PB88-218979

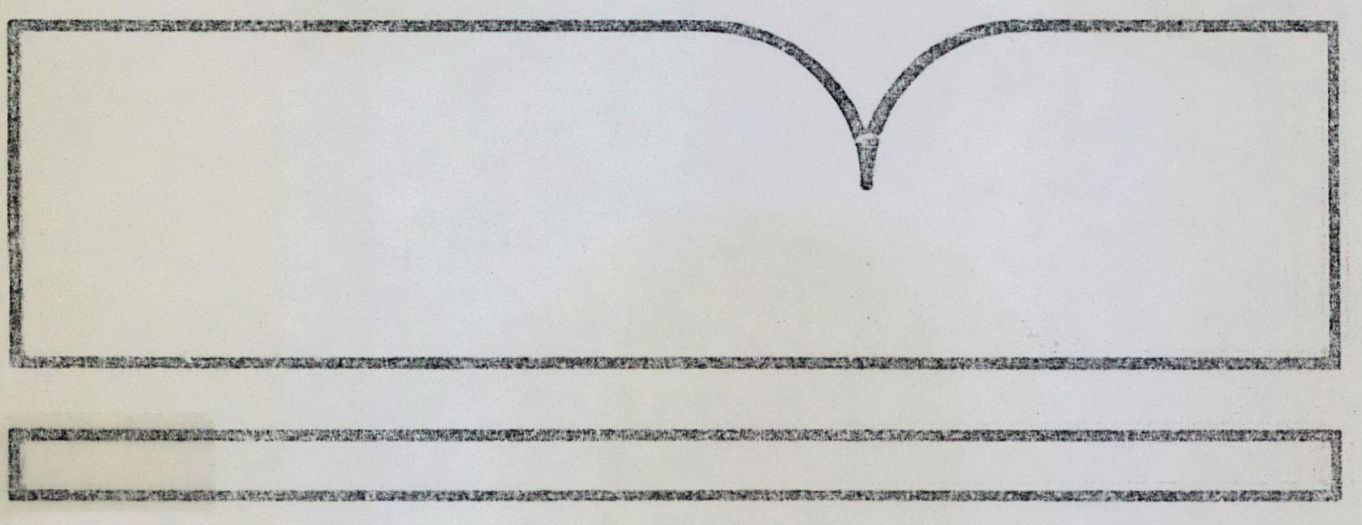
Estimating the Risk of Lung Cancer from Inhalation of Radon Daughters Indoors Review and Evaluation

Colorado State Univ., Fort Collins

Prepared for

Environmental Monitoring Systems Lab.
Las Vegas, NV

Jun 88



TECHNICAL REPORT DATA
(Please read Instructions on the reverse before completing)

1. REPORT NO.	2.	3. RECIPIENT'S ACCESSION NO.
EPA/600/6-88/008		PB88-218970/AS

4. TITLE AND SUBTITLE	5. REPORT DATE
ESTIMATING THE RISK OF LUNG CANCER FROM INHALATION OF RADON DAUGHTERS INDOORS: Review and Evaluation.	June 1988
	6. PERFORMING ORGANIZATION CODE
7. AUTHOR(S)	8. PERFORMING ORGANIZATION REPORT NO.
Thomas B. Borak and Janet A. Johnson	
9. PERFORMING ORGANIZATION NAME AND ADDRESS	10. PROGRAM ELEMENT NO.
Department of Radiology & Radiation Biology Colorado State University Fort Collins, CO 80523	CCVN1A
	11. CONTRACT/GRANT NO.
	CR 813606-01
12. SPONSORING AGENCY NAME AND ADDRESS	13. TYPE OF REPORT AND PERIOD COVERED
Nuclear Radiation Assessment Division Environmental Monitoring Systems Laboratory P.O. Box 93478 Las Vegas, NV 89193-3478	Final - Oct. 86 to Apr. 88
	14. SPONSORING AGENCY CODE
	EPA/600/07

15. SUPPLEMENTARY NOTES
Work performed under cooperative agreement between Colorado State University and U.S. Environmental Protection Agency. The Project Officer was Stuart C. Black, EMSL-LV.

16. ABSTRACT

A review of the dosimetric models and epidemiological studies with regard to the relation between indoor radon exposure and lung cancer indicates that the Working Level is an appropriate unit for indoor radon exposure; that the uncertainty in applying risk estimates derived from uranium miner data may be reduced by determining nose vs. mouth breathing ratios, residential aerosol characteristics, and lung cancer risk vs. age at exposure; that there is persuasive evidence of an association between radon exposure indoors and lung cancer; and theat epidemiological studies in progress may provide a basis for revision or validation of current models but only is experimental designs are employed that will permit pooling of data to obtain greater statistical power.

17. KEY WORDS AND DOCUMENT ANALYSIS

a. DESCRIPTORS	b. IDENTIFIERS/OPEN ENDED TERMS	c. COSATI Field/Group
	U.S. Environmental Protection Agency Region 5, Library (5PL-16) 77 West Jackson Boulevard Chicago, IL 60604-3590	

18. DISTRIBUTION STATEMENT	19. SECURITY CLASS (This Report)	21. NO. OF PAGES
Release to the public	Unclassified	130
	20. SECURITY CLASS (This page)	22. PRICE
	Unclassified	A07 19.95

EPA Form 2220-1 (Rev. 4-77) PREVIOUS EDITION IS OBSOLETE

PB88-218379

EPA/600/6-88/008
June 1988

ESTIMATING THE RISK OF LUNG CANCER FROM INHALATION OF RADON DAUGHTERS INDOORS: Review and Evaluation

by

Thomas B. Borak and Janet A. Johnson
Department of Radiology and Radiation Biology
Colorado State University
Fort Collins, CO 80523

Cooperative Agreement
Number CR813606

Project Officer

Stuart C. Black
Nuclear Radiation Assessment Division
Environmental Monitoring Systems Laboratory
Las Vegas, NV 89193-3478

ENVIRONMENTAL MONITORING SYSTEMS LABORATORY
OFFICE OF RESEARCH AND DEVELOPMENT
U.S. ENVIRONMENTAL PROTECTION AGENCY
LAS VEGAS, NV 89193-3478

NOTICE

The information in this document has been funded in part by the U.S. Environmental Protection Agency under cooperative agreement number CR 813606 with Colorado State University. It has been subject to the Agency's peer and administrative review, and it has been approved for publication as an Agency document. Mention of trade names or commercial products is for illustration only and does not constitute endorsement or recommendation for use.

