A CASE-CONTROL STUDY OF RADON AND LUNG CANCER AMONG NEW JERSEY WOMEN

SUMMARY REPORT - PHASE I

AUGUST, 1989

NEW JERSEY STATE DEPARTMENT OF HEALTH

DIVISION OF EPIDEMIOLOGY AND DISEASE CONTROL
DIVISION OF OCCUPATIONAL AND ENVIRONMENTAL HEALTH

THOMAS H. KEAN
GOVERNOR

MOLLY JOEL COYE, MD, MPH
COMMISSIONER OF HEALTH

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EXECUTIVE SUMMARY

The New Jersey State Department of Health (NJDOH) has been conducting an epidemiologic study of radon and lung cancer in New Jersey women. This study focuses on the questions of whether and to what extent radon in homes is associated with increased lung cancer risk. The importance of this question arose from the 1985 finding of very high levels of radon, a known cause of lung cancer among underground miners, in some Eastern Pennsylvania residences.

The New Jersey research reported here is the first large-scale epidemiological study of radon and lung cancer based on actual measurements in homes and detailed smoking histories for individual subjects. It is an extension of a case-control study of lung cancer which previously had been conducted among New Jersey women. The cases in that study were women newly diagnosed with lung cancer from August 1982 through September 1983, while the controls were women without lung cancer but similar in age and race to the cases. Information on smoking, residential, occupational and dietary histories was collected for 994 cases and 995 controls.

The radon substudy initially focused on those New Jersey dwellings which met a residence criterion, i.e., where subjects had lived the longest and for at least 10 years during the period from 10-30 years prior to lung cancer diagnosis or control selection. Both long-term and short-term radon measurements were made in these houses. Radon exposures for subjects were estimated by year-long alpha track detector measurements in the living areas. Four-day measurements of radon were made using charcoal canisters in basements to provide quick screening measurements for current residents, in case radon levels were so high that immediate remediation was needed, and to provide back-up data in case year-long measurements of radon were not completed.

This report is based on radon exposure data from 433 cases and 402 controls. Some of the original cases and controls were not included in the radon substudy because address-specific information could not be collected, because no house met the

residence criterion, or because radon tests could not be conducted at a house which did meet this criterion.

The overall distribution of radon exposure was generally low: only 24 cases (5.6%) and 12 controls (3.0%) had year-round living area radon concentrations of 2 pCi/L or greater. After smoking, age and occupation were taken into account, the estimated lung cancer risk for those exposed to the highest radon category (2-11 pCi/L) was 80% greater than the risk for those at the lowest exposure level (less than 1.0 pCi/L). Because the number of subjects in the higher exposure category was small, however, the relative risk estimate was not statistically significant. In contrast, the trend for increasing risk with increasing radon exposure was statistically significant; the probability that this trend was due to chance alone was only 4%.

When duration of exposure was also taken into account, similar patterns of increasing risk with increasing cumulative radon exposure were seen. The estimated lung cancer risk for those exposed to the highest cumulative radon category (50-155 pCi/L-years) was 40% greater than the risk for those at the lowest exposure level (less than 25 pCi/L-years). Furthermore, the increase in lung cancer risk over background risk per unit of cumulative exposure was consistent with that generally found in the studies of underground miners.

Study analyses also showed that lung cancer risk for women who smoked about one pack a day was 1,000% greater than risk for lifetime nonsmokers. This again confirmed that **smoking is the major cause of lung cancer.**

Some of the results of this study must be interpreted cautiously because of the small number of subjects in the highest radon exposure categories. Extensive data analyses and discussion throughout the technical report and its appendices are designed to consider the extent of any possible biases introduced by reduction of the potential study population to those with actual radon exposure estimates.

Nevertheless, the study suggests that the findings of radon-related lung cancer in miners can be applied to the residential setting. Excess radon exposures typical of homes may increase risk of lung cancer; extremely high residential exposures would be associated with very serious lung cancer risks. These results support the comprehensive interdepartmental radon-related effort initiated in 1985 by the NJDOH and the New Jersey Department of Environmental Protection, including provision of technical information and services, citizen education, and research activities. The study also confirms that smoking avoidance education should be strongly emphasized along with radon reduction activities.

The exposure data yielded by this study also suggest that the relationship between screening measurements and year-round living area measurements need better characterization for public policy purposes and clearer understanding by the public before remediation decisions are made. In addition, building code modification to prevent radon entry may be an effective means for reducing overall population risks from radon exposure.

Further data analyses may refine the results of this study. A second, still ongoing phase of data collection will add more subjects to the substudy, and will result in more complete exposure histories from additional houses for those subjects already included.

The findings of this study also need to be corroborated by other residential radon studies currently underway worldwide. In the meantime, existing actions to reduce radon exposure to the lowest feasible levels should be maintained. Remedial action should be taken in residences when follow-up testing indicates that typical exposures of occupants are above 4 pCi/L. This recommendation is not based upon the absence of any risk below 4 pCi/L; rather, it is based upon the limited feasibility of remediating residences below that level.

INTRODUCTION

The New Jersey State Department of Health (NJDOH) has been conducting an epidemiologic study of radon and lung cancer in New Jersey women. This study focuses on the questions of whether and to what extent radon in homes is associated with increased lung cancer risk. The importance of this question arose from the 1985 finding of very high levels of radon in some Eastern Pennsylvania residences. In response to this finding, the NJDOH and the New Jersey Department of Environmental Protection (NJDEP) initiated a comprehensive, interdepartmental effort to address radon-related issues. This program has included provision of technical information and services, citizen education, and research activities. Much of this effort was funded by a special New Jersey Legislative appropriation; the epidemiologic study was also partially funded by the National Cancer Institute (NCI).

Lung cancer is caused primarily by smoking[1,2]. Evidence is also strong regarding other risk factors, including various occupations[3] and diet[4]. The roles of environmental pollution and other potential risk factors are not as clear[5].

Prolonged exposures to high levels of radon have been identified as a cause of lung cancer in underground miners; epidemiologic studies of miners have shown a strong and consistent dose-response relationship between lung cancer and radon exposure[6,7]. Based on the miner data, the levels of radon exposure found in some houses may result in a substantial risk for the residents of these houses[8-11]. However, it is not clear to what extent radon contributes to the occurrence of lung cancer in the general population. It is important to clarify the degree of lung cancer risk from indoor radon, because of the vast public and private resources needed to identify and remediate residences with high radon levels.

