Delaware Health and Social Services
Division of Public Health

Cancer Cluster Investigation
Indian River Area
Delaware Health and Social Services
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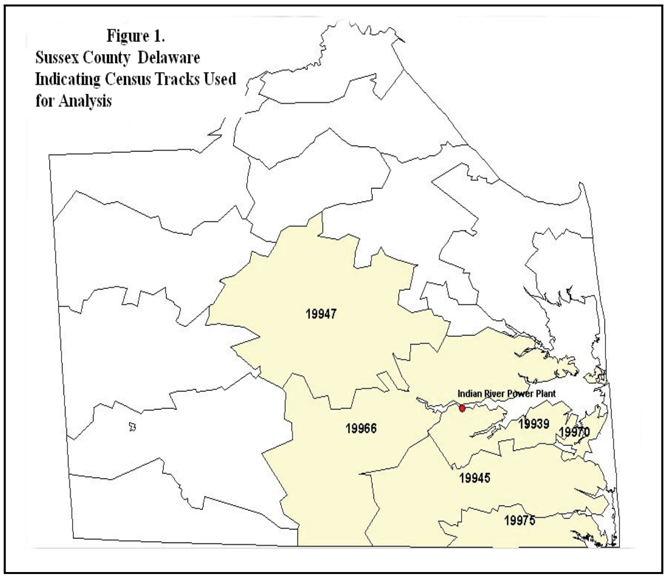
Introduction

The Delaware Division of Public Health (DPH) was asked to investigate the occurrence of cancer in the Indian River area of Sussex County. The request was made because of future power plant options and concerns about cancer resulting from the current coal burning facility.

An annotated bibliography is provided as an appendix to this report. The literature shows some evidence that exposure to particulates may cause cancer. However, evidence that coal burning power plants specifically cause cancer is not clear.



Methods

For investigative purposes DPH handled this request as a cancer cluster investigation. Concerned citizens defined the area of interest as zip codes 19939, 19945, 19947, 19966, 19970 and 19975 (Figure 1). To provide an overall assessment, 2000-2004 average annual cancer incidence rates were calculated for this area and compared to cancer incidence rates for the nation and Delaware as a whole. U.S cancer rates were estimated by the National Cancer Institute's Surveillance Epidemiology and End Results program. All rates were age-adjusted using the 2000 U.S. population as the standard.

The frequency of cancer was produced by age group and site for the years 1994-2004 for the six zip code area, Sussex County and Delaware as a whole.

Statistical significance was determined by calculating the 95 percent confidence intervals. Confidence intervals on graphs are shown as vertical bars. Intervals that do not overlap are statistically significant.

U.S. Census data was used to examine length of residence in Indian River as compared to Delaware.

Results

Table 1 and Figure 2 show the incidence rate of all cancer in the six zip-code area, Sussex County, the U.S., and Delaware. The incidence rate for cancer in Indian River is significantly higher than the rate for Sussex County, Delaware and the U.S. for the five-year time interval compared. Figure 3 compares the lung cancer incidence rate for these same geographic areas. The rate in Indian River is again higher than both Sussex County and Delaware.

Table 1

Age-adjusted Cancer Rate per 100,000 people, 2000-2004, Delaware and the United States

	Rate per 100,000	Lower 95% CI	Upper 95% CI
Indian River	553.9	530.4	577.3
Delaware	501.3	494.6	508.0
United States	473.6	472.5	474.8

Table 2 and Figure 4 show the 10 year frequency of cancer by site for the Indian River zip codes and Delaware as a whole. Lung cancer cases as a percentage of all cases are significantly higher in the Indian River zip codes (19.5 percent) than Delaware (15.0 percent). Breast cancer cases as a percentage of all cases are higher in Delaware (16.8 percent) than in the Indian River zip codes (14.1 percent).

