6	2.7	2.1	0.8–5.4
<i>Gasoline exhaust-kidney cancer</i>					All others					28	1.4	1.4	1.0–2.1
Exposure level					<i>Wood combustion-esophageal cancer</i>								
Short-low	15	1.4	1.5	0.9–2.3	Exposure level								
Short-high	7	0.7	0.7	0.4–1.4	Nonsubstantial					3	2.1	2.0	0.7–5.5
Long-low	24	1.1	1.1	0.8–1.7	Substantial					5	2.4	2.6	1.2–6.0
Long-high	34	1.4	1.4	1.0–2.0	Both combined					8	2.3	2.3	1.2–4.5
All combined	80	1.2	1.2	0.9–1.6	<i>Wood combustion-stomach cancer</i>								
<i>Diesel exhaust-colon cancer</i>					Exposure level								
Exposure level					Nonsubstantial					11	2.1	1.6	0.9–2.9
Short-low	6	0.7	0.7	0.3–1.4	Substantial					6	1.1	1.0	0.5–2.1
Short-high	5	0.6	0.6	0.3–1.3	Both combined					17	1.6	1.3	0.8–2.1
Long-low	27	1.5	1.5	1.0–2.2	<i>Coal combustion-pancreatic cancer</i>								
Long-high	30	1.7	1.7	1.2–2.5	Exposure level								
All combined	68	1.3	1.3	1.0–1.7	Nonsubstantial					2	0.9	0.7	0.2–2.4
<i>Diesel exhaust-squamous-cell lung cancer</i>					Substantial					8	4.1	3.5	1.7–7.3
Exposure level					Both combined					10	2.4	1.9	1.0–3.6
Short-low	13	1.5	1.4	0.8–2.7	<i>Coal combustion-nonadenocarcinoma lung cancer</i>								
Short-high	16	1.6	1.5	0.9–2.7	Exposure level								
Long-low	24	1.0	1.0	0.7–1.6	Short-low					9	1.5	1.9	0.9–4.1
Long-high	28	1.1	1.2	0.8–1.8	Short-high					14	1.9	2.3	1.1–4.7
All combined	81	1.2	1.2	0.9–1.6	Long-low					12	1.5	1.4	0.8–2.7
Occupation					Long-high					13	1.2	1.1	0.6–2.2
Mining & quarrying	11	3.2	2.8	1.4–5.8	All combined					48	1.5	1.6	1.1–2.3
All others	70	1.1	1.1	0.8–1.5	Occupation								
<i>Diesel exhaust-prostatic cancer</i>					Railway transport					9	2.1	1.7	0.6–4.9
Exposure level					All others					39	1.4	1.3	0.9–2.1
Short-low	8	1.1	1.1	0.5–2.1	<i>Coal combustion-prostatic cancer</i>								
Short-high	11	0.9	0.8	0.5–1.5	Exposure level								
Long-low	21	1.5	1.5	0.9–2.3	Short-low					6	1.2	1.1	0.5–2.4
Long-high	46	1.2	1.3	0.9–1.7	Short-high					10	1.9	1.6	0.8–3.3
All combined	86	1.2	1.2	0.9–1.5	Long-low					10	1.7	1.5	0.7–3.0
Occupation					Long-high					9	1.3	1.1	0.5–2.2
Materials handling	10	2.7	2.7	1.3–5.5	All combined					35	1.5	1.3	0.9–1.9
All others	76	1.1	1.1	0.9–1.4	Occupation								
<i>Propane exhaust-squamous-cell lung cancer</i>					Railway transport					7	2.7	2.3	0.9–5.6
Exposure level					All others					28	1.4	1.2	0.8–1.8
Nonsubstantial	4	1.4	1.3	0.4–4.0	^a These are the associations which were significant in at least one of the two screening runs and which had at least five exposed cases. A few associations which were of borderline significance were also selected.								
Substantial	13	1.3	1.2	0.7–2.3									
Both combined	17	1.3	1.3	0.7–2.2	^b Exposure level was divided into two or four categories depending on whether there were fewer or more than 20 exposed cases. When the total number was less than 20, the level of exposure was defined by the cumulative exposure index used in the Mantel-Haenszel analyses and dichotomized at the same point along the scale of that index to provide two categories which have been called nonsubstantial and substantial. When the total number exceeded 20, four categories were defined by the dichotomization of the duration of exposure and the								
Occupation													
Materials handling	9	2.3	2.3	1.0–5.3									
All others	8	0.9	0.8	0.4–1.7									
<i>Propane exhaust-melanoma of the skin</i>													
Exposure level													
Nonsubstantial	1	1.0	0.9	0.1–5.8									
Substantial	4	3.4	3.6	1.5–9.0									
Both combined	5	2.5	2.5	1.1–5.8									