ABSTRACT

A review of the dosimetric models and epidemiological studies with regard to the relation between indoor radon exposure and lung cancer indicates that the Working Level is an appropriate unit for indoor radon exposure; that the uncertainty in applying risk estimates derived from uranium miner data may be reduced by determining nose vs. mouth breathing ratios, residential aerosol characteristics, and lung cancer risk vs. age at exposure; that there is persuasive evidence of an association between radon exposure indoors and lung cancer; and that epidemiological studies in progress may provide a basis for revision or validation of current models but only if experimental designs are employed that will permit pooling of data to obtain greater statistical power.

TABLE OF CONTENTS

TABLE OF CONTENTS (continued)

LIST OF TABLES

ACKNOWLEDGMENTS

The authors gratefully acknowledge the assistance of the following individuals:

S. C. Austin
R. Brownson
O. Castren
B. L. Cohen
F. T. Cross
S. C. Darby
N. H. Harley
W. Jacobi
A. C. James
J. B. Klotz
E. Lacombe
E. M. Lanctot
E. G. LeTourneau
C. R. Muirhead
G. Pershagen
P. Rand
J. M. Samet
K. J. Schlager
J. B. Schoenberg
J. H. Steboings
H. G. Stockwell
E. Stranden
C. Svensson
S. Takacs

SUMMARY

Public concern for the health effects of exposure to indoor radon has made it necessary to make risk estimates based on inadequate and incomplete data. The challenge to the professional community is to evaluate available information on occupational exposure and adapt it to non-occupational environments using basic concepts of radiation dosimetry. The results must then be validated on the basis of epidemiologic evidence and data on residential exposures.

Dose conversion factors for inhalation of radon daughters have appeared in the literature since 1956. They range from 0.7-29 mGy WLM^{-1} (Ja87). Recently the range of values has been reduced considerably. The results shown in Table 1 indicate that the spread between models is greater than the conversion from occupational to environmental exposures within each model.

Each model has been formulated by distinguished scientists who have selected input variables according to their interpretation of available and often identical data. At this time there is no indisputable evidence that permits ranking or elimination of any of the computations.

The average of all three models gives a ratio of dose conversion factors for residential to occupational exposure of 1.3 ± 1.3. The only conclusion that can be made with confidence is that the ratio of dose conversion factors is greater than 1. The added uncertainty of deriving risk coefficients using data from underground miners may not be significant.

The concept of cumulative potential alpha energy is sufficient for describing the exposure of individuals and there is no justification for redefining or modifying the WLM or J h m^{-3}. However, there are several important factors which influence the conversion from exposure to dose. Improved data on the following could reduce the uncertainty in the risk estimates to the general public:

- Fraction of time nose breathing vs. mouth breathing.
- Unattached fraction.
- Aerodynamic median diameter and geometric standard deviation of attached aerosols.
- Age dependence.
- Location of radiosensitive targets.

The common denominator for dose conversion factors is cumulative exposure to potential alpha energy (WLM). Most epidemiological studies of indoor environments measure radon gas only. It is important to understand the relationship between radon gas and radon daughter concentrations.

James (Ja87) has reported that the conversion to dose can be related directly to radon concentrations indoors. The reason is that for a constant level of radon the potential alpha energy, WL, increases as the concentration of room aerosols increases. However, the availability of condensation nuclei reduces the unattached fraction, f_p. These compensating factors tend to dampen variations in the dose conversion factor for a given concentration of radon gas. These concepts should be carefully evaluated in future studies.

The epidemiologic evidence of an association between indoor radon exposure and lung cancer in the general population is persuasive but by no means definitive. Twenty-one papers, published in the general literature,

have been summarized in this report. In addition, the results of five unpublished studies have been summarized.

Two general types of epidemiologic studies are represented in this body of literature: ecological and case-control. Ecological studies may have an inherent systematic bias towards showing no association between lung cancer and indoor radon due to the effect of population migration. A second source of bias in such studies may involve secondary characteristics of geographic regions studied which may either dilute or enhance an apparent association. Due to the inherent problems with interpretation of ecological studies they can be weighted less heavily than case-control studies in the assessment of the strength of the evidence for a causative role of radon daughter exposure in lung cancer etiology.

The majority of the case-control studies relied on surrogate measures of radon daughter exposure. However, at least these measures were determined on an individual home basis. The studies are so diverse in design and execution that the data cannot be pooled or combined in order to increase the statistical significance. However, each of the published studies can be treated as an independent trial to test the hypothesis of an association between radon and lung cancer.

Six of the seven published case-control studies have indicated a relative risk or odds ratio greater than one. If there is no association between indoor radon and lung cancer and there is no systematic bias among the studies, it can be assumed that there would be a 50% chance of finding a positive association (relative risk or odds ratio greater than one) and a 50% chance of finding a negative association. Using the binomial probability distribution, the probability of six of seven such studies

showing a positive association if, in fact, none exists, is approximately 0.06. This analysis depends on the assumption that the results of the published studies represent a random sample from a binomial population of results of all possible studies. The question of bias in publication of studies could invalidate this analysis.

The studies in progress are generally of case-control design and will use actual radon measurements. Several also have common design features. Collectively, they have the potential to show an association between indoor radon exposure and lung cancer which would withstand a more rigorous statistical analysis if such an association truly exists. It is much more difficult to provide definitive evidence that an association does not exist if, in fact, this is the case.

Even under the best circumstances, the exposure data from studies in progress may not be sufficiently refined to allow for development of risk models and risk coefficients independent of the information already obtained from studies of underground miners. It is likely that the studies in progress will provide a means for validating the adaptation of risk models derived from miner data to non-occupational exposures among the general population.

INTRODUCTION

Inhalation of radon gas was the first situation in which radiation was implicated as a cause for cancer. The problem can be traced back for more than 400 years. In the sixteenth century an unusual fatal disease was occurring among underground miners in Bohemia. About 100 years ago this disease was diagnosed as lung cancer and at that time about 50% of the miners in the region died from lung cancer.

