

Effects of low-dose radiation — A correlation study

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EDLING C, COMBA P, AXELSON O, FLODIN U. Effects of low-dose radiation — A correlation study. *Scand j work environ health* 8 (1982): suppl 1, 59—64. The effects of low-dose radiation have been a matter of controversy over the years, and the epidemiologic results have been conflicting. A couple of recent studies have indicated a possible impact on lung cancer mortality from exposure to indoor levels of radon and radon daughters. In this study, selected mortality rates, ie, lung cancer, pancreatic cancer, breast cancer (females only), leukemia, and multiple myeloma were correlated for the counties of Sweden with estimates of average background radiation exposure in these areas. Significant correlations were obtained for lung cancer (males, $r = 0.46$; females, $r = 0.55$) and pancreatic cancer (males, $r = 0.59$; females, $r = 0.40$), and there was a borderline correlation ($r = 0.36$; $p = 0.04$) for leukemia in males. In all, there were positive correlations for eight out of the nine computations made. Since background radiation correlates with urbanization and therefore with smoking, air pollution, etc, the correlations might be spurious due to confounding; on the other hand confounding is a reciprocal phenomenon which suggests that background radiation should to be taken into consideration when widespread risk factors like smoking, coffee drinking, general air pollution, etc, are studied.

Key terms: breast cancer, correlation study, leukemia, lung cancer, multiple myeloma, pancreatic cancer.

The health effects of low-dose radiation have attracted increasing interest over the past decade, especially because of the potential hazards involved in nuclear energy utilization. Since animal experiments on the effects of low-dose radiation near the background level are impractical, as requiring very large animal populations, epidemiologic studies are needed to elucidate the risks. Until now, some 20 epidemiologic studies seem to have been devoted to the oncogenic effects of background radiation, but many of these studies might be criticized because of poor design and uncertain data on both exposure and outcome.

Usually background radiation has been thought of in terms of gamma radiation

from the ground and cosmic radiation, but during the past few years there has also been concern about the increasing indoor concentrations of radon and radon daughters as a potential lung cancer hazard through the alpha radiation to the bronchial epithelium (30). Preliminary observations of an association between lung cancer and stone-house residency, as presumably reflecting a higher exposure to radon and its daughters, have been made in Sweden (3), and there is also a recent report from the state of Maine in the United States that suggests a positive and significant correlation between lung cancer and radon levels in tap water (18), ie, one important source of indoor radon.

The studies on background radiation and cancer have recently been reviewed (1). Some of these investigations have not shown any association, whereas others are suggestive of a possible effect. Because of this discrepancy in the results, there is certainly a need for further studies utilizing the new information on death rates

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and exposure measurements that might become available. This paper is one such attempt; it correlates some specific and adequately standardized cancer rates for Swedish counties with estimates of the average background radiation of these areas as recently reported by the Swedish Institute for Radiation Protection (30).

Based on information in the literature, five types of malignancies were chosen as probably respondent to radiation induction and therefore likely to correlate with background radiation if this exposure would have any pertinent effect. Thus, the earlier observations from Sweden (3) and the state of Maine (18) suggested that lung cancer should be considered; the rather well-established relationship between leukemia and ionizing radiation (10, 21) motivated the inclusion of this disease; similarly there have been suggestions of radiation-induced myeloma (20, 21, 23, 24). Several studies have also indicated that breast cancer might be induced by radiation (4, 6, 9, 31), and pancreatic cancers have appeared in several irradiated groups

(5, 12, 23, 28). These cancers were therefore chosen for the present study, although some other types might have been included as well, or chosen as alternatives.

Materials and methods

Age- and sex-specific death rates for lung cancer, breast cancer, and leukemia for the different Swedish counties in 1969–1978 were computed from data at the National Bureau of Statistics as part of a specific research project (15). Directly standardized rates were based on the 1974 Swedish population of the ages of 40 and above in 5-a age groups. For pancreatic cancer and multiple myeloma the absolute numbers of deceased cases during 1961–1973 were provided by the Swedish National Cancer Register, also as a part of the research project already referred to (15), and age- and sex-specific death rates were computed for the counties from an estimate of the 1965 population through the averaging of 1960 and 1970 census data; the reason for

Table 1. Mortality rates age-standardized directly for lung and breast cancer and leukemia during 1969–1978 in the counties of Sweden and for persons aged 40 and over, along with estimates of background radiation (cosmic radiation excluded), Pearson correlation coefficients and p-values.