Figure 2

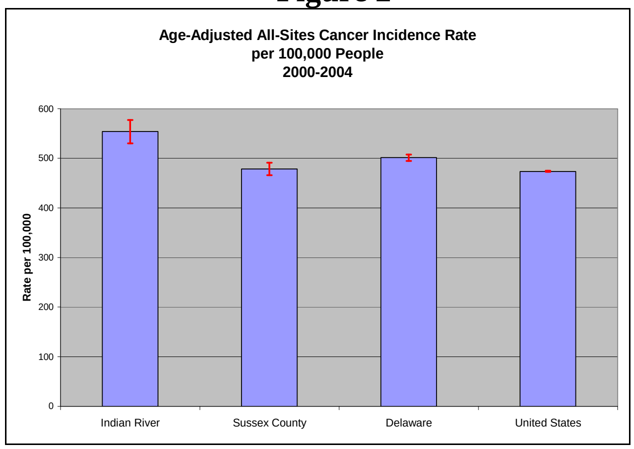
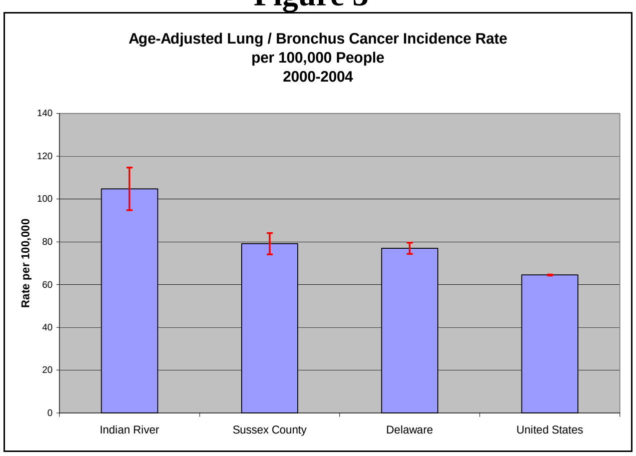


Table 3 and Figure 5 show the 10 year frequency of cancer by age group for the Indian River zip codes and Delaware as a whole. Cancer cases did not occur at a younger age in Indian River as compared to Delaware. For Indian River, 10.8 percent of the cases occurred below the age of 51 years, compared to 16.2 percent of cancer cases in Delaware.

Figure 3



With respect to length of residency, in 2000, 21.9 percent of Indian River residents had moved into the area from a different county, state or country. This is compared to 16.3 percent of the Delaware residents, who had moved from a different state or country.

Table 2
Incident Cancers by Site 1995-2004, Delaware

	Indian River				Delaware			
	Number	Percent	Lower 95% CI	Upper 95% CI	Number	Percent	Lower 95% CI	Upper 95% CI
lung & bronchus	771	19.5%	18.2%	20.7%	6,509	15.0%	14.6%	15.3%
prostate	574	14.5%	13.4%	15.6%	6,172	14.2%	13.9%	14.5%
breast	559	14.1%	13.1%	15.2%	7,282	16.8%	16.4%	17.1%
colorectal	447	11.3%	10.3%	12.3%	4,853	11.2%	10.9%	11.5%
urinary bladder	201	5.1%	4.4%	5.8%	1,855	4.3%	4.1%	4.5%
skin - melanoma	166	4.2%	3.6%	4.9%	2,077	4.8%	4.6%	5.0%
non-Hodgkin lymphoma	101	2.6%	2.1%	3.1%	1,124	2.6%	2.4%	2.7%
kidney & renal pelvis	96	2.4%	2.0%	3.0%	1,098	2.5%	2.4%	2.7%
leukemia	90	2.3%	1.9%	2.9%	810	1.9%	1.7%	2.0%
corpus uteri	86	2.2%	1.8%	2.7%	1,078	2.5%	2.3%	2.6%
pancreas	64	1.6%	1.3%	2.1%	871	2.0%	1.9%	2.1%
stomach	53	1.3%	1.0%	1.8%	677	1.6%	1.5%	1.7%
larynx	52	1.3%	1.0%	1.7%	432	1.0%	0.9%	1.1%
brain & other nervous system	46	1.2%	0.9%	1.6%	830	1.9%	1.8%	2.0%
ovary	46	1.2%	0.9%	1.6%	696	1.6%	1.5%	1.7%
esophagus	44	1.1%	0.8%	1.5%	505	1.2%	1.1%	1.3%
miscellaneous	38	1.0%	0.7%	1.3%	147	0.34%	0.29%	0.4%
cervix uteri	37	0.9%	0.7%	1.3%	422	1.0%	0.9%	1.1%
thyroid	37	0.9%	0.7%	1.3%	702	1.6%	1.5%	1.7%
multiple myeloma	36	0.9%	0.7%	1.3%	392	0.9%	0.8%	1.0%
liver	32	0.8%	0.6%	1.2%	287	0.7%	0.6%	0.7%
Hodgkin lymphoma	21	0.5%	0.3%	0.8%	262	0.6%	0.5%	0.7%
skin - not melanoma	19	0.5%	0.3%	0.8%	238	0.6%	0.5%	0.6%
Other	346	8.7%	7.9%	9.7%	4,161	9.6%	9.3%	9.9%
Total	3,962	100%			43,480	100%		