Direct information on residential risk from radon has been very limited so far. Most reports involve only correlation studies, i.e., those comparing lung cancer rates and average radon exposures in different geographical areas[12-16]. Such correlation

studies do not include individual information on risk factors known to cause lung cancer, particularly on smoking. These studies also do not take into account how long individuals have lived in the area. Strong conclusions cannot be drawn from these studies alone. Moreover, their results have been conflicting.

The public health policy questions can be addressed more directly by epidemiologic studies based on individuals. This includes case-control studies and cohort studies. In case-control studies, persons with lung cancer and similar persons who do not have lung cancer are characterized with respect to past exposure to radon and other factors, such as smoking. In cohort studies, a group of individuals is identified and characterized with respect to exposures, and then followed forward in time to determine who gets lung cancer. Several small primarily Swedish case-control studies[17-22] as well as a small New Jersey cohort study[23] suggested an association between residential radon and lung cancer risk. However, most of these studies did not include actual measurements of radon in the houses of all subjects, and did not account adequately for smoking.

It was recognized in 1985 that some questions on residential radon risk could be addressed by extending a statewide female lung cancer case-control study which had been recently conducted in New Jersey. This study had already collected extensive data on smoking, diet, and occupation. The extension of this study to collect data on radon exposures was designed to help resolve the public health policy questions about the applicability of the underground miners studies to residential settings. Consequently, the study could help guide public agencies and citizens on radon testing and remediation decisions. The collaborators in this study extension included the Division of Epidemiology and Disease Control and the Division of Occupational and Environmental Health of the NJDOH, the Division of Environmental Quality of the NJDEP, and both the Radiation Epidemiology Branch and the Environmental Epidemiology Branch of the NCI.

More detailed information on this study is available in the Technical Report and its Appendices.

NEW JERSEY RADON STUDY - METHODS

ORIGINAL FEMALE LUNG CANCER STUDY.

The original study cases included all female New Jersey residents who were newly diagnosed with cancer of the lung (confirmed by various methods) from August 1982 through September 1983[24]. For cases who were interviewed themselves, controls similar in age and race were selected during the same time period from New Jersey drivers' license files and from files of persons enrolled for Medicare. For deceased or incapacitated cases with next of kin interviews, controls were selected from state death certificate files.

During the original study, an extensive personal interview was administered for 994 cases (76% of the 1,306 cases originally identified) and for 995 controls (69% of the 1,449 controls originally identified). The questionnaire included a lifetime brand-specific smoking history, information on smoking by other household members, lifetime residential and occupational histories, and a dietary history concerning foods containing vitamin A.

RADON STUDY DATA COLLECTION.

In order to collect data on radon exposures, the original female lung cancer study was extended. Based on the literature available in 1985, a minimum 10 year period was assumed to elapse between relevant exposure to radon and diagnosis of lung cancer. It was necessary to estimate radon exposure over a sufficient time interval, while remaining within available budgetary resources for radon measurements. Therefore, those residences in New Jersey at which each subject had lived the longest and for at least 10 years during the twenty-year period 10-30 years prior to case diagnosis or control selection (approximately 1953-1972) were selected for study.

Residential information which had been collected previously specified only the towns in which each subject had lived. Therefore, the subjects or their next of kin were recontacted to determine their exact street addresses during the period 1953-1982 and to identify an "index residence" which met the above residence criterion (10+ years, approximately 1953-1972). For each index residence, the current occupant was then requested to participate in the radon measurement portion of the study.

Measurements at these index residences started in October 1986. At each residence, house construction and ventilation information was collected, including any changes in construction which had occurred since the current occupants had lived in the house. Four-day measurements of radon were made using charcoal canisters provided and analyzed by the NJDEP. The charcoal canister measurements served two purposes: first, to provide a relatively quick "worst case" screening measurement of radon for current residents, to identify any dangerously high levels which would need immediate remediation; second, to provide back-up data, in case long-term measurements of radon (see below) were not completed.

Year-long measurements of radon were made using alpha track detectors. Those alpha track measurements from the living areas of the house (non-basement) were believed to provide the best estimate of the average radon levels to which the subjects had been exposed while they were residents of these houses.

The number of years of exposure to the radon levels measured in the index house was determined from the dates provided by the respondent (original subject or next of kin) in the residential history. Tax office records also were used to validate the residential histories.

DATA ANALYSIS.

The radon measurements were grouped into categories for analysis, because of concern about the precision of measurements at the low concentrations found in this

study. Results were expressed as <1, 1-1.9, 2-3.9, and 4.0+ picocuries per liter (pCi/L). These groups are useful because they are consistent with the "log-normal distribution" of radon, and they also agree with the categories generally used by the NJDEP.

Relative risks (RR) measure the frequency of lung cancer among persons exposed to a factor, such as radon, compared to the frequency of disease among persons not exposed. The RR was estimated using a statistic called the odds ratio (OR), including its 90% confidence interval (CI). The CI is a range of values within which the true value of the lung cancer relative risk is thought to be, given a specified degree of chance variation. A statistical method called multiple logistic regression analysis[25] allowed relative risks for radon to be calculated, while taking into account other factors, such as smoking and age. Trends in risk with increasing radon exposure were also calculated.

RESULTS

INCLUSION IN THE RADON STUDY.

Of 1,989 subjects (994 cases, 995 controls) in the original lung cancer study, 835 subjects (433 cases, 402 controls) were included in the radon study (see Table 1). Actual radon measurements were conducted at the index residence for 796 subjects (411 cases, 385 controls). Living area alpha-track measurements were completed for 664 of these subjects (346 cases, 318 controls); living area alpha-track measurements were estimated from basement alpha-track measurements or from canister measurements for 132 subjects (65 cases, 67 controls). Another 39 subjects (22 cases, 17 controls) who lived in apartments above the second floor were assumed to have negligible radon exposures. The remaining 1154 subjects (561 cases, 593 controls) were not included in the radon study because no address-specific information could be collected, no address met the residence criterion, or radon tests could not be conducted at the index residence.

TABLE 1
Distribution of the original New Jersey female lung cancer cases and controls by their status in the radon substudy
New Jersey radon-female lung cancer case-control study, 1982-1988

	No. of cases (%)		No. of controls (%)	
INCLUDED IN RADON STUDY	**433**	**(43.6%)**	**402**	**(40.4%)**
Radon testing at index address	411	(41.4%)	385	(38.7%)
Index address is apartment above second floor	22	(2.2%)	17	(1.7%)
NOT INCLUDED IN RADON STUDY	**561**	**(56.4%)**	**593**	**(59.6%)**
No address-specific information	140	(14.1%)	126	(12.7%)
No address met residence criterion	253	(25.5%)	256	(25.7%)
No radon testing at index address	168	(16.9%)	211	(21.2%)
TOTAL	994		995	

DISTRIBUTION OF RADON CONCENTRATIONS.