County	mGy	Lung cancer		Breast cancer	Leukemia	
		Males	Females	Females	Males	Females
Stockholms	0.79	155.4	34.4	76.1	9.8	6.8
Uppsala	0.57	84.8	23.8	63.2	10.8	7.9
Södermanlands	0.77	112.6	22.2	74.7	11.8	8.4
Östergötlands	0.75	90.2	24.7	72.8	9.3	7.5
Jönköpings	0.52	61.2	13.8	79.3	10.7	7.5
Kronobergs	0.52	51.5	13.9	76.0	8.9	8.6
Kalmar	0.45	70.5	19.7	72.0	10.4	7.9
Gotlands	0.15	72.3	16.0	87.0	8.5	6.4
Blekinge	0.50	80.6	20.2	65.1	10.2	8.8
Kristianstads	0.42	63.9	17.6	68.3	9.5	8.8
Malmöhus	0.34	123.8	24.9	79.5	9.7	8.0
Hallands	0.37	68.0	22.3	66.7	9.4	7.8
Göteborgs-Bohus	0.60	101.5	26.9	73.7	9.3	6.7
Älvsborgs	0.39	55.3	17.9	72.5	9.2	7.4
Skaraborgs	0.63	43.5	16.8	79.6	10.6	7.9
Värmlands	0.48	65.2	18.4	74.5	10.1	7.8
Örebro	0.64	82.1	19.5	73.7	9.4	6.4
Västmanlands	0.67	94.8	25.5	68.0	9.0	7.7
Kopparbergs	0.58	68.7	19.2	71.9	8.6	6.9
Gävleborgs	0.44	84.0	17.8	68.4	9.5	8.3
Västernorrlands	0.39	73.7	17.1	63.7	7.2	5.5
Jämtlands	0.30	55.7	17.2	63.5	10.1	7.9
Västerbottens	0.41	61.1	17.3	58.6	8.9	8.9
Norrbottens	0.45	75.9	17.5	52.5	9.1	7.1
Coefficient of correlation		0.459	0.546	0.075	0.363	0.004
p-Value (one-tailed)		0.012	0.003	0.365	0.040	0.493

this somewhat different approach for multiple myeloma and pancreatic cancer was due to the lack of directly obtained age- and sex-specific rates for the counties.

The estimates of the average levels of background radiation in the various counties were provided by the National Institute for Radiation Protection (30), as based on a countrywide investigation of gamma radiation in 1,500 Swedish dwellings picked out at random.

Pearson's correlation coefficient, along with one-tailed p-values, were computed to test the association between background radiation and the cancer death rates from the aforementioned malignancies.

Results

The result of the correlation studies between background radiation and various cancer rates are shown in tables 1 and 2. There was a significant correlation between the estimates of background radiation and lung cancer, for both males and

females, and a similar correlation was obtained for pancreatic cancer in both sexes. Leukemia showed a correlation of borderline significance for males, and there was an even weaker correlation for females. Breast cancer (in women only) and multiple myeloma did not show any significant correlation, the correlation coefficient being negative for multiple myeloma in women (ie, the only negative correlation obtained from the nine correlations made).

Discussion

Lung cancer has a well-known, strong association with smoking, as has been shown in a number of epidemiologic studies. However, lung cancer also exists among nonsmokers and might even be increasing in this sector of the population (16). In an ongoing Swedish case-referent study on lung cancer (14), smoking and various environmental factors have been ascertained, until now showing 86 % of the male cases to be smokers or recent exsmokers (less

Table 2. Mortality rates age-standardized directly for pancreatic cancer and multiple myeloma during 1961–1973 in the counties of Sweden and for persons aged 40 a and over, along with estimates of background radiation, etc, as in table 1.

County	mGy	Pancreatic cancer		Multiple myeloma	
		Males	Females	Males	Females
Stockholms	0.79	34.2	24.8	7.7	5.9
Uppsala	0.57	26.7	22.0	5.0	4.4
Södermanlands	0.77	31.3	20.8	8.4	7.6
Östergötlands	0.75	27.6	20.2	7.0	5.2
Jönköpings	0.52	22.4	18.2	6.4	5.7
Kronobergs	0.52	30.8	23.1	9.8	7.0
Kalmar	0.45	23.4	19.3	7.8	5.3
Gotlands	0.15	16.0	20.3	5.0	6.7
Blekinge	0.50	19.5	15.7	7.9	4.3
Kristianstads	0.42	21.0	18.9	7.6	4.3
Malmöhus	0.34	27.8	17.4	7.6	6.2
Hallands	0.37	23.2	15.8	5.3	4.7
Göteborgs-Bohus	0.60	28.8	21.9	7.5	5.7
Älvsborgs	0.39	22.7	17.2	8.2	6.1
Skaraborgs	0.63	26.1	19.4	9.1	6.4
Värmlands	0.48	24.9	18.4	11.2	7.6
Örebro	0.64	22.0	21.0	8.9	6.2
Västmanlands	0.67	25.0	18.7	7.6	6.4
Kopparbergs	0.58	22.1	19.3	7.0	6.2
Gävleborgs	0.44	23.8	21.4	6.6	5.1
Västernorrlands	0.39	31.1	22.2	7.7	6.2
Jämtlands	0.30	21.8	18.7	7.8	9.6
Västerbottens	0.41	23.7	19.9	10.1	7.9
Norrbottnens	0.45	23.4	19.8	7.4	6.7
Coefficient of correlation		0.591	0.396	0.205	— 0.146
p-Value (one-tailed)		0.001	0.028	0.168	0.248

Table 3. Risk estimates for lung cancer per working level month (WLM) and per 10^6 person-years for persons above 50 a of age in various Swedish populations and estimates given in BEIR III (8). For the underlying assumptions and calculations see Axelsson & Edling (2).