Discussion

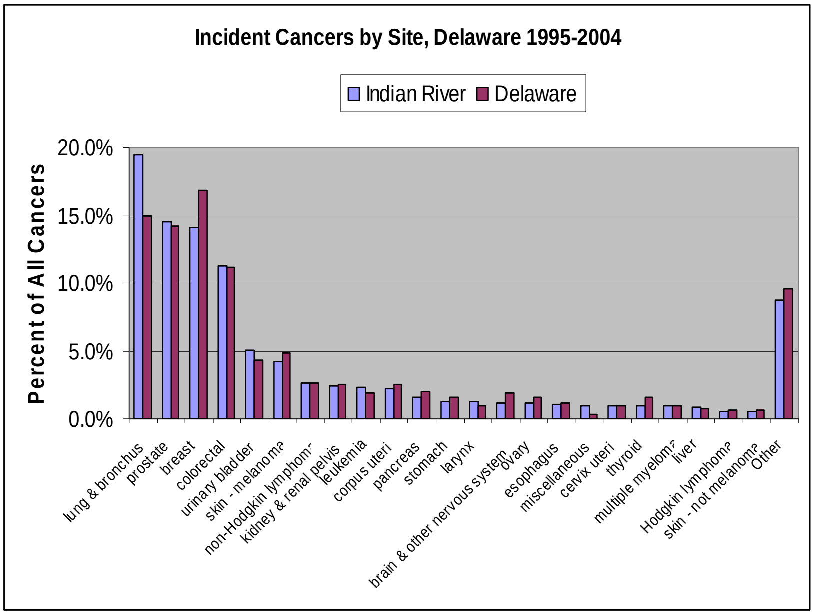
This analysis has significant limitations. No adjustments were made for other potentially relevant factors, such as smoking incidence, socio-economic status, or access to health care. In addition, exposure or dose data was not available or considered.

Tobacco use is a hypothesis that should be further explored to explain the higher rate of lung cancer cases in Indian River than in the state, and possibly for the higher rate of cancer overall.

This is because cigarette smoking causes about 85 percent of all lung cancer. Data on tobacco use in this area and for these cases would be required to explore this hypothesis further, but is not available.