Around 1924 it was suggested that the high rate of lung cancer may be attributed to elevated concentrations of the radioactive noble gas, radon. In many ways it was difficult to reconcile the fact that an insoluble gas could be responsible for the disease. However, in 1950 it was recognized that the true cause of high absorbed doses to the lung was inhalation of the short lived radioactive descendants (daughters) of radon which are initially created by the decay of radon in air.

It has recently become evident that this same mechanism could be responsible for the induction of lung cancer in the general public. Measurements of radon in dwellings indicate that 20-60% of the dose commitment from natural background radiation is due to radon. It is generally more pronounced in regions where dwellings must be closed and insulated to protect the occupants from the weather.

Over the past several years, energy conservation has developed into a popular and patriotic theme. One of the easier ways to accomplish this is to increase the insulation in houses and reduce ventilation. This could result in elevated levels of toxic gases, including radon, and increase

the incidence of fatal lung cancers. Thus, an apparent cost effective means for conserving energy could actually be unacceptably expensive in terms of lives lost or life shortening. Approaches to resolving this dilemma will depend on an understanding of the true risk for induction of lung cancer from inhalation of radon daughters.

The objective of this report is to summarize state of the art methodologies for deriving risk estimates from this environmental pathway. It also includes an evaluation of the uncertainties of each method and suggestions for improving the risk-estimation process. The report is divided into the following major sections:

- DOSIMETRY
- EPIDEMIOLOGY
- RISK MODELS

Sections on dosimetry and epidemiology are included since each discipline has contributed to the derivation of risk models employed to assess public health detriment due to indoor radon exposure.

Current risk models are based on epidemiologic data from underground miners. The intent of this report is to summarize the epidemiologic data available from indoor radon studies and investigate its usefulness as a basis for estimating risk coefficients or validating those derived from miner data. In addition, studies in progress are summarized and their potential contribution to quantitative risk estimation discussed.

The section describing epidemiologic risk models is included simply to enhance the usefulness of this report. No attempt was made to evaluate the merits and deficiencies of each of the models.

A summary that includes results from all three major topics is presented and followed by a condensed list of conclusions.

DOSIMETRY

INTRODUCTION

Risk estimates for the induction of lung cancer from occupational exposure to the short-lived descendents of radon (daughters) have been derived primarily from epidemiological studies of underground uranium miners. The risks are related to the total accumulated exposure to potential alpha energy of radon daughters in air (J h m^{-3} or WLM; see Appendix A for a description of quantities and units). However, there are large uncertainties in this method since the exposure for most miners has been reconstructed from estimations of the concentration of radon daughters underground. Nevertheless, there is a basis for confidence in the risk estimate for accumulated exposures down to 100 WLM (Th85).

Classically, the response of biological systems to ionizing radiation is related to the absorbed dose received by the tissue or cells of interest. Since many organs appear to have different sensitivities to radiation, weighting factors have been proposed to accommodate the variation in the appearance of late stochastic effects (ICRP77). There is, therefore, a strong precedent to apply a similar methodology for describing the induction of lung cancer by the inhalation of radioactive aerosols such as the short-lived descendants of radon.

It has not been possible to measure the absorbed dose to lung tissue from inhalation of radon daughters; it must be calculated using models which simulate the sequence of events leading to energy deposition. This

requires a quantitative description of the physiological properties of the respiratory system as well as the physical and chemical properties of the inhaled aerosol.

Cancer of the respiratory tract is one of the most common forms of fatal cancer in industrialized countries. Exposure to radon daughters in domestic environments may be an important factor for induction of this disease in the general public (USEPA86). Controversy arises since an estimate of the rate of incidence is derived by combining concentration measurements in dwellings with risk factors obtained from underground mines (ICRP87).

It has been proposed that principles of radiation dosimetry might be capable of resolving this dilemma. This requires a hybrid procedure whereby the occupational exposure is converted into absorbed dose in the lung using aerosol characteristics and breathing patterns in mines. The incidence of lung cancer in miners is then related to dose rather than exposure. These risk factors would then be applied to dose estimates computed for the general public based on aerosols and breathing patterns in domestic environments.

The following sections describe the underlying principles of the dose models and methods for adapting these to environmental and occupational situations.

DOSIMETRIC MODELS

There have been a number of attempts to model the absorbed dose to the lung and portions of the respiratory track from inhalation of radon daughters. These have been reviewed and summarized by the National Council

on Radiation Protection and Measurement (NCRP84) and James (Ja87). Many of the later calculations incorporated methods or concepts from previous works. This report will focus on three recent models which were developed by Harley (Ha72, NCRP84, Ha86), Jacobi (Ja80, OECD83) and James (Ja87, Ja86, Ja84).

Each model includes three basic components: deposition, clearance and energy absorption. There are subcategories within each that control the result of the calculation. The assumptions employed by each model are summarized in Table 1. The objective is to identify which parameters have the greatest influence on calculations of absorbed dose and the implications of converting from occupational to environmental conditions.

DEPOSITION

All models assumed that the air flow in the lower airways is laminar. For unattached and attached daughters, diffusion is the dominant mechanism, and expressions exist which compute the deposition due to this process (Go49, In75). For the upper respiratory track, turbulence can exist and the deposition may be enhanced by this secondary flow. When the aerodynamic median diameter (AMD) or geometric standard deviation (σ_g) of the attached aerosols becomes large, deposition can also increase due to gravitational settling and inertial impaction.