(continued)

(continued)

cut which of these steps provided the most “valid” odds ratio estimate (4). Space limitation mitigates against presenting all five, and in any event the variation in the odds ratio estimates across steps was generally minor, especially across the last three steps. We decided to present the estimates from two models, ie, that based on a priori confounders only and that based on all variables except for the other nine exhausts and combustion substances. If the results from the full model differed from the latter, it has been mentioned in the text and its meaning has been discussed.

For each association there was a distinct regression model containing from 5 to 25 covariates, depending on which covariables were earmarked in the data-based search for confounders. While there may be some interest in showing which variables went into the respective models, in fact it is not important for the interpretation of the disease-exposure odds ratios because we have “adjusted” for all variables in our data set, either by confirming in the initial step that their inclusion in the model does not affect the odds ratio estimate or by including them in the regression model. Because it would take considerable space to present them all, we have chosen not to present the covariables included in each model.

Discussion

There were several statistically significant findings, some undoubtedly by chance and some because of real cause-and-effect relations. While acknowledging the possibility of false positive results, we must also note the possibility of false negatives. As implied by the width of the confidence intervals in tables 4 and 5, the power to detect risks was only moderate for most of the associations analyzed. Power may have been

further compromised because of a misclassification error in the exposure assessment. Furthermore the strategy of employing other cancer patients as referents for each case series was a “conservative” strategy, possibly leading to some attenuation of risk estimates. Finally, the inclusion of data-based confounders in the models may also have been a conservative strategy. On the one hand, including more variables than is strictly necessary increases the variability of estimates; on the other it may also introduce some overadjustment.

The main focus of the in-depth analysis was to try to delineate between false positives and true positives. In this process we used criteria such as stability of statistical significance once the confounders were included in the model, strength of association, dose-response, and coherence with experimental or other epidemiologic information. Unfortunately, there have been very few other epidemiologic studies bearing directly on the carcinogenicity of any of these mixtures. The available evidence, such as it is, derives indirectly from studies of occupational or industrial groups who may have been exposed to the mixture. Most of these studies were based on the occupations mentioned on death certificates or tumor registers. Such evidence suffers from several deficiencies (31).

When we discuss the odds ratios without qualification, it can be assumed that we are referring to the more fully adjusted odds ratio in table 6, namely, OR_2 .

Lung cancer and engine exhaust

Of the various associations examined in this paper, the associations between lung cancer and engine exhausts have been the subject of most previous attention and even controversy. Gasoline exhaust and, to a less extent, diesel exhaust have long been ubiquitous components of the urban environment. Our exposure-coding procedure was designed to assign exposure only when it occurred at higher-than-background levels. But because of the widespread nature of the exposure it is important to note that there can be no truly unexposed group in a study among urban dwellers. The background levels of exposure, which we call “unexposed” may not be innocuous.