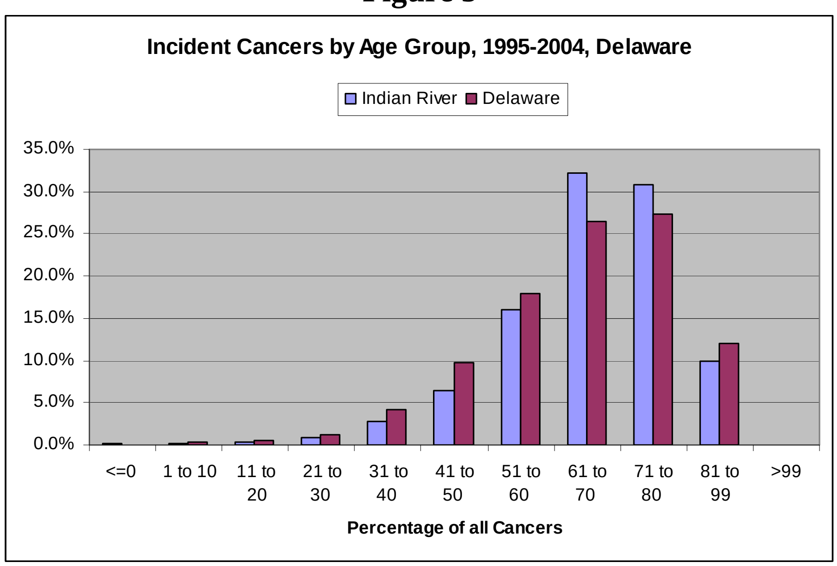
Migration may be another factor that could account for some of the increased rate of lung cancer in Indian River. The cancer incidence data reflects the zip code location of the individual when the cancer diagnosis was recorded, but does not reflect the duration of "exposure" of individuals at that location. In some cases, the individuals may have lived in these zip codes – with associated exposures - their entire lives, or they may have moved recently from another location. A higher proportion of Indian River residents move into the area than the state as a whole, based on 2000 census data. It is not known what proportion of the cancer cases contributing to the excess lung cancer in Indian River occurred among long-time as opposed to recently-arrived residents. Lung cancer among long term residents is consistent with a hypothesis involving a local environmental etiology. Lung cancer among recently-arrived residents would not be consistent with this hypothesis.

Figure 4



In addition to tobacco use and migration unknowns, no information about actual exposure to environmental carcinogens is available to study as part of this investigation. It is not known if the prevailing winds would deposit respirable particulates in the Indian River community or if such particles would be carried east out to the ocean. Air quality studies in the Indian River area are not available

Figure 5



to compare with what is known in other areas of the state. Further, since lung cancer usually results from exposures that occurred decades ago, measurements of environmental conditions today may not reflect conditions relevant to recent cancer rates. In addition, some of the contaminants from the power plant (e.g. mercury) would not necessarily have the greatest impact in a plume touchdown area, based on air modeling. The biologically-relevant human exposures to mercury occur predominantly from oral ingestion of contaminated fish flesh, which has been converted to a methylated form and concentrated in the food chain, not direct inhalation of air.

Table 3
Incident Cancers by Age Group, 1995-2004, Delaware

	Indian River				**Delaware**			
	Number	**Percent**	**Lower 95% CI**	**Upper 95% CI**	**Number**	**Percent**	**Lower 95% CI**	**Upper 95% CI**
<=0	6	0.2%	0.1%	0.3%	23	0.05%	0.03%	0.08%
1 to 10	5	0.1%	0.0%	0.3%	187	0.4%	0.37%	0.5%
11 to 20	16	0.4%	0.3%	0.7%	215	0.5%	0.4%	0.6%
21 to 30	30	0.8%	0.5%	1.1%	548	1.3%	1.2%	1.4%
31 to 40	111	2.8%	2.3%	3.4%	1,815	4.2%	4.0%	4.4%
41 to 50	258	6.5%	5.8%	7.3%	4,234	9.7%	9.5%	10.0%
51 to 60	632	16.0%	14.8%	17.1%	7,785	17.9%	17.5%	18.3%
61 to 70	1,279	32.3%	30.8%	33.8%	11,528	26.5%	26.1%	26.9%
71 to 80	1,226	30.9%	29.5%	32.4%	11,866	27.3%	26.9%	27.7%
81 to 99	397	10.0%	9.1%	11.0%	5,249	12.1%	11.8%	12.4%
>99	2	0.05%	0.01%	0.2%	30	0.07%	0.05%	0.1%
Total	3,962	100%			43,480	100%		

These unknowns illustrate the complexity of the carcinogenic process and the difficulty of evaluating the impact of cancer clusters in a community. More generally, cancer clusters may occur for a variety of reasons.