The Jacobi model assumes diffusion based on laminar flow and enhanced deposition in the upper airways based on experiments using a plastic dichotomous symmetrical branching device. Harley also assumes that laminar diffusion is the only mechanism with enhanced deposition in the

Table 1. Comparison of Dosimetric Models

Category	James	Jacobi	Harley
Lung Morphometry	Yeh & Schum Weibel A UCI	Weibel A	Yeh & Schum
Bronchial Deposition	Laminar Diffusion + Impaction + Sedimentation	Laminar Diffusion + Turbulent Enhancement in Upper Airways	Laminar Diffusion + Turbulent Enhancement in Upper Airways
Nasal Deposition:			
Unattached	50%	50%	60%
Attached	0%	4%	2%
Clearance:			
Mucociliary Transport	Model constrained to keep mucus thickness constant	Model based on mucus velocity in trachea in TB region	Mucus production constant over surface of TB region
Solubility	10% $T_{1/2}$ = 15 min 30% $T_{1/2}$ = 10 h	Attached $T_{1/2}$ = 10 h Unattached $T_{1/2}$ = 15 min	Neglected
Location of Activity	Distributed in mucus and mucosa	Uniformly distributed in 15μm layer of mucus	Uniformly distributed in 15μm layer of mucus
Sensitive Cells	All stem cells in bronchial epithelium at each generation	Basal cells distributed at variable depth at each generation	Basal cells located 22μm below mucus layer in segmented bronchi
Dose	Dose averaged over all cells in epithelium and over all bronchial generations	Dose to basal cells averaged over generations 2-15	Dose to shallow basal cells in bronchial generations 2-4

Table 1. Comparison of Dosimetric Models

Category	James	Jacobi	Harley
Breathing Rate:			
Occupational	1.2 m^3h^{-1}	1.2 m^3h^{-1}	1.1 m^3h^{-1}
Residential	0.75 m^3h^{-1}	0.75 m^3h^{-1}	1.1 m^3h^{-1} Active (67%) 0.54 m^3h^{-1} Resting (33%)
Aerosol Characteristics:			
Size:			
Unattached	0.001μm	Diff. Coef. = 0.054 $cm^2\ s^{-1}$	Diff. Coef. = 0.0025 $cm^2\ s^{-1}$
Attached			
Occupational	AMD = 0.2μm	AMD = 0.2μm	AMD = 0.17μm
Residential	AMD = 0.1μm	AMD = 0.15μm	AMD = 0.12μm
Unattached Fraction			
Occupational	f_p = 0.03	f_p = 0.025	f_p = 0.01 [1/0.6/0.3/0.2]
Residential	f_p = 0.05	f_p = 0.03 (ICRP50)	f_p = 0.017 [1/0.9/0.6/0.4]
Dose Conversion [mGy/WLM]			
Occupational	6.3 + 180 f_p	4.6 + 35 f_p	3.6
Residential	10 + 140 f_p	5.3 + 15 f_p	4.2
Scale Factors:			
Breathing Rate	$\bar{D}_B \propto [BR]^{1/2}$		
Age Dependence	Insignificant	$\frac{\bar{D}\ \text{Ages 0-10}}{\bar{D}\ \text{Adult}} = 1.5$	

upper airways determined using casts prepared from autopsy specimens of the human bronchial tree.

The James model uses diffusion equations for laminar flow without turbulent enhancement in the upper airways. His justification is based on results of deposition using ventilated pig lungs. The model does however include gravitational sedimentation and inertial impaction for larger particles.

LUNG MORPHOMETRY

The geometrical configuration and size of the respiratory system influences deposition of aerosols. Most models initially used airway dimensions described by the Wiebel A dichotomous model (Wi63). It gives the diameter and length of bronchial airways and assumes that airways at each level of branching are identical. Jacobi uses this description exclusively.

Extensive measurements of airway size were reported by Yeh and Schum (Ye80). They prepared a replica cast by injecting silicone rubber into a lung in situ in the thorax of a human cadaver. This procedure preserved the in vivo shape of the lung but gave rise to enlargement of some airways. Harley has adopted a scaled down version of the Yeh-Schur model that corresponds to the normal functional residual capacity of an adult.

More recently Phalen has reported measurements of airway sizes from replica casts of twenty lungs (Ph85). They derived regression formulae to give the variation of airway diameter and length as a function of age. James uses the average of all three lung models since "there is no overriding reason to prefer a particular model" (Ja87).

CLEARANCE

In the bronchial region, the aerosols are deposited on the surface of the mucus. They move from this location either by mucociliary clearance toward the throat or absorption through the epithelium and elimination into the blood stream.

In the pulmonary region the daughters are deposited on a thin surface fluid in close proximity to the blood capillaries. For short-lived radon daughters this clearance mechanism can be neglected since the dissolution time is longer than the physical half lives.

The model of Harley assumes that both attached and unattached daughters are insoluble and are cleared by mucociliary transport only. Jacobi assumes that in addition to mucociliary transport attached daughters have a solubility characterized by a 10 hour half-time while the unattached daughters are transferred through the epithelium with a half-time of 15 min.

James has developed a compartmentalized model for clearance where 60% of the radon daughters are insoluble, 10% have a rapid clearance through the mucosa with a half-time of 15 min. and 30% enter a compartment of protracted retention with a half-time of 10 hours. He does not distinguish between attached and unattached daughters.

The mucociliary transport velocities are similar for all models with values ranging from ~10 mm min^{-1} in the trachea to ~0.01 mm min^{-1} in generation 14.

LOCATION OF RADIOACTIVITY

The location of the radioactivity on the walls of the airways following deposition is critical to dosimetry since the range of the alpha particles is similar to the dimensions of the material surrounding the cells. Harley and Jocobi assumed that the activity is uniformly distributed in the mucus layer which is 15μm thick. James assumes deposition in a thin layer of mucus gel only 7μm thick and that the activity penetrates through the mucous and enters the mucosa containing the epithelium, basement membrane and lamina propria. He assumes a concentration gradient which falls to zero at the base of the mucosa where blood capillaries are found and that the epithelium occupies the top half of this mucosal layer.

LOCATION OF TARGET CELLS

Lung cancers observed in uranium miners are primarily bronchial in origin and usually localized in the first few generations of the bronchial tree. It is generally assumed that the target cells are undifferentiated stem cells located in the bronchial epithelium.

Harley identifies the targets as basal cells attached to the basement membrane of the epithelium. Her model assigns a fixed depth for these cells at 22μm below the mucus-epithelium interface for generations 1-9 and 10μm after the ninth generation. However, the model focuses upon the dose to these shallow basal cells in the segmented bronchi, specifically generation 4.

Jacobi also assumes that the targets are basal cells of the bronchial epithelium. However, his model uses a distribution of depths below the base of the cilia which decreases as the generation number increases. The

model computes the dose to basal cells at a mean depth for each generation and then averages over generation 2-14 to derive a single value for the bronchial region.