In the screening results and in the logistic regressions, there were elevated odds ratios between both diesel and gasoline exhaust and squamous-cell lung cancer. The association with gasoline exhaust showed evidence of a dose-response relation with a significant odds ratio of 1.4 in the long-high exposure group. For diesel exhaust there were higher risks among those with short exposure than among those with long exposure. The OR_2 results in table 6 were based on logistic regression models in which the various exhausts were not included in the same model. There was no effect on the odds ratios between gasoline exhaust and lung cancer when diesel exhaust was added to the model. And there was virtually no effect on the odds ratios for diesel

Table 6. Continued.

dichotomization of the degree of exposure. Short- and long-term exposures were defined by a 10-year cut point. Low and high exposures were defined by the median of the distribution of values of the index comprising the following characteristics of the exposure: concentration, frequency, and the chemists' confidence that the exposure occurred. See reference 33 for a description of index E, used in the two-category definition, and index A, used in the four-category definition.

^c Occupation refers to the occupation in which the subject was exposed to the substance. Selected for presentation were one or two occupations in which the odds ratio differed from the overall odds ratio. If the odds ratios were constant across the main occupations in which the substance was found, then no occupations were listed. Each man was classified into only one occupation category; if he was exposed to the substance in two different occupations, the job of longest duration was used. Thus the sum of the number across occupations is the same as that across exposure levels, and it equals the total number of men with this site of cancer and exposure to this substance. Note that the odds ratios corresponding to each occupation refer to the risk for those men in the occupation who have been exposed to the substance of interest, not for all men in the occupation. The level of exposure was ignored in these occupation-substance analyses.

^d Odds ratio (OR_1) estimates for each association are based on a logistic regression model including the following five a priori covariates: age, ethnic group, socioeconomic status, smoking, blue/white-collar job history.

^e Odds ratio (OR_2) estimates for each association are based on a logistic regression model including all potential confounders identified in the confounder searching procedure described in the Methods section, except for other substances examined in this paper.

exhaust-lung cancer when gasoline exhaust was added to that model. Thus the apparent elevated risks due to both of these mixtures were not due to mutual confounding. Since our work previously reported an association between squamous-cell lung cancer and exposure to diesel fuel itself (32), we also included that exposure variable in the model for diesel exhaust-lung cancer; again there was virtually no impact on the odds ratios from those presented as OR_2 in table 6.

The definition of unexposed in all of the analyses in tables 4, 5, and 6 was substance specific. The use of this definition could lead to some attenuation of risk estimates if two substances are carcinogenic but do not behave as independent multiplicative factors in a relative risk model. If diesel and gasoline exhaust act via the same mechanisms, their joint effects may not be multiplicative. To examine further the relationship between gasoline and diesel exhaust on the one hand and squamous-cell lung cancer on the other, we carried out an analysis, summarized in table 7, of persons exposed to different combinations of diesel and gasoline exhaust. The unexposed in this analysis consisted of those unexposed to both gasoline and diesel exhaust, and the others were divided into eight mutually exclusive exposure subgroups formed through trichotomizing exposure to each exhaust (none, non-substantial, substantial). The results were not clear-cut. All combinations of diesel and gasoline exhaust showed some excess. Two of the three cells in the substantial gasoline column showed significant or borderline significant excess over the reference category, as did two of the three cells in the nonsubstantial diesel row. There was a suggestion of a dose-response relationship with gasoline exhaust, particularly in the large subgroup with no diesel exhaust exposure (first row).

The components of gasoline and diesel exhaust are not dissimilar, though under normal operating conditions, and for today's vehicles, diesel engines produce much more (30 to 100 times) in the way of respirable particulates (21). These particles are made up essentially of elemental carbon and serve as vehicles for organic compounds such as polycyclic aromatic

hydrocarbons (PAH) and their derivatives, which can then be deposited in the lung. The condensates of both gasoline and diesel engine exhausts have been found to be mutagenic and carcinogenic in biological test systems. Recently diesel exhausts were shown to induce lung cancers in rats exposed at high levels by inhalation (20).