- Environmental exposure – The scientific literature can document the clustering of rare types of cancer among highly exposed occupational and medical populations where the exposure is high, prolonged, and well defined.[1] For example, in the late 1960s the connection between Vinyl Chloride and angiosarcoma was proposed when doctors discovered that workers at a B.F. Goodrich polyvinyl chloride plant who were exposed to above average rates of the chemical exhibited significantly higher rates of this rare liver cancer.[2] More research was performed after this initial discovery, for it seemed odd that so many workers in one place would suffer from such a rare disease by coincidence. However in the community setting in which the exposures are low and poorly defined, and where the cases involve a mix of unrelated, relatively common types of cancer, it is much more difficult to show that a cluster is caused by a specific environmental cause. This is further complicated by the fact that most

[1] Thun MJ, T Sinks**.** Understanding Cancer Clusters .CA Cancer J Clin 2004; 54:273-280

[2] Creech JL Jr, Johnson MN. Angiosarcoma of liver in the manufacture of polyvinyl chloride. J Occup Med 1974; 16: 150–151.

cancers occur decades after the initial exposure. Thus measurement of environmental pollution in the community today tells us little about its relationship to recent cancer cases.

- Better access to care – Ironically, a population that is more likely to have access to cancer screening services may be identified as having higher than average cancer incidence rates. This is because more screening means earlier identification of cancer, which is then reported to the state cancer registry. The cluster is really an artifact and not truly related to a higher risk of cancer. In Indian River, the elevated cancer was lung, which historically has no screening test. Therefore it is unlikely that access to screening is a cause of this cluster.

- Personal habits - Personal habits have a very strong influence on the risk of developing cancer. For example, tobacco use is known to cause about 85 percent of all lung cancer, which is the leading cause of cancer death in the U.S. among both men and women. It is associated with at least 15 cancers and responsible for 30 percent of cancer deaths overall. Therefore any analysis of a cluster involving higher than expected tobacco related cancers needs to explore whether or not the community is more likely to have smoked than the population at large. Other personal habits to consider are nutrition and physical activity, which are thought to account for about one third of all cancers.[3]

- Random variation – Cancer clusters occur randomly. About one of every two men and one in every three women will develop cancer over full life expectancy. Given that the occurrence of cancer is a frequent event, some spatial clustering is inevitable. However, the communities affected by clustering may perceive their experience not as part of a larger random pattern, but rather as the direct consequence of some local underlying cause. To further emphasize this point, Figure 6 was generated by randomly assigning numbers to x and y coordinates. The points represented on the graph are random. Imagine the space defined by the graph to be a community and each point to be a person with cancer among the inhabitants of that community. It is easy to identify clusters of these random cancers, as shown in Figure 7. Anyone living inside the circles or squares would rightly believe their community is experiencing a cancer cluster, but may wrongly conclude that there is some underlying cause to the cluster.

[3] American Cancer Society. Cancer Facts and Figures 2007. Atlanta. American Cancer Society. 2007.

Figure 6.
Scatter Gram Generated by Random X,Y Coordinates

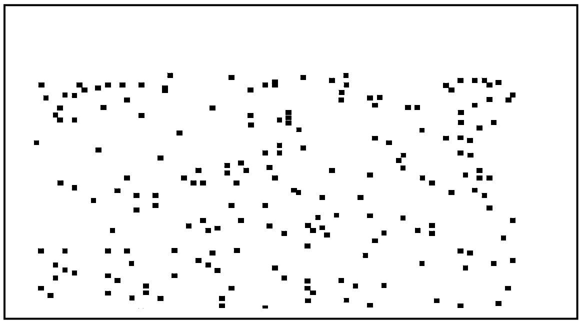
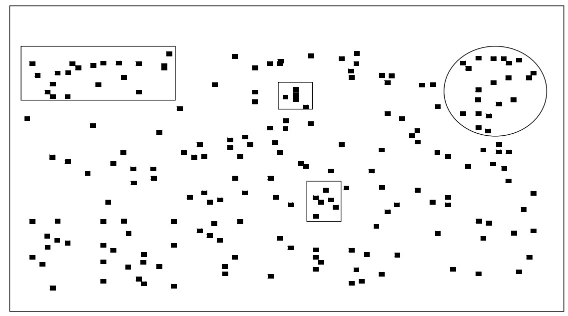


Figure 7.
Arbitrary Clusters From Figure 6



More than 1,000 suspected cancer clusters are reported to state health departments each year. [4] Investigations of these clusters very rarely lead to definitive conclusions because of the difficulties briefly reviewed above.