James postulates that the radiosensitive cells responsible for the induction of lung cancer are distributed throughout the bronchial airways. He assumes that these cells are not restricted to basal cells attached to the basement membrane, but extend over the entire thickness of the epithelium. Thus, the dose is computed to all cells in the epithelium which has a thickness determined by measurements of clinical biopsy specimens made by Gastineau (Ga69). The final result is the mean dose to all epithelial cells in each generation and averaged over all generations.

DISCUSSION

In any theoretical exercise such as this it is important to recognize the difference between postulates which are axiomatically true without need for proof and assumptions which are educated guesses. Unfortunately, there are precious few axioms in radiation biology.

The conjecture that lung cancer is directly related to average energy deposited per unit mass is a clear example of this. Harley states that the underlying risk factor for radon daughter induced lung cancer "ought" to be the alpha dose to target cells (Ha84). The OECD states that an increased risk of bronchogenic cancer is the "expected" consequence of absorbed dose in bronchial tissues (OECD83). The NCRP takes a firmer stance saying that absorbed dose to cells in the epithelium of the upper

airways in the tracheobronchial tree "is" the significant dose for cancer induction (NCRP84). These are at best intelligent speculations.

A popular description of carcinogenesis is that radiation is responsible for initiation of the disease which remains dormant until acted upon by one or more promoters (We83). There have been several studies of oncogenic transformation of mammalian cells in vitro. Lloyd et al. reported no excess transformation in mouse embryo fibroblasts for doses less than 20 rad when irradiated with α particles having a LET of 85 KeV/μm (Ll79). Robertson et al. shows an excess transformation frequency in mouse fibroblasts of $2x10^{-4}$ per irradiated cell at 25 rad using alpha particles with a mean LET of 150 KeV/μm (Ro83). Hieber et al. obtained a transformation frequency of $1.6x10^{-4}$ per irradiated cell for an α dose of 25 rad (Hi87). They also report that the effect is not dependent on dose rate down to 200 mrad/min.

A linear interpolation of this data yields the transformation frequency at low doses of ~ $1x10^{-5}$/rad cell. Similar experiments with human epithelial cells have not been successful in generating enough transformation to obtain an estimate of the frequency at low doses. However, since the mouse cell lines already have one damaged locus, it might be necessary to have two independent events to produce a transformation in normal cells (i.e. $[1x10^{-5}] \times [1x10^{-5}] = 1x10^{-10}$ transformation/rad. cell).

The approximate number of basal cells at risk in bronchial generations 2-4 is ~ $5x10^5$ (airway area = 5 cm^2; 1 basal cell/1000μm^2). An indoor exposure to 4 pCi ℓ^{-1} (0.02 WL; 0.8 WLM a^{-1}; 0.5 rad WLM^{-1}) for 50 years yields ~ 10^{-3} oncogenic transformation. This example is flawed

for many reasons; however if each transformation develops into a cancer, the risk estimate is similar to that obtained by other methods. It illustrates the importance of understanding the transformation process in order to assign reliable risk factors to absorbed energy.

Therefore, risk estimates from dosimetric considerations must include the human experience. At this time the most complete information comes from cancer incidence in underground uranium mines. Dosimetry cannot include carcinogenic co-factors such as diesel fumes and dust, but on the other hand houses are not necessarily as pure as one would like to believe (Ga85). Thus, it is recommended that dosimetry should focus upon scaling factors that reflect both the physical properties of the aerosols in each environment and the physiological factors associated with respiration, deposition and clearance.

Quality factors are used to account for the relative biological effectiveness of different types of radiations. In general, the exposure rates from external gamma rays in domestic environments are low and can be neglected. Gamma exposure rates in underground mines are higher than houses, but there is a large uncertainty in the exposure to the population of miners currently used to obtain risk estimates. Most probably the accumulated gamma dose to the lung was only a small fraction of the alpha dose from inhaled radon daughters.

Weighting factors have been derived by the ICRP to adjust for differences in the sensitivity of organs with regard to the development of cancer following an absorbed dose of ionizing radiation (ICRP77). This has been extended to include separate weighting factors for the pulmonary and bronchial regions of the lung (OECD83, ICRP81). Since the toxic agent

is alpha particles from radon daughters and the biological end point is strictly bronchogenic cancer, it is not necessary to include these adjustments.

The concepts of microdosimetry can be used to obtain information concerning mechanisms on the subcellular level. These could ultimately lead to an improved understanding of the initiation processes associated with carcinogenic transformation. At present this experimental methodology is restricted primarily to invitro investigations.

Since the objective is to derive risks for the general public based on exposure of uranium miners, absorbed dose is a sufficient basis of comparison. The subcellular mechanisms of radiation action and macroscopic weighting factors for dose equivalent are similar for both groups and do not need to be included. The models should be restricted to physical and physiological properties which can be verified with measurements whenever possible.

TARGET CELLS

There is a general consensus that transformed stem cells or their differentiated progeny do not migrate large distances within the respiratory system. Since most of the observed primary tumors are located in the upper regions of the bronchial tree, that is where the dose should be calculated. Combining the dose to basal cells over all generations (2-14) does not produce a large effect compared to considering only generations 2-4. However, the dose is increased if the deposited activity migrates below the mucus into the epithelium according to the James model.

DEPOSITION

It is reasonable to assume that there is some turbulence in the upper airways. Cohen (Co86) reports a larger deposition correction factor in the trachea than previously suggested by Jacobi (Ja80). By not using correction factors the deposition is shifted toward lower generations which increases the dose to the segmental bronchi.

Increasing the breathing rate will increase the intake of radon daughters. However, there is a corresponding increase in flow rate in the bronchial tree which decreases the fractional deposition. Although these two effects are not completely compensating the effect on dose is small and James suggests a scaling factor depending on the square root of the breathing rate.

The most important factor controlling deposition is nose vs. mouth breathing. Miners are generally involved in light to heavy activity which could result in intermittent or continuous mouth breathing. A large fraction of the exposure in indoor environments occurs when people are sleeping and therefore nose breathing. The nasal passage is an effective filter for unattached daughters which preferentially deposit in the first few generations of the tracheobronchial tree. This factor must be understood to effectively compare absorbed dose in the two environments.