Table 2 shows the distribution of year-round living area radon levels (measurements and estimates) for index residences of the 835 subjects. Radon levels were less than 1 pCi/L for 666 (79.8%) subjects, 1-1.9 pCi/L for 133 (15.9%), 2-3.9 pCi/L for 28 (3.4%), and 4+ pCi/L for only 8 subjects (1.0%). There are several reasons that only one percent of the houses in this study had living area alpha track measurements greater than 4 pCi/L:

(1) Surveys of radon are often based on screening measurements, i.e., charcoal canister measurements in the basement during the winter under closed house conditions, which are "worst case" measurements. This study based its results on year-round radon measurements in the living areas, which are better estimates of actual exposures to people. Table 3 shows the relationship between basement screening measurements and year-round living area measurements. Screening measurements below 4 pCi/L generally result in year-round measurements less than 1 pCi/L. Even screening measurements from 8-20 pCi/L result in average year-round living area measurements which average 2.4 pCi/L, and few alpha-track measurements which exceed the 4 pCi/L guidelines.

(2) The original female lung cancer study was population-based; the subjects were identified systematically from the entire state. Therefore, many of the subjects lived in the heavily-populated urban areas of the state (e.g., Bergen, Essex, Hudson counties), which happen to have lower radon levels. Surveys of radon conducted for the DEP have focused on the high-radon areas, and have included more houses from areas of the state such as Warren and Hunterdon counties which are not as heavily populated.

(3) A house included in this study had to be the residence of a subject for at least 10 years from 1953-1972. This meant that the house would have been built in 1962 or earlier. A radon survey conducted by the NJDEP has found that older houses in New Jersey often have lower radon levels than newer houses[26].

TABLE 2

Distribution of lung cancer cases and controls by radon level
(year-long living area alpha track measurements, n=664; estimates, n=171)
New Jersey radon-female lung cancer case-control study, 1982-1988

	Radon (pCi/L)				
	<1.0 [a]	1-1.9	2-3.9	4-11.3	Total
Cases	342 (79.0%)	67 (15.5%)	18 (4.2%)	6 (1.4%)	433
Controls	324 (80.6%)	66 (16.4%)	10 (2.5%)	2 (0.5%)	402
TOTAL	666 (79.8%)	133 (15.9%)	28 (3.4%)	8 (1.0%)	835
Adjusted OR[b] (90% CI)	1.0	1.1 (0.79,1.7)	1.3 (0.62,2.9)	4.2 (0.99,17.5)	
			1.8[c] (0.89,3.5)		

[a] Includes subjects whose index address was an apartment above the second floor or a trailer.

[b] Odds ratios (OR) and 90% confidence interval (CI): Estimate of the lung cancer risk associated with exposure to a given level of radon, after taking into account other factors such as cigarette smoking, age, occupation, and respondent type. Test for trend in OR with increasing radon: p=0.04.

[c] OR for radon exposure of 2.0+ pCi/L.

TABLE 3
Relationship between basement canister measurements
and year-round living area alpha-track measurements,
New Jersey radon-female lung cancer case-control study, 1982-1988

Basement canister (4-day) measurement group	Year-round living area alpha track measurements: Average[a] (pCi/L)	Range (pCi/L)	percent of basement canister (average)[a]
< 1 pCi/L	0.4	0.1-2.0	64%
1-2 pCi/L	0.6	0.1-2.0	36%
2-4 pCi/L	0.7	0.1-3.7	24%
4-8 pCi/L	1.0	0.2-3.4	18%
8-20 pCi/L	2.4	0.3-11.3	20%

[a] geometric mean

LUNG CANCER RISK ASSOCIATED WITH RADON.

Table 2 also shows the lung cancer risks (as estimated by the odds ratios) for the different categories of radon exposure in this study. Note that these are "adjusted" ORs, i.e., they take into account cigarette smoking by the subject (number of cigarettes smoked per day and number of years since smoking cessation, if any) as well as age, respondent type, and occupation. By definition, the OR for the lowest exposure level (< 1.0 pCi/L) is assumed to be 1.0. The findings show that lung cancer risk increases with increasing radon exposure, from an OR of 1.1 for 1-1.9 pCi/L to an OR of 1.8 for 2-11 pCi/L. When the small numbers of subjects with exposures above 2 pCi/L are subdivided, the OR is 1.3 for 2-3.9 pCi/L and 4.2 for 4-11 pCi/L. However, there is substantial statistical uncertainty in these latter estimates, because of the small numbers of subjects. None of the OR for any single category is statistically significant, i.e., there is a greater than 5% possibility that the results are due to chance. However, there is a statistically significiant trend (p=0.04) of increasing risk with increasing radon exposure, i.e., there is only a 4% probability that such a trend is due to chance.

For comparison purposes, Figure 1 shows relative risks for the associations of lung cancer with radon and with smoking. The OR for lifetime nonsmokers (0 cigarettes/day) is assumed to be 1.0. The risk increases substantially with increasing numbers of cigarettes smoked per day. Smokers of about one pack a day have a greater than eleven-fold increase in risk relative to lifetime nonsmokers.

Other data analyses are not shown in the tables or figures in this Summary Report, but are included in more detail in the Technical Report. Analyses by separate smoking groups showed some differences in the patterns of radon-related risk. The light smokers showed the greatest increase in odds ratios with increasing radon exposure. The heavy smokers showed a pattern of decreasing odds ratios with increasing radon exposure. However, the number of subjects who were both heavy smokers and exposed to higher radon concentrations was very small, suggesting that

FIGURE 1

ASSOCIATION OF LUNG CANCER WITH LONG-TERM RADON EXPOSURES OR WITH CIGARETTE SMOKING IN WOMEN, NEW JERSEY RADON-FEMALE LUNG CANCER CASE-CONTROL STUDY, 1982-1988