Although there has been greater concern of late about the carcinogenicity of diesel exhaust than gasoline exhaust, it is not self-evident that this should be the case. There is meager and conflicting evidence concerning levels of exposure to PAH and their derivatives originating from gasoline- versus diesel-powered vehicles. Perera (26) reported higher emission rates of benzo(a)pyrene from diesel vehicles than from catalyst-controlled gasoline vehicles; however Nikolaou et al (25), in their review, reported similar or higher emissions of six PAH, including benzo(a)pyrene, from gasoline vehicles. What the exposure situation was before the 1970s and what the effect was of the introduction of control equipment on gasoline-powered vehicles remains difficult to estimate from present data. For instance, emissions from gasoline engines that use regular fuel have been reported to contain over 50 times the particle concentrations found in emissions from gasoline engines that use catalytic converters and unleaded fuel (5). It is reasonable to assume that emissions of PAH and analogues from leaded gasoline engines were far higher in the past than they are today, and it is quite possible that they were higher than for diesel-powered vehicles. In addition workers exposed to gasoline exhaust are exposed to lead, while those exposed to diesel exhaust are not.

It appears that diesel exhaust is more potent in the Ames test than gasoline exhaust, and this phenomenon has been attributed to the formation of nitro derivatives of PAH (25). However, results from other biological test systems are equivocal as indicators of the relative carcinogenic potencies of the two types of exhausts (6). On balance, there is no compelling evidence that diesel particle extracts are more potent than gasoline exhaust extracts.

Table 7. Associations between squamous-cell lung cancer and different combinations of exposure to diesel and gasoline exhaust. (90 % CI = 90 % confidence interval)

Exposure to diesel exhaust	Exposure to gasoline exhaust								
	None			Nonsubstantial			Substantial		
	N ^a	OR ₂ ^b	90 % CI	N ^a	OR ₂ ^b	90 % CI	N ^a	OR ₂ ^b	90 % CI
None	155	1.0		23	1.0	0.7–1.6	100	1.3	1.0–1.7
Nonsubstantial	13	1.9	1.0–3.5	8	2.3	1.0–5.2	21	1.1	0.7–1.7
Substantial	9	1.2	0.6–2.4	3	1.2	0.4–3.8	27	1.4	0.9–2.1

^a Number of squamous-cell lung cancers with this combination of diesel- and gasoline-exhaust exposure.

^b The odds ratio (OR₂) estimates for each association are based on a logistic regression model including five a priori covariates, ie, age, ethnic group, socioeconomic status, smoking, and blue/white-collar job history, and all potential confounders identified in the confounder searching procedure described in the Methods section. The reference category for the odds ratios is the group of subjects unexposed to both diesel and gasoline exhaust. The referents consisted of other types of cancer as indicated in table 1.

Previous epidemiologic evidence is characterized by studies based on crude exposure information (eg, job titles on death certificates), lack of control for smoking and other potential confounders, and low statistical power. Despite the limitations of each study there has been a pattern of excess lung cancer among truck drivers in several studies, and this is a group with potentially high exposure to diesel exhaust, as well as exposure to gasoline exhaust (6, 18, 23, 24, 35). Bus and taxi drivers, many of whom would not have driven diesel-powered vehicles, or, if they had, the level of exposure to diesel exhaust would have been low, have also generally exhibited excess lung cancer rates (6, 9, 23). There have been more studies of workers exposed to diesel exhaust than of workers exposed to gasoline exhaust. Among London Transit Authority workers there was no evidence of lung cancer excess (38). Nor did Wong et al (40) find any convincing excess of lung cancer among operators of heavy construction equipment. Howe et al (17) found some excess among Canadian railway workers exposed to diesel exhaust. No excess was detected in an analogous, but much smaller, study in the United States (29); whereas a larger study currently in progress suggests in preliminary reports that there is some excess lung cancer (28).

The aggregate epidemiologic evidence may be said to be compatible with the hypothesis of excess lung cancer risk related to diesel exhaust exposure and even to gasoline exhaust exposure, though the evidence is weak. It should be recalled that the use of diesel engines only became widespread in the 1950s. It may be that the latency has been too short to pick up any human carcinogenic effects due to diesel exhaust.