Population ^a	WLM/lifetime	Lung cancers per WLM and per 10^6 person-years
Male zinc-lead miners	412.5	34.8
Rural wooden house residency		
Male	2.4	26.7
Female	2.4	24.2
Rural stone and mixed house residency		
Male	4.4	27.7
Female	4.4	32.3
Women ≥ 50 a of age in 1972	4.6	32.8
BEIR III estimates for males with Swedish men ≥ 50 a of age in 1972 as the age standard	—	27.6

^a The Swedish populations include (estimated) nonsmokers only.

than 10 a before diagnosis), in comparison to 51 % of the referents. For women the corresponding figures were 60 % of the cases and 19 % of the referents. Calculation of the etiologic fraction with regard to smoking resulted in 75 % for the males and 55 % for the females. Certainly these figures are preliminary and based on 52 cases and 113 referents only, but nevertheless they indicate the magnitude of smoking- and nonsmoking-related lung cancers. As suggested by the etiologic fractions, there is apparently room for other etiologies of lung cancer than smoking, eg, radiation, especially among women, and it is interesting that the correlation is the highest for women ($r = 0.55$), similarly to what was found in the state of Maine ($r = 0.65$).

Based on estimates given in the so-called BEIR III Report (8) and as obtained through some estimations from various Swedish populations, including zinc-lead miners with exposure to radon and radon daughters (2), it might now be estimated that some 25–35 cases per 10^6 person-years and per working level month (WLM) ³ for persons aged 50 and over might result from radon daughter exposure (table 3). It

could be added that the estimated background gamma radiation and indoor exposure to radon and radon daughters should correlate reasonably well when the exposure situation for large population groups is considered.

With regard to leukemia and low-dose radiation there are substantial discrepancies between various evaluations in the literature. Several authors have been unsuccessful in finding an association between leukemia mortality and different measures of background radiation (10, 11, 13, 19, 27), whereas a relationship between background radiation and leukemia has been suggested in a Polish study (25).

A recent Swedish investigation (17) seems to indicate a distinguishable effect of background radiation on myeloid leukemia. That study also revealed a rather complex situation of effect-modification and interconfounding with regard to other, earlier suggested risk factors, particularly solvent exposure, but also exposure to pesticides and animal contacts for population groups with low exposure to background radiation. This complex, interconfounding pattern, mainly operating in a negative and therefore obscuring direction, makes it unlikely that crude correlation studies should be able to reveal any effect of background radiation on leukemia. However, as derived from the study (17), low linear-energy-transfer radiation at the low-dose rate of background exposure might produce about three to nine leukemias per 10^6 person-years and per rad,

³ One "working level" is any combination of short-lived radon daughters (through ^{214}Po , ^{214}Pb , ^{214}Bi) leading to a total emission of 1.3×10^5 MeV of alpha energy per liter of air. A working level month (WLM) is inhalation of air containing a radon daughter concentration of one working level for 1 work month (170 h) or any combination of these two factors yielding the same product.

which is consistent with some of the earlier suggested, higher estimates (7).

As already indicated, correlation studies like the present one have apparent weaknesses because of insensitivity, but also because there might be many correlates of both the cancer incidence rates and the background radiation. [See the report of Saracci (26) for a general view of this problem.] For instance, there is a relationship between background radiation and degree of county urbanization, and there is also a well-known correlation between cigarette smoking and urbanization. Confounding from smoking cannot be effectively controlled in such a study and might well be an explanation for the obtained correlation of background radiation and lung cancer rates. Similarly there is a relationship between pancreatic cancer and smoking (29), the risk ratios being about two to three. However, it seems questionable to attribute the about 25 % of variance "explained" by the correlation in this study to the variations in smoking patterns between the counties. Recently, coffee drinking has also been suggested to be a risk factor for pancreatic cancer (22), and it might be assumed that coffee drinking is also somewhat more common in urbanized populations.

Confounding is a reciprocal phenomenon, however, and the conclusion of the present study might be, therefore, that background radiation could be a phenomenon worth considering in various studies of cancer effects from widespread risk factors like smoking, coffee drinking, general air pollution, etc. A similar view might also be relevant in selecting a reference population for an urbanized occupational group, ie, national rates might not be acceptable for comparison when an industry population in a (large) city is studied, the reasons being the tendency towards generally elevated cancer rates in urban areas, which might have to do with the increased background radiation in addition to other factors.

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