Conclusion and Recommendations

By definition, a cancer cluster occurs when a statistically higher rate of cancer exists in a defined community as compared to the region as a whole. The higher rate of cancer - lung cancer in particular - in the Indian River area is a cancer cluster. However, a review of 10 years of cancer data did not identify a disproportionate number of cancer cases among young people in Indian River. It also did not identify a cluster of unusual cancers or cancers with a known, rare cause. The absence of any abnormalities such as these provides no clues as to the origin of this cluster and suggests that further investigation is unlikely to be fruitful.

New rules promulgated by the Department of Natural Resources and Environmental Control are intended to reduce emissions from coal burning power plants. Regardless of the unknowns regarding the causal relationship between power plant emissions and cancer, both generally and in Indian River in particular, these rules are a major step forward in providing a clean environment. In addition, the Division of Public Health recommends the following:

1. Consideration should be given to locating air quality monitors maintained by the Department of Natural Resources and Environmental Control to the Indian River area, and to studying deposition patterns to provide further information about the potential for exposure to carcinogens and small particulates in the area. Such studies may also be useful in documenting the impact of the new emission control rules.

2. This investigation has reached the limits of evaluation with available data. However, further epidemiologic studies which may provide additional perspectives are possible by collecting new data from lung cancer patients or their survivors in Indian River, as well as from an

[4] Thun MJ, T Sinks**.** Understanding Cancer Clusters. CA Cancer J Clin 2004; 54:273-280

appropriate control group. Especially valuable would be information about tobacco use and residence history. The potential benefit of such studies must be weighed against the diversion of resources from other cancer control efforts. For this reason, the Division recommends that the Environmental Committee of the Delaware Cancer Consortium consider whether such studies should be done.

Appendix
Annotated Bibliography

Pope AC, Burnett RT, Thun MJ, Calle EE, Krewski D, Ito K, & Thurston GD. Lung Cancer, Cardiopulmonary mortality, and long-term exposure to fine particulate air pollution. *Journal of the American Medical Association.* 2002; 287(9): 1132-1141.

Design, setting & participants: Vital stats and cause of death data were collected by the ACS as part of the Cancer Prevention II Study, on on-going, prospective mortality study, which enrolled ~2.1M adults (age 30+) in 1982*. Participants completed a questionnaire detailing individual risk factor data (age, sex, race, weight, height, smoking history, education, marital status, diet, alcohol consumption and occupational exposures). The risk factor data for ~500,000 adults were linked with air pollution data for metro areas through the US and combined with vital stats and COD data through Dec 31, 1998.

* Participants resided in all 50 states, DC and Puerto Rico.

This study: Expanded follow-up time to >16 years; restricted to those participants who lived in metro areas for which pollution data were available. An average of 51 metro areas – and an average of 319,000 participants – were included in the analysis of $PM_{2.5}$; 102 metro areas – and 415,000 participants – were included in the analysis of PM_{10}.

Results: Fine particulate- and sulfur-oxide-related pollution were associated with all-cause, lung cancer and cardiopulmonary mortality. Each 10-µg/m^3 elevation in fine particulate air pollution was associated with ~4%, 6% and 8% increased risk of all-cause, cardiopulmonary and lung cancer mortalities, respectively. Measures of coarse particle fraction and total suspended particles were not consistently associated with mortality.

Summary Table: Adjusted Mortality Relative Risk (RR) Associated with a 10-µg/m^3 Change in Fine Particles Measuring Less Than 2.5 µm in Diameter.