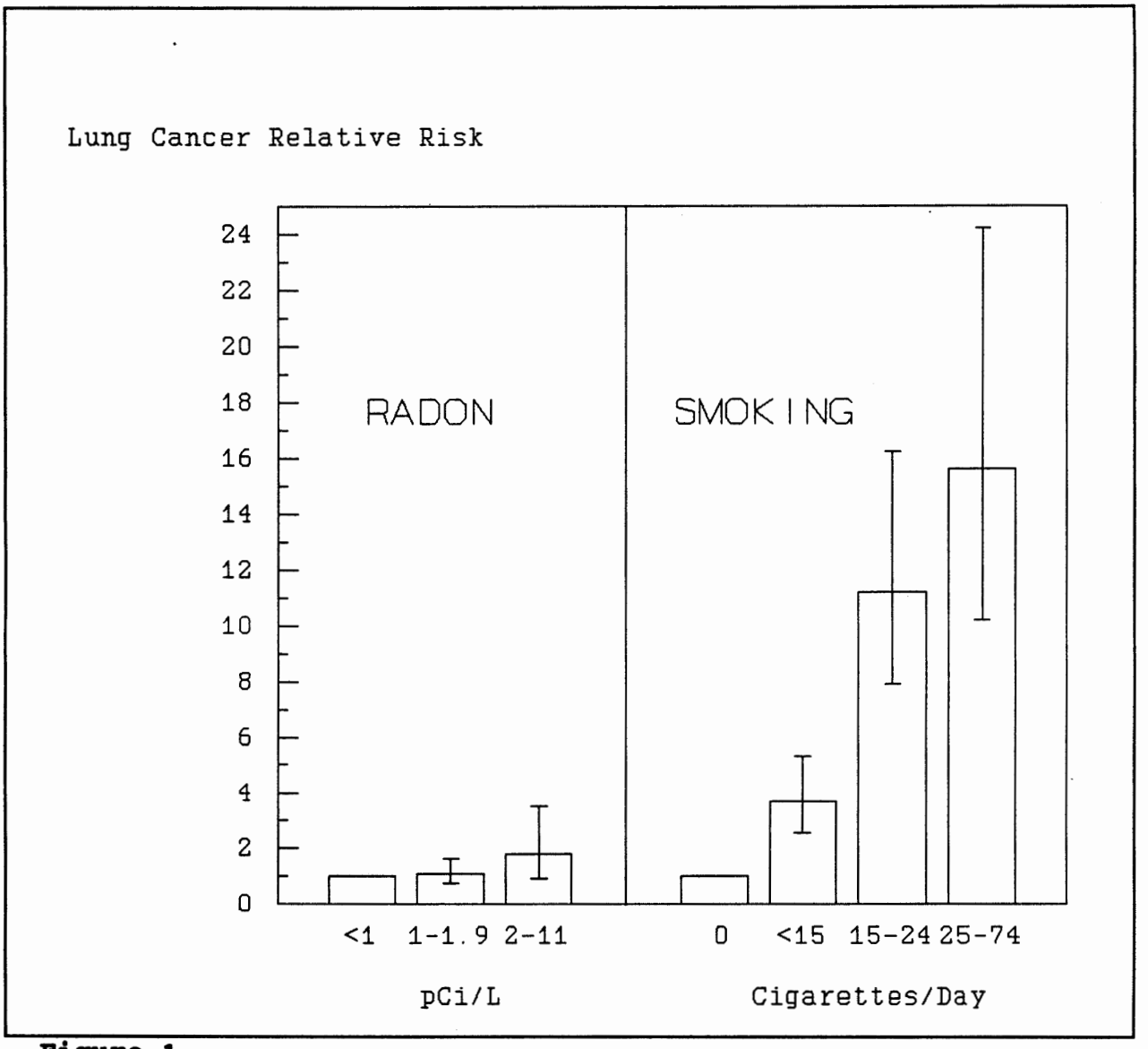

Figure 1

Lung cancer risk increases both with radon and with smoking, but much more with smoking. Bars (and error lines) represent relative risks ± 90% confidence intervals for association of lung cancer in New Jersey women with year-round living area radon concentration in index residence (at least 10 years exposure) or with lifetime average number of cigarettes smoked per day. Relative risk is assumed to equal 1.0 for radon < 1 pCi/L or for nonsmokers.

these observations were due to chance variation or to some selection biases (see Discussion and Technical Report). Also, there were very few cases among nonsmokers, making it difficult to observe any pattern in this group.

Analyses were also conducted according to the histologic type of lung cancer. The pattern of increasing risk with increasing radon level was found for all histologic types, with the possible exception of squamous cell carcinoma.

ANALYSES OF CUMULATIVE RADON EXPOSURES.

All of the analyses described above have considered only the radon concentration measured in the living area of the index residence. The number of years of residence at the index address had not yet been taken into account. **A cumulative exposure index multiplies the radon concentration by years of residence.** In developing the cumulative exposure index used in these anslyses below, several assumptions were made:

(1) A minimum period of five years between relevant radon exposure and diagnosis of lung cancer has been assumed, rather than ten years. This makes the exposure period of interest the years from 5-30 years prior to case diagnosis or control selection. This assumption is based on recently published analyses of data from miner studies[7,27].

(2) Based on the median radon concentration for control subjects in this study, an exposure of 0.6 pCi/L has been assumed for each year during the 5-30 period when a subject lived in any house other than the index residence. These other houses were not tested for radon in this part of the study.

The resulting cumulative radon exposure distribution has been divided into subgroups of <25, 25-49, 50-99, and 100+ pCi/L-years. Each level represents the equivalent of 25 years of exposure at <1, 1-1.9, 2-3.9, or 4+ pCi/L, respectively.

Table 4 shows the distribution of cumulative radon exposure estimates for the 835 subjects. Cumulative exposures were less than 25 pCi/L-years for 701 (84.0%) of the 835 subjects, 25-49 pCi/L- years for 108 (12.9%), 50-99 pCi/L-years for 21 (2.5%) and

100-155 pCi/L-years for only 5 (0.6%) of the subjects. Table 4 also shows the OR for the association of lung cancer with cumulative radon exposure, adjusted for cigarette smoking and other factors. Again, the lowest exposure level (<25 pCi/L-years) is assumed to have an OR of 1.0. The risks increase with increasing cumulative radon exposures, from an OR of 1.2 for 25-49 pCi/L-years to 1.4 for 50-155 pCi/L-years. When the small numbers of subjects with exposures above 50 pCi/L-years are subdivided, the OR is 0.94 for 50-99 pCi/L-years and 7.2 for 100-155 pCi/L-years. The OR of 7.2 is significantly high (the lower 90% confidence limit is greater than 1.0); however, there is substantial uncertainty in these separate estimates. The trend of increasing risk with increasing cumulative radon exposure is marginally significant (p=0.09), i.e., there is a 9% probability that such a trend is due to chance.