CLEARANCE

Changes in the rate of mucociliary clearance do not have a large effect on absorbed dose. Assumptions about solubility and transfer into the blood make an appreciable change in absorbed dose to epithelial cells. Jacobi assumes a rather high solubility and correspondingly short half

life in the mucus which tends to lower the dose to epithelial cells. Harley concludes that the effects of the clearance mechanism are small, and the James model is somewhere in between these two extremes.

AGE

It is important to recognize that indoor exposure is not limited to healthy middle-aged males. Children spend large amounts of time indoors especially in the winter months. The OECD reports that the dose to the tracheobronchial tree is about a factor of 1.5 higher for children than adults (OECD83). James concludes that the mean bronchial dose is only marginally increased in young children and can be regarded as insignificant (Ja87). Hofmann has computed age dependent modifying factors for alpha dose rates to the respiratory track (Ho79). He obtains values of 1.9 for infants with a maximum value of 2.4 at age 6.

The uncertainty is a result of assumptions on the thickness of the mucus layer and epithelium in children. This issue needs to be resolved along with determinations of nose vs. mouth breathing for the general public.

AEROSOL CHARACTERISTICS

Unattached

All of the unattached daughters that penetrate the nasal passage will be deposited in the tracheobronchial tree. There is some difference of opinion as to the size distribution of these particles. The Harley model uses a diffusion coefficient of 0.0025 cm^2/s corresponding to a particle

size of 0.005μm (Kn83). Jacobi and James use a diffusion coefficient of 0.054 corresponding to a particle size of 0.001μm.

The nasal passage will filter out 40-60 percent of the unattached radon daughters independent of size range between 1 and 5 nm. However, the smaller particles will have an increased deposition in the trachea and thus a smaller fraction will be available for deposition in the following generations. This size effect is, however, not large and does not appreciably alter the dose conversion factor for unattached radon daughters.

The major factor is not so much the size of the unattached particles, but the quantity. All dose models are sensitive to f_p, the fraction of potential alpha energy which is unattached. Although only 3 to 5% of the potential alpha energies is unattached it accounts for up to 50% of the absorbed dose to the bronchial epithelium. Measurements of this quantity are essential for comparing mine and residential atmospheres.

Attached

Radon daughters attached to condensation nuclei or other aerosols are responsible for the largest contribution to potential alpha energy. However, they are not aerodynamically suitable for efficient deposition in the upper airways of the human respiratory tract. In general less than 2% of these particles are filtered by the nasal passage and about 5-10% are deposited in the tracheobronchial region.

Deposition in the first few generations depends on the aerodynamic diameter of the carrier aerosols. Underground mines are dusty and can have high concentrations of fumes from internal combustion engines. Measurements indicate an AMD ranging from 0.1 - 0.3μm in mines.

Atmospheric conditions in dwellings tend to produce smaller aerosols: measurements range from 0.03 - 0.1μm. The AMD can change rapidly depending on the activities of the occupants.

Deposition by diffusion increases in the upper airways as the AMD of the attached aerosol decreases. However, as particles become larger or the distribution broader (i.e., σ_g large) there is an increase in deposition due to impaction. The models do not specifically address deposition at bifurcations which can be enhanced (Ma72, Co87).

Harley indicates that the dose conversion factor can be a factor of 4 higher for aerosols having an AMD of 0.03μm compared to an AMD of 0.12μm (Ha86). It has also been mentioned that aerosols might grow after entering the humid airways of the respiratory tract. This would decrease deposition in the tracheobronchial region.

The type and concentrations of condensation nuclei can also affect the mixture of suspended radon daughters. However, changes in the daughter ratios do not have a large influence on the dose conversion factors based on potential alpha energy.

EPIDEMIOLOGY

Exposure to radon daughters has been generally accepted as a causative factor in the observed excess risk of lung cancer among underground miners. Epidemiologic studies spanning three decades have been reported in the literature with relatively good agreement among them as to risk coefficients (Th85). The data are continually being updated and reanalyzed as the follow-up period for miners increases.

Due to basic differences between miners and members of the general public in terms of lung morphometry, breathing patterns and the aerosol characteristics of their environment, the applicability of the miner derived risk coefficients to the general public has been questioned. As described in the previous section, dosimetric analyses have been used to adjust the coefficients. However, validation of the dosimetric models using epidemiologic data is at least desirable if not essential.

Since it is generally accepted that radon daughters cause lung cancer, the concern of indoor radon epidemiology need not be to prove the causal relationship. The objectives should be to determine if the risk is significant under the conditions and levels associated with residential exposure and to develop or validate risk coefficients.

SUMMARY OF CURRENTLY AVAILABLE EPIDEMIOLOGIC DATA

The emphasis on energy conservation during the previous decade led to a concern about radon daughter exposures in residences. As a consequence, a significant role in the etiology of lung cancer in the general

population has been proposed for this agent. From 5,000 to 20,000 lung cancer deaths per year are postulated due to radon daughter exposure from indoor radon (USEPA86). However, much of the epidemiologic data with regard to non-occupational radon daughter exposures has only recently been published and at this time the information is still relatively sparse. Summaries of the individual studies published in the open literature to date are given in Appendix B.

There are some studies which have been completed but are as yet unpublished. Summaries of unpublished studies are given in Appendix C. In addition to the unpublished completed studies, some preliminary results are available from pilot studies and studies in progress. Where this information has been published in the open literature it is included in Appendix B.

The information in the appendices is organized to give a brief summary of each study with regard to basic method and results. Very few of the studies are quantitative with respect to radon or radon daughter exposure. All of the studies which include quantitative data suffer from a lack of statistical power due to low numbers of lung cancers included. The studies are too varied in design, type of surrogate for radon daughter exposure used, method and type of data collection and reporting, and control for confounding variables to allow for pooling of results by any reasonable statistical method for the purpose of examining exposure-response quantitatively. This is unfortunate since, collectively, they provide persuasive evidence of an etiologic role of indoor radon in lung cancer in the general population.

No estimate of risk coefficients can be made on the basis of these studies taken together. However, several individual studies provided enough information on which to base an estimate of risk coefficients. These estimates are noted in the appendices.