	Adjusted RR (95% CI)		
Cause of Mortality	**1979-1983**	**1999-2000**	**Average**
All-cause	1.04 (1.01-1.08)	1.06 (1.02-1.10)	1.06 (1.02-1.11)
Cardiopulmonary	1.06 (1.02-1.10)	1.08 (1.02-1.14)	1.09 (1.03-1.16)
Lung cancer	1.08 (1.01-1.16)	1.13 (1.04-1.22)	1.14 (1.04-1.23)
All other cause	1.01 (0.97-1.05)	1.01 (0.97-10.6)	1.01 (0.95-1.06)

* Estimated and age-adjusted based on the baseline random-effects Cox proportional hazards model, controlling for age, sex, race, smoking, education, marital status, body mass, alcohol consumption, occupational exposure and diet.

Laden F, Neas LM, Dockery DW & Schwartz J. Association of fine particulate matter from different sources with daily mortality in six US cities. *Environmental Health Perspectives.* 2000; 108(10): 941-947.

Study expands upon previous study which reported that fine particle mass ($PM^{2.5}$), which is primarily from combustion sources, but not coarse particle mass, which is primarily from crustal sources, was associated with daily mortality in six eastern US cities. Researchers used the elemental composition of size-fractionated particles to identify distinct source-related fractions of fine particles and examined the association of those fractions with daily mortality in each of the six cities.

Factors: Silicon (soil/crustal material)
Lead (motor vehicle exhaust) (study done pre-unleaded gas)
Selenium (coal combustion)
Etc.

Time period: 1979-1988

Results: In the combined analysis, a 10 µg/m3 increase in $PM^{2.5}$ from mobile sources accounted for a 3.4% (1.7-5.2%) increase in daily mortality; equivalent increase in fine particles from coal combustion sources account for a non-significant 1.1% increase (0.3-2.0%). (In city-specific analysis, significance was achieved in one city, demonstrating a 2.8% [1.2-4.4%] increase.) PM2.5 crustal particles were not associated with daily mortality.

Samet JM, Dominici F, Curriero FC, Coursac I & Zeger SL. Particulate air pollution and mortality in 20 US cities: 1987-1994. *New England Journal of Medicine.* 2000; 343(24): 1724-1749.

Study assesses the effects of five major outdoor air pollutants - PM_{10}, ozone, carbon monoxide, sulfur dioxide and nitrogen dioxide – on daily mortality in 20 of the largest cities in the US.

Results: Found consistent evidence that PM_{10} is associated with total and cardiorespiratory mortality after taking into account potential confounding by other pollutants. For total mortality, the estimated relative rate was ~0.5% increase in mortality per $10\mu/m^3$ increase in PM_{10}, and the effect was not likely due to chance.

Pisani, P., Srivatanakul, P., Randerson-Moor, J., et al. (2006). GSTM1 and CYP1A1 polymorphisms, tobacco, air pollution, and lung cancer: A study in rural Thailand. *Cancer Epidemiol Biomarkers Prev*, 15(4), 667-674.

Pisani et al conducted a case control study in the Lampang Province in northern Thailand. The study was designed to evaluate the causes of the relatively high incidence of lung cancer in a province where several coal powered power plans were a source of public concern.

Methods: Controls were residents of a rural community surrounding a coal-burning power plant (n=197) and patients admitted to the local hospital for non-tobacco related conditions (n=211).

Cases were individuals with primary lung cancer recruited at the hospital (n=211). Cases and controls were matched by sex, age and residence. There were no relevant differences in socioeconomic level between the three groups. Four percent and 13% of the male and female cases, respectively, had never smoked. The prevalence of never smoked among female controls was 33% and 37%, versus 10% and 6% among males. Seventy-eight percent of smokers consumed unfiltered traditional products. The OR was 4.9 (95%, CI, 2.5-9.7) among smokers reporting the highest levels of consumption (> 7 cigarettes per day). The cumulative index of exposure to SO_2, NO_2, suspended particulate and domestic fumes was also analyzed. There was no increased risk of lung cancer associated with air pollution exposure from the power plant or domestic sources of fumes.

Results: Besides tobacco smoking, which alone explained 96% of male and 64% of female lung cancer incidence, none of the other environmental factors or three polymorphisms analyzed was associated with increased risk of lung cancer.

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