Figure 2 shows lung cancer relative risks for cumulative radon exposures in this study, and compares these to the average risks seen in occupational studies of underground miners.[7] The exposure scale is in units of "working level months" (WLM), which is the unit of cumulative exposure used in the miner studies. For comparison, 25 pCi/L-years equals 5 WLM, while 50 pCi/L-years equals 10 WLM. The pattern of increasing risk with increasing cumulative radon exposure seen in the residential study is quite consistent with the pattern seen in the occupational studies.

RELATIVE RISK COEFFICIENTS.

Another method of comparing the results of this study with the miners studies is to calculate a "relative risk coefficient." This is the increase in risk per unit of exposure, i.e., per pCi/L-year or WLM. The relative risk coefficient estimated for this study is 3.4% per WLM, which means there is a 3.4% increase in lung cancer risk over background risk for every one WLM or every 5 pCi/L-years. The miner studies have generally shown relative risk coefficients of 0.5%-4%, so again the results of this study seem to be consistent with the occupational data.

TABLE 4

Distribution of lung cancer cases and controls by cumulative radon exposure[a]
New Jersey radon-female lung cancer case-control study, 1982-1988

	Cumulative radon (pCi/L-years)				
	<25	25-49	50-99	100-155	Total
Cases	361 (83.4%)	56 (12.9%)	12 (2.8%)	4 (0.9%)	433
Controls	340 (84.6%)	52 (12.9%)	9 (2.2%)	1 (0.2%)	402
TOTAL	701 (84.0%)	108 (12.9%)	21 (2.5%)	5 (0.6%)	835
Adjusted OR[b] (90% CI)	1.0	1.2 (0.83,1.9)	0.94 (0.41,2.2)	7.2 (1.0,50.3)	
			1.4[c] (0.65,3.0)		

[a] Cumulative radon exposure during 25 years from 5-30 years prior to case diagnosis or control selection; assumes exposure of 0.6 pCi/L (median for controls) for any of the 25 years during which the subject did not live in the index address where the measurements were made.

[b] Odds ratios (OR) and 90% confidence interval (CI): Estimate of the lung cancer risk associated with exposure to a given cumulative level of radon, after taking into account other factors such as cigarette smoking, age, occupation, and respondent type. Test for trend in OR with increasing cumulative radon exposure: p=0.09.

[c] OR for cumulative radon exposure of 50.0+ pCi/L-years.

FIGURE 2

ASSOCIATION OF LUNG CANCER WITH CUMULATIVE RADON EXPOSURES IN OCCUPATIONAL STUDIES OF MINERS AND IN THE NEW JERSEY RADON-FEMALE LUNG CANCER CASE-CONTROL STUDY, 1982-1988

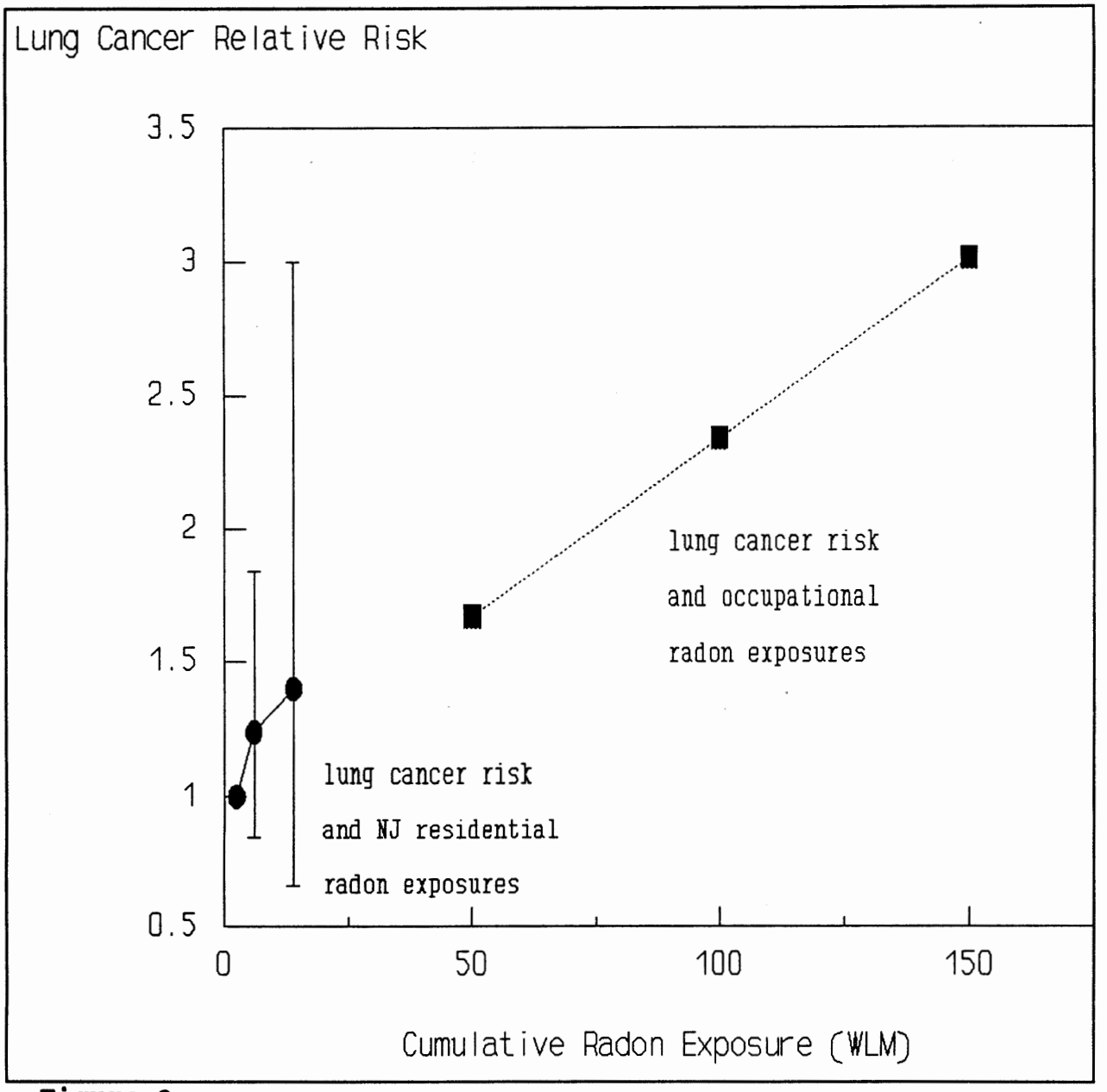

Figure 2

Lung cancer risk increases with cumulative radon exposures. There is consistency between the increase in risk seen in average data from occupational studies of miners and the increase in risk seen in data from the New Jersey case-control study. The error bars represent 90% confidence intervals for the New Jersey data.