The judgment as to whether excess risk of lung cancer due to indoor radon exposure is demonstrated by a study depends on the magnitude of the point estimate of relative or absolute risk, the reliability of the data, the degree to which confounding variables were taken into account and the statistical significance of the results. In each appendix, the statement of whether excess risk was demonstrated by each study is the opinion of the authors of this report and is based on the above mentioned considerations. The conclusions of the investigator are also explicitly stated. In most cases the investigators for the individual studies used conservative statistical requirements (i.e. 95% confidence limits) in postulating an effect of indoor radon on lung cancer risk. Since the objective of this report is to look more generally at the evidence, an element of judgment was used in deciding whether an excess risk was demonstrated. As stated previously, the methodological variations among the studies precluded any statistical pooling of the data to obtain results with greater statistical significance.

Some of the studies listed in the appendices were more general than others and covered cancers other than lung cancer and risk factors other than indoor radon. The appendices include only those results pertinent to lung cancer risk from indoor radon. Table 2 is a brief summary of all of the published studies.

Table 2. Overall Summary of Results of Published Studies with Regard to Indoor Radon and Lung Cancer

Author (date)	Results	Approx. Range Rn Daughter Concentration (WL)	Approximate Relative Risk	Estimated Risk Coefficient
CASE CONTROL STUDIES				
Axelson (Ax79)	++	na	1.8-5.4	na
Ouimette (Ou83)	0	na	1.2	na
Pershagen (Pe84)	+/0	na	na	na
Edling (Ed84, Ed86)	++	0.011-0.046	1.2-5.1	5-7 E-6 per PY-WLM
Damber (Da86)	+	na	1.4-2.0	na
Lees (Lee87)	+	na	1.4-2.4	na
Svensson (Sv87)	++	na	2.2	na
ECOLOGICAL STUDIES				
Bean (Be82)*	++	na	1.3-1.7	na
Dousset (Do85)	0	na	na	na
Forastiere (Fo85)	+/0	na	1.2	na
Hofmann (Ho85, Ho86)	0	0.2-0.4 WLM/a	na	na
Archer (Ar87)	++	na	na	na
Fleischer (Fl81)	++	na	na	na
Edling (Ed82)	++	na	na	na
Hess (He83)	++	na	na	na
Letourneau (Let83)	0	na	na	na
Fleischer (Fl86)	++	na	na	na
Walter (Wa86)	0	na	na	na
Stranden (Str86, Str87)	++	na	na	RR coeff. 0.003-0.009 per WLM
Castren (Ca87))	0	na	na	na
OTHER				
Simpson (Si83)	0	na	na	na

++ — Significant positive association
+ — Positive association not significant
0 — No association
+/0 — Equivocal
na — Not Applicable

* The surrogate for indoor radon used in this study, radium concentration in water, has not been correlated with indoor radon.

In general, epidemiologic studies are considered "positive" only if they show a statistically significant effect. Studies which show an increased risk of disease which is not statistically significant are considered "inconclusive". However, such studies should not be considered "negative" as that term implies a finding of no effect. For that reason, the term "positive" as used in the context of Table 2 indicates only that the study showed an increased risk of lung cancer with increased indoor radon concentration, or its surrogate, as indicated by a point estimate of the relative risk greater than 1.0 or a positive correlation.

ROLE OF INDOOR RADON IN LUNG CANCER ETIOLOGY

By itself, no single published or unpublished study reviewed provides definitive or even persuasive evidence of an association between indoor radon exposure and lung cancer. However, taken collectively, they constitute persuasive evidence of such an association. In Table 2, nearly all of the case-control studies show an effect of indoor radon exposure on the measure of lung cancer risk even though in only three studies were the effects statistically significant. One study that showed no effect was a part of a general study of cancer in Mesa County, Colorado, and involved homes contaminated with mill tailings (Ou83). Any effect of indoor radon exposure would have been masked by the presence of large numbers of retired uranium miners. Among the case-control studies, it should be noted that only two (Ed84, Lee87) used actual radon measurements. The other case-control studies relied on surrogate measures.

Results of the ecological or geographic studies are equivocal with little more than half of the studies showing a significant positive

association between radon daughter exposure and lung cancer incidence or death rates. In some of these studies, migration may have played a large role in exposure misclassification which diluted the observed effect of indoor radon. In other studies, the statistical power was just not great enough to have shown an effect even if it did exist.

As noted previously, all but two of the case-control investigations used surrogate measures for radon daughter exposure such as area geology, housing characteristics or background gamma radiation. Such surrogate measures are not a good substitute for real data. However, it is interesting to note that studies using independent measures show a similar association between lung cancer and the exposure surrogate. Surrogate measures used in these epidemiologic studies are, presumably, independent factors which may be associated with indoor radon concentration.

In assessing the strength of the evidence for a true association between indoor radon and lung cancer, it is essential to consider the potential for systematic bias among the studies. A possible source of such bias is the tendency for positive studies to be submitted and accepted for publication, whereas negative or inconclusive results are often considered uninteresting and never published. No other systematic bias among the case-control studies is apparent.

Retrospective or case-control epidemiologic studies can show an association of a particular agent with a specific disease state but do not necessarily establish causation. However causation can be inferred from epidemiologic studies on the basis of a set of criteria which historically has been applied for this purpose (Sc82). These criteria are by no means intended to be a "checklist". Under some conditions, such as low levels

of association, they may be irrelevant. However, such criteria can provide a systematic basis for examining causal inference, which is "at best tentative and still a subjective process" (Ro86).

1. Temporal Sequence — In order for causation to be inferred, the temporal sequence of the exposure and the disease must be reasonable. Basically, that is, the period of exposure must precede the onset of the disease. In the case of lung cancer and radon daughter exposure, the latent period must also be taken into account. The designs of all of the studies reported in Appendices B and C are in accordance with this criterion. However, the relatively long latent period for lung cancer (> 5 yr) and the difficulty of estimating past exposure levels from current measurement data inject a degree of uncertainty in this regard.