While our study entailed several advantages over most studies — exposure assessment based on detailed job descriptions, control of key confounders, reasonable statistical power — the results insofar as these exhausts are concerned were not unambiguous.

The gasoline exhaust-lung cancer association was not concentrated in a single occupation category. The odds ratio was high in a small group of farmers who had been exposed to gasoline exhaust in the era before diesel-powered farm equipment became prevalent. As the levels of exposure were very low, we are not inclined to attach importance to this finding. Among other workers exposed to gasoline exhaust, taxi drivers exhibited a somewhat higher odds ratio than others. In the diesel exhaust-lung cancer association, the excess risk was concentrated among mine and quarry workers. An examination of these files indicated that most of these workers were exposed to diesel exhaust for short periods of time. There may have been confounding due to some factor which was not adequately adjusted for however.

There was evidence of excess risk with both types of engine exhaust, though the dose-response pattern of risk was more persuasive for gasoline exhaust than for diesel exhaust. Nevertheless, in the light of previous

experimental and epidemiologic evidence, our study supports the hypothesis of a lung cancer risk associated with vehicle-exhaust exposure. This risk seems to be limited to squamous-cell tumors.

Even propane engine exhaust exhibited a somewhat elevated risk of squamous-cell lung cancer in the screening analyses, though this risk virtually disappeared in the logistic regression runs.

Other associations with engine exhausts

Apart from the associations with lung cancer already discussed, there were a number of other noteworthy associations. Gasoline exhaust was associated with rectal cancer and diesel exhaust with colon cancer, and both of these associations exhibited dose-response tendencies. In fact, as can be seen in table 4, the odds ratios between both gasoline and diesel exhaust and the three subsites of colorectum were all in excess of 1.0, possibly indicating a generalized effect of these exhausts on the entire colorectum. An alternative hypothesis to explain these results may derive from the fact that the major occupation groups with these exposures have sedentary jobs. Colorectal cancer has been linked with lack of physical activity (13, 14).

Less persuasive from a statistical perspective were the gasoline exhaust-kidney cancer and diesel exhaust-prostatic cancer associations. We could find no evidence to support these hypotheses in either the epidemiologic or the experimental literature. There has however been some conflicting evidence concerning the association between exposure to gasoline in liquid or vapor form and kidney cancer (8, 11, 22, 27, 39). Based on only five exposed cases, our results showed a significant association between propane engine exhaust and melanoma of the skin.

Another type of cancer which has been linked to vehicle engine exhaust is bladder cancer. There have been both positive (16, 34) and negative (37, 41) reports in the literature. Our evidence, in the screening analyses, indicated no excess risk of bladder cancer for either gasoline or diesel exhaust.

There were no statistically significant associations with jet engine exhausts, though this was a relatively rare exposure with little statistical power.

Associations with combustion products of natural gas and propane

There were only two noteworthy associations with the combustion products of natural gas and propane. The propane combustion-lung (oat cell) cancer association virtually disappeared once confounders were included in the model. The natural gas combustion-bladder cancer association remained statistically significant. The only supporting evidence was tenuous. Cooks comprise an occupation group with potential exposure to natural gas. In an interview-based case-referent study of bladder cancer, there was an elevated risk among food counter cooks (30).

Associations with combustion products of liquid fuels

Only the association between combustion products of liquid fuels and prostatic cancer was elevated. This association was particularly strong among water transport workers and stationary engineers, though the excess risk was also evident among the other workers exposed to liquid-fuel combustion. Adelstein (1) reported high proportional and standardized mortality ratios for prostatic cancer among deck and engine-room workers, barge workers, and boatmen.

Wood combustion

Both esophageal and stomach cancer were related to wood combustion exposure, and both were based on small numbers. While the association with stomach cancer was not statistically persuasive, that with esophageal cancer was significant at the substantial exposure level. In our study, men who had been farmers in Italy represented one of the main groups with wood combustion exposure. Risk of cancer of the digestive tract is known to be high among farmers (3) and, in

our study, among persons of Italian origin. It is therefore likely that the stomach cancer-wood combustion association was an artifact due to confounding. Nevertheless, it is of interest that particulates from wood combustion have been shown to contain significant amounts of benzo(a)pyrene, and their extracts showed significant activity in the Ames test (7).