DISCUSSION

As described above, the study was designed to investigate whether higher radon levels in residences are associated with excess lung cancer risk. Although there is a definite cause-effect link between radon and lung cancer at the high concentrations which have been found in underground mines, many have questioned whether that link applies to the lower radon concentrations usually seen in homes.

This study suggests that a radon-related lung cancer risk may exist in residences, but some of the results must be interpreted cautiously for reasons which are described below.

EVALUATION OF CAUSALITY IN EPIDEMIOLOGIC DATA.

First, it is important to consider how epidemiologists interpret data on the relationship between an exposure and a health outcome, and how they draw conclusions about cause and effect[28].

1. Consistency with previous findings. In a specific study, an association between exposures and health effects may be considered causal if it is consistent with other research and if similar findings have been previously reported in other populations. There is a vast body of evidence indicating that exposure to radon and its decay products increases lung cancer risk. The results of this study results are consistent with those of miners[7] (see Figure 2) and with those of other residential case-control studies already reported from Sweden[17-21].

2. Biological plausibility. When there is a biologically plausible basis for relating an exposure to a health effect, there is support for concluding that the association is causal. There is much information from human and animal observations and from radiation biology to predict independently that radon causes lung cancer.

3. Dose-response issues. Causality is supported when an exposure-effect association increases in strength as the exposure increases. This study found that overall relative risks increased directly with exposure.

4. Strength of association. The method used to assess strength of association is the "relative risk" (RR) as estimated by the "odds ratio" (OR). A strong association (one with a higher RR) supports the interpretation that the association is causal. For example, the RR of lung cancer is about 11 times greater for women who have smoked about a pack of cigarettes a day than for women who are lifetime nonsmokers. This is a very strong association.

In the current study, the RR for women with higher radon exposure intensity (2-11 pCi/L on an annual basis) was 1.8, compared to the risk of 1.0 for background indoor concentrations of less than 1.0 pCi/L. Similarly, the RR for women who accumulated 50 to 155 pCi/L-years during the twenty-five-year exposure period under study was 1.4, 40% greater than baseline. This is a relatively weak association, but is consistent with predictions for low exposures (again, see Figure 2). For the occasional household in New Jersey with much higher radon levels, such as 200 pCi/L, lung cancer risks are probably much higher.

5. Specificity. In communicable disease, a classic cause-effect relationship depends upon a unique microbe's association with a particular clinical syndrome. However, in environmental health, it is very rare to find a disease caused by only one agent. Lung cancer is no exception. Lung cancer is caused primarily by cigarette smoking. For that reason, the effect of smoking was carefully controlled in the analyses. Residential radon, occupation, and diet are other risk factors.

6. Sequence (timing) of exposure and health effect. In a cause-effect relationship, the exposure precedes the disease. However, the long latency of cancer, i.e., time between the start of exposure and diagnosis, is a factor which makes epidemiologic research on

cancer causality so difficult. Exposure was estimated for each individual subject for the years five to thirty years prior to lung cancer diagnosis or control selection.

7. Internal consistency of results among subgroups. Causality is supported when all subgroups of important variables which could affect the study show similar results. Therefore, the difference among smoking subgroups in these findings (see p. 12) weakens the causal inferences.

8. Adjustment for other variables. The observed association between lung cancer and radon became stronger when other lung cancer risk factors, such as smoking, age and occupation, were taken into account. This strengthens the causal inference.

KEY FEATURES OF THE STUDY: STRENGTHS AND WEAKNESSES.

Key features of this study include the quality of the health outcome data, the possibility of selection biases, the quality of the exposure data, the adjustment for potential confounders, and the number of subjects and measurements.

Health outcome data. The quality of the health outcome data is a strength of the study. The original cases and controls were drawn systematically from the entire New Jersey population. The cases were all clinically validated through review of pathology reports and other medical records.

Selection biases. The possibility of selection biases is a weakness of the study. The residence criteria and the need to have the cooperation of both the original subjects and the current occupants of homes reduced the number of subjects included in the study. This could have introduced some biases, which may result in observing either a smaller or greater radon-lung cancer association than would be found if all of the original subjects were included.

These possible selection biases are described and discussed in detail in the Technical Report and Appendices.

Exposure Data. Another strength of the study is that actual radon measurements were made in each index house except for apartments above the second floor. In addition, year-long radon measurements in the living areas were used as the main index of exposure. Short-term measurements were used only for screening purposes, as consistency checks, and as contingency measurements (when long-term measurements were not completed). Screening conditions (heating season, "closed-house", and lowest floor) are best used for making decisions on whether further testing is needed. However, screening results are usually exaggerations of the typical radon concentrations actually inhaled by people on a year-round basis (see Table 3). Year-long measurements also have the advantage of smoothing over the daily and seasonal radon fluctuations due to weather changes, different proportions of time spent at home, and varying amounts of time spent on each floor of the house.

A weakness in all case-control studies is that exposure data are collected in the present time when the exposure of interest actually occurred in the past. Changes in house construction, heating, ventilation, occupants' activity, and variation in hours per week of occupancy could cause inaccuracies in the exposure estimates. It is also possible that high or low radon exposure during the years in which subjects lived in other houses (not measured in this study) could have caused some significant exposure misclassification. However, there is no reason to believe that there was any systematic exposure misclassification which would have resulted in higher (or lower) measurements for cases than for controls. Furthermore, the overall distribution of measurement results agree well with those of NJDEP[26], after taking into account differences in the location and age of the houses tested.

Potential confounders. Confounders are factors which can influence both the exposure observations and the health effect observations, and may distort an observed association between the exposure and effect of interest. Because smoking is by far the most important cause of lung cancer, it can confound the association between radon and lung cancer. Therefore, another strength of the study is the availability of detailed information on smoking habits of all study subjects which was taken into account in the analyses.

In addition, detailed occupational and dietary histories and data on demographic characteristics such as age and educational level were also available. Occupation and age were taken into account in the final analysis along with the detailed smoking information. However, it is still possible that the observed relationship between lung cancer and the low levels of radon in this study is distorted due to other, unevaluated confounding factors.

Numbers of Subjects and Measurements. Another weakness of the study is the small number of houses which had high exposure measurements, especially the very few above 4 pCi/L. Because the risk estimates have large statistical uncertainty, the results must be interpreted cautiously. Nonetheless, the total number of subjects for whom residential measurements were made exceeds most previous individual-based residential studies; this is another strength of the study.

RISK PER UNIT OF EXPOSURE.

In comparing studies of miners, and in deriving predictions about the degree of hazard from radon exposure under various scenarios, the concept of **excess risk per unit radon exposure** has been useful. In this study, "relative risk coefficients" based on excess risk per pCi/L-year or per WLM of radon exposure were derived. As described in the Results section (see p. 16) and as shown in Figure 2, the findings are consistent

with those of the miner studies. This suggests that the conclusions about lung cancer risk from radon based on the studies of miners can be applied to radon exposures in the residential setting.

SMOKING INTERACTION.

Cigarette smoke contains a mixture of potent carcinogens (cancer-causing substances). Other studies have suggested that a combination of both radon and cigarette exposure produces a greater carcinogenic effect than either exposure by itself. The finding of different radon risk patterns in different smoking subgroups may be influenced by small numbers of heavy smokers and nonsmoking cases and by possible selection biases (see Technical Report). The fact that the strongest radon effects were seen in light and moderate smokers emphasizes the importance of avoiding both smoking and radon exposure.

Moreover, smoking is by far the most serious risk factor for lung cancer. Risks are increased about eleven-fold in women who have smoked about one pack per day (see Figure 1) compared to the overall less than two-fold risk from the radon exposures found in this study.

HISTOLOGY.

Particular cell or histological types of lung cancer which are more or less associated with radon exposure could have medical significance for early diagnosis and treatment. Underground miner studies suggested that small cell and squamous cell lung cancers were the major types induced by radon. In this study, other types were also found to be associated with higher radon exposure. Since females tend to have a somewhat different distribution of lung cancer cell types than males, these histological findings are of particular interest. Data from future studies in other locations will be needed to substantiate these observations.

AGE AND GENDER COMPARISONS.

Since underground miner research was conducted only on working age males, only residential studies can compare radon risks for persons of all ages and for men with women. The design of this study did not permit the consideration of childhood exposures, but it contributes a new and important set of data on females to the body of knowledge on radon risks.

IMPLICATIONS OF EXPOSURE FINDINGS.

The year-round average exposures in the study houses were lower than had been expected on the basis of a statewide survey which included primarily screening measurements[26]. This finding has several important implications.

(1) The results support the use of follow-up tests rather than screening tests for making remediation decisions. Such procedures are already advised by the USEPA, NJDEP and NJDOH, but are not necessarily understood by the public.

(2) If the findings concerning the relationship of average annual concentrations to screening measurements are confirmed by other studies, remediation may not be necessary for as many dwellings in the state (and the nation) as had been predicted on the basis of screening measurement distributions.

POLICY IMPLICATIONS.

The results of this study have important implications with respect to the policies which have been followed concerning radon-related issues.

Degree of health concern about radon exposure. The results of this study, in combination with previous occupational, residential, and experimental data, suggest that radon is a carcinogen in the residential setting. The excess lung cancer risk per unit

of radon exposure found in this study appears to be consistent with underground mining studies. **Therefore, these findings suggest that exposures typical of dwellings may increase risk of lung cancer and that extreme exposures would be associated with very serious lung cancer risks.**

Governmental Radon Programs. The observation that residential radon exposures may increase lung cancer risk supports governmental radon activities. These include educating citizens, providing technical information and services, and conducting research on health effects, testing, and remediation. Furthermore, smoking avoidance education should be included and strongly emphasized in all governmental radon risk education activities. The distinction between radon screening and annual average tests should be emphasized.

Remedial action level recommendations. **Given that radon appears to be a lung carcinogen even at low, unavoidable exposures, the recommended action levels must be based on feasibility of remediation. The current guidance remains:**

1) Follow-up testing should be conducted when the result of a screening test is greater than 4 pCi/L. A screening test is conducted for 3-7 days under worst case conditions (heating season, ground level, closed house). The purpose of follow-up testing is to characterize the typical exposures to occupants in the living area of the dwelling. The length of the follow-up testing should depend upon the screening result: over 20 pCi/L, follow-up tests should be short term (a few days); below 20 pCi/L, long-term measurements (up to a year) are better, but short-term tests may also be useful under certain circumstances.

2) Remedial action should be taken when follow-up testing indicates that typical exposures of occupants are high and when remediation is feasible, i.e., typical exposures are above 4 pCi/L.

A true health-based guideline for a carcinogen such as radiation would be zero or close to zero exposure, because the weight of evidence suggests that there is no amount of exposure which does not entail some amount of risk. However, outdoor radon levels are about 0.1 - 0.2 pCi/L, and baseline indoor levels are 0.2 - 1.0 pCi/L. The future does not appear to hold any promise for changing this unavoidable exposure or the associated risks. The 4 pCi/L recommendations are based upon the practical feasibility of remediating and constructing residences such that most are below this action level.

There are two types of practical limitations to reduction of radon exposure:

(1) Ability to remediate: As the indoor concentrations approach the background (0.2-1.0 pCi/L), there are diminishing returns in radon reduction as a result of remedial action. As remediation progresses, a point is reached where further actions are increasingly expensive and decreasingly effective. (This phenomenon is true of pollution control generally.)

(2) Validation of remediation: As the indoor radon concentrations are reduced closer to background, normal daily/weekly/seasonal fluctuations due to weather ventilation, etc., can easily mask any improvements in radon gas levels which result from further remediation. In order to be sure whether any action has succeeded, testing must be done for increasingly long time periods and must be more expensive and technically sophisticated. Therefore, it becomes even more difficult to reduce radon concentrations below a certain point because the results of such actions cannot be easily verified.

There has been consensus from national radon technology experts that 4 pCi/L is currently an achievable goal for most dwellings. There is also intensive research underway throughout the world to increase the effectiveness of both new construction and remediation techniques for citizens. It is hoped that these efforts will contribute to the long-range goals of decreasing indoor radon concentrations.

Meanwhile, it has been the policy of the NJDOH and NJDEP (1) to recommend the lowest radon exposure which is currently feasible for citizens, (2) to support a decrease in the officially-recommended exposure limit as soon as such technology is considered practical, and (3) to support the implementation of building construction codes so that radon entry resistant dwellings will be built in areas with high exposure potential. The findings of this case-control study on lung cancer and radon in New Jersey women support these policies, since they are consistent with the belief that even radon concentrations at or below the current guidance levels probably cause small increases in the chances of lung cancer.