Coal and coke combustion

Exposure to coal combustion products was initially related to pancreatic and prostatic cancers, as well as to nonadenocarcinoma lung cancers. While the association with pancreatic cancer remained highly significant at the substantial exposure level, this association was based on only eight exposed cases. The association with nonadenocarcinoma lung cancer was marginally significant but did not manifest a dose-response relation; that with prostatic cancer was not statistically significant or convincing. There were no previous reports to support these hypotheses, except for that of Howe et al (17) showing excess lung cancer among railway workers exposed to coal dust, and thus presumably to coal combustion products as well. The composition of coal combustion products, including as it does varying amounts of respirable particulates, including PAH and gases which may be adsorbed such as aldehydes and hydrocarbons, would make it a plausible lung carcinogen. Coke, one of the cleanest-burning of the substances examined in this report, produced no significant associations.

Table 8. Brief summary (by site of cancer) of the strength of evidence for each association selected for the in-depth analysis.

Association	Strength of evidence ^a	
	Statistical ^b	Dose-response ^c
Esophageal cancer — wood combustion	+	+
Stomach cancer — wood combustion	—	—
Colon cancer — diesel exhaust	+	++
Rectal cancer — gasoline exhaust	+	++
Pancreatic cancer — coal combustion	+	++
Lung (oat cell) cancer — propane combustion	—	—
Lung (squamous cell) cancer — gasoline exhaust ^d	+	+
Lung (squamous cell) cancer — diesel exhaust ^{d,e}	+	—
Lung (squamous cell) cancer — propane exhaust	—	—
Lung (nonadenocarcinoma) cancer — coal combustion	+	—
Prostatic cancer — diesel exhaust	—	—
Prostatic cancer — liquid fuel combustion	+	+
Prostatic cancer — coal combustion	—	—
Bladder cancer — natural gas combustion	+	+
Kidney cancer — gasoline exhaust	—	+
Melanoma of the skin — propane exhaust	+	+

^a + + = moderate to strong evidence of excess risk, + = weak evidence of excess risk, — = no evidence of excess risk, — — = evidence against the hypothesis of excess risk (eg, inverse dose-response).

^b Based on the results of the logistic regression for "any" exposure. It takes into account the magnitude of the odds ratios, its statistical significance, and the number on which it is based.

^c Refers to the trend among subgroups at different levels and/or durations of exposure and to the odds ratios in the highest exposure subgroup.

^d Some experimental evidence which supports this association is presented in the text.

^e Some previous epidemiologic evidence which supports this association is presented in the text.

General comments

While we presented and discussed the associations in substance order, some readers may be interested to see them grouped by cancer site. In addition it is useful to briefly summarize the evidence presented. Table 8 presents an admittedly rough summary of the evidence on each association that was examined in-depth in our study.

The most important results were the associations between squamous-cell lung cancer and both gasoline and diesel exhaust. Given the findings reported in previous literature and the plausibility of these associations, our results add support to the notion of a lung cancer risk due to these engine exhausts.

Among the associations that have not been subjected to previous attention, the most promising leads to follow-up from our results are the following: (i) the effects of exposure to gasoline and diesel exhaust on the occurrence of colorectal cancers; (ii) the effects of exposure to gasoline exhaust on the occurrence of kidney cancer; (iii) the effects of exposure to coal combustion products on the occurrence of pancreatic cancer and possibly on nonadenocarcinoma lung cancer; (iv) the effects of exposure to combustion products of liquid fuels on the occurrence of prostatic cancer; and (v) the effects of exposure to natural-gas combustion products on the occurrence of bladder cancer.

Some of the hypotheses suggested will be followed up in our own data set with additional analyses regarding latency, interaction with smoking and other factors, effect modification, and more complex regression models. Such analyses were beyond the scope of this initial paper.

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