Recommendations on specific geographic areas. This study did not address potential radon exposures in specific counties or municipalities of New Jersey. The ongoing data collection and updated guidance in this regard by the NJDEP continues to be the best guide to citizen testing.

Maximum individual risks vs population risks. Indoor radon is an example of a public health hazard in which some individuals are subject to much higher exposures than most others. It is appropriate for public health policy to address reduction of risk both to the most highly exposed individuals and to the public as a whole.

Occupants of houses with extreme radon levels (e.g. over 200 pCi/L) are exposed to higher concentrations than those typical of some uranium miners and may have lung cancer risks approaching or even exceeding those of cigarette smokers. While identification and remediation of such houses do not make a large impact on population lung cancer rates, they may have a dramatic effect on reducing the lung cancer risks for the specific occupants.

The findings of this and other studies indicate that the excess risks to each individual occupant of houses with low radon exposures are quite modest compared to

other causes of lung cancer such as smoking. However, in the population as a whole, most of the lung cancer due to radon is a result of relatively low exposures.

Moreover, because remediation is not yet feasible at levels less than 4 pCi/L, revised building codes designed to render new dwellings more resistant to radon entry may have a far reaching effect on overall population lung cancer rates. To be effective such codes need to be widely implemented, especially in areas with high radon potential.

FUTURE ANALYSES.

This report is neither a final point in the data collection nor an end to the data analyses for this study. Nonetheless, it is important to share with the New Jersey public and the scientific community the findings to this point because of their important implications in validating the activities conducted and recommended so far by the NJDOH and the NJDEP. Several important additions to the study are planned for the near future.

1. A second phase of data collection is currently underway. Since 1985, data from miner studies have been published which indicate a shorter time period (five years) between relevant radon exposure and lung cancer than had been assumed previously[7,27]. Also, the NJ State Legislature provided a supplemental appropriation to test additional residences of the original subjects. To date, as part of Phase II, approximately 200 additional houses have had canister measurements completed and year-long alpha track detectors installed. These measurements will result in more complete exposure histories for some subjects already included in Phase I of the study, and provide some exposure measurements for subjects not yet included in Phase I.

2. Further statistical analysis of the interaction of smoking and radon will be conducted.

3. In a subsequent analysis, municipality-specific or county-specific radon data from the NJDEP study will be used to estimate other non-measured radon exposures for the subjects.

4. There have been several indications that the urban or rural character of a locality may affect the ability to observe a link of radon with lung cancer. In a subsequent analysis, population density and the subjects' own characterization of the urban-rural nature of their residence will be analyzed.

5. Data on changes of house construction, ventilation, and heating will be considered in some analyses.

6. Details on occupation of the subjects will be used to improve estimates of number of hours per week spent at home.

7. The frequency with which subjects moved their residence will be analyzed in order to consider factors which could have influenced the results due to the residency requirement.

CONCLUSIONS

Radon exposure is universal; everyone is exposed to radon to some degree. This report is intended to contribute to decisions by public agencies and individuals regarding the importance of limiting radon exposure, wherever it is feasible to do so.

The findings of the first phase of the New Jersey epidemiologic study of radon and lung cancer in women are consistent with recommendations to reduce exposure which have been made by the New Jersey Department of Health, New Jersey Department of Environment Protection, U.S. Environmental Protection Agency, and other federal agencies. These recommendations have been in effect since the widespread problem of high radon exposure from naturally-occurring sources became known in the mid-1980's.

This study found statistically significant or marginally significant increasing trends in lung cancer risk with increasing radon exposure. However, the number of subjects in this study with annual exposures above 4 pCi/L was very small; therefore, the results should be interpreted cautiously. The degree of excess risk per unit of radon exposure which was found is consistent with the few previous individual-based residential studies and with the many studies of underground miners. Forthcoming analyses of additional measurement data may improve the confidence of the risk estimates from this study.

The exposure data yielded by the study suggest that a relatively small percentage of New Jersey houses which are more than 25 years old have year-round living area exposures above 4 pCi/L, although in certain geographic areas, the proportion is larger. Moreoever, the relationship of screening to annual average exposures may need better characterization for public policy purposes and clearer understanding by the public before remediation decisions are made.

One potentially important finding was that the strongest effects of radon exposure were seen in light and moderate smokers. However, possible misclassification of smoking and selective underrepresentation of heavy smokers in the study cannot be ruled out. It is clear that cigarette smoking, even at the level of one pack per day, remains by far the most important risk factor for lung cancer in most women and men.

GLOSSARY

alpha-track detector - a small plastic device used for measuring radon gas concentrations over a long period of time, generally one month to one year.

bias - any effect which produces results which are systematically different from the true results.

case-control study - a study in which cases (persons with a given disease) and controls (persons who do not have the disease) are compared with respect to factors thought to be related to the occurrence of the disease.

charcoal canister - a metal can filled with charcoal used for measuring radon gas concentrations over a short period of time, generally three to seven days.

cohort study - a study in which some persons exposed to a factor and other persons not exposed are followed in time and compared with respect to whether or not they get a particular disease.

confidence interval - a range of values within which the true value of a statistic is thought to be, given a specified degree of chance variation.

confounder - one factor which distorts the apparent effect of another factor on risk.

cumulative exposure - exposure over a given period of time.

epidemiology - the study of the distribution and causes of disease in populations.

histologic types of lung cancer - subgroups of lung cancer in which the cancer cells have similar features, when examined by a pathologist under a microscope.

log-normal distribution - a distribution in which the logarithm of the variable is itself normally distributed, i.e., follows a "bell-shaped curve".

odds ratios - a statistic used to estimate the relative risk in a case-control study.

picocuries per liter (pCi/L) - a unit of radon exposure, measured by alpha-track detectors or charcoal canisters.

picocuries per liter-years (pCi/L-yrs) - a unit of cumulative radon exposure, which equals the radon exposure multiplied by the number of years of exposure.

radon - a radioactive gas found in low concentrations everywhere on earth; it can come out of the soil and rock and can enter buildings through cracks or other openings.

relative risk - the ratio of the rate of disease among persons exposed to a given factor, compared to the rate of disease among the unexposed; in a case-control study, the relative risk is estimated by the odds ratio.

relative risk coefficient - the difference between the relative risk and the background risk for each unit of exposure

remediation - reducing the radon concentrations in a building.

statistically significant result - a finding which could occur by chance less than a given percentage of time, usually 5%.

Working Level Month (WLM) - a unit of cumulative radon exposure, often used in studies of radon exposure among miners; 1 WLM equals 5 pCi/L-years.

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