2. Consistency — The association must be observed under a variety of conditions. Repetition in epidemiologic studies by different researchers using various populations provides support for this criterion. As with the temporal sequence, the epidemiologic studies summarized in Table 2, for the most part, show the same effect even though the magnitude of the effect cannot be compared among the studies. The majority of the studies showed an association between lung cancer and indoor

radon (or its surrogate) even though, in some cases, that association was not statistically significant at the 95% confidence level. In general, the studies showing no effect were "ecological" studies which are subject to exposure misclassification that tends to bias results towards the null or have very low statistical power. Animal studies and epidemiologic studies of uranium miners consistently show a causal association between radon daughter exposure and lung cancer.

3. Strength of Association — The greater the magnitude of the observed effect the more likely it is to be causative. This is not always the case as an observed association may be due to a second factor which is the true cause. The observed association would then depend on the magnitude of the effect of the true causative agent. In the case of the indoor radon studies, the strength of the association is variable and is obviously dependent on the indoor radon daughter concentrations for the populations studied.

4. Biological Gradient — An obvious dose-response effect is good evidence of causation. Several of the indoor radon studies showed an exposure-response effect (Ed84, Lee87). However, the majority of the studies used surrogate measures of indoor radon daughter exposure so

an exposure-response demonstration was often not appropriate. At low levels of exposure, the exposure-response may be difficult to discern. Therefore, lack of an exposure-response gradient should not be considered as evidence against a causal association.

5. Specificity of Effect — The issue of specificity of effect is a questionable criterion in the case of radiation induced cancer. This criterion is met if the factor (radon daughter exposure) always produces the same effect (lung cancer) and if the effect disappears when the factor is removed. Obviously the etiology of cancer in general and lung cancer in particular is complex and this criterion cannot be met. Therefore, it is reasonable to conclude that specificity would strongly support a causative inference but that lack of specificity should not be a reason for concluding that an exposure is not causative in the presence of other evidence or conformity with the other criteria.

6. Biological Plausibility — The effect should be a logical consequence of the exposure in terms of what is known about biological processes and the results of collateral studies. This criterion is often ignored in the assertions of causation with regard to radiation exposure. However, in the case of indoor radon, the studies of

occupational exposure to radon daughters and animal research support the inference of causation. There is little doubt that radon daughter exposure causes an increased risk of lung cancer in miners. The major question with regard to indoor radon exposures is whether that effect occurs at much lower levels of exposure, i.e. is there an effective threshold.

ESTIMATED RISK COEFFICIENTS

While it may be concluded from the epidemiologic data available that indoor radon exposure is a causative factor for lung cancer, the magnitude of the effect (risk coefficient) is very much in question. Only two of the published studies provided sufficient information with which to estimate risk coefficients and even in those instances many assumptions had to be made with regard to occupancy, equilibrium fractions, and other critical factors (Ed86, Str86). It is interesting to note that considering the inherent problems in making these estimations, the estimated risk coefficients from these two studies were within the range of the risk coefficients determined for underground miners.

CONFOUNDING VARIABLES

In almost all of the studies described in Appendix B the investigators tried to take into account confounding variables to the extent possible. In order to be considered a confounding variable the factor must be associated with both the disease and the exposure of interest but not directly caused by the exposure. Confounding variables

must be taken into account in any epidemiologic study. Other variables which are known to be associated with the disease but not the exposure need not necessarily be taken into account as they may be assumed to be randomly distributed among all groups if there is no bias in selection of study subjects. Some of the variables potentially confounding in both published studies and studies in progress are tobacco use, diet (vitamin A consumption), socioeconomic status, occupational exposures, and urban vs. rural environment.

Socioeconomic Status

Socioeconomic status is known to be associated with lung cancer, that is, the risk is greater with low socioeconomic status (Wy77). This may be a function of the prevalence of cigarette smoking and other factors affecting health status. Socioeconomic status may also influence indoor radon exposure through housing characteristics such as living in an apartment versus single family dwelling, degree of home insulation, type of construction materials and method of heating and/or air conditioning. In addition, the exposure and consequent dose to individuals in lower socioeconomic classes may be affected by the proportion of time spent outdoors as well as breathing characteristics associated with manual labor.

Smoking

Cigarette smoking is the most common variable accounted for in these indoor radon studies. However, in many studies this was not possible. This would not be a major problem if smoking were not a true confounder, that is associated with both indoor radon concentration and lung cancer.

Smoking is unquestionably associated with lung cancer (Wy83). Smoking may directly influence the dose to the lung from indoor radon exposure due to many factors including airborne particulate concentration affecting the unattached fraction and the effect of smoking on the thickness of the mucus lining the upper respiratory tract and to a lesser extent the clearance rate. It also may be associated with indoor radon concentration through a common association with socioeconomic status. Lung cancer risk is inversely associated with socioeconomic status (Wy77). Indoor radon may also be associated with socioeconomic status through housing characteristics as described previously. In one situation, smoking, low socioeconomic status increases the risk; in the other, indoor radon concentration, low socioeconomic status may tend to decrease the risk due to the higher probability of living in an apartment building or an older, less energy efficient home. None of the published studies referenced had enough data to contribute to an understanding of the relationship between smoking risk and radon risk. The question of whether an additive relationship exists or the effect is multiplicative for non-occupational exposure to radon daughters is not adequately addressed by the published studies.

Diet

None of the published studies took into account the role of diet in lung cancer risk. Dietary Vitamin A has been suggested to reduce the risk of lung cancer (Si84). As with smoking, diet is associated with socioeconomic status and thus may be a confounding variable.

Ambient air quality

There has been some suggestion that outdoor air pollution has an etiologic role in lung cancer (Ve82). Since air quality is related to the urban characteristic of an area, living in an urban area may increase the risk of lung cancer from outdoor air pollution. However, an urban-rural gradient in indoor radon concentrations has been indicated with rural homes having higher concentrations than urban homes (Co87a). In addition, urban dwellers are more likely to live in apartments above the ground floor also indicating lower average indoor radon concentrations. Therefore, as with socioeconomic status, urban air pollution could tend to weaken any observed effect of radon.

Other variables which have been associated with lung cancer may be considered in future studies. The number of confounding variables included in an analysis will affect the statistical power, therefore, for greatest efficiency without sacrificing accuracy, that number should be kept as low as reasonable.

ECOLOGICAL STUDIES

Many of the published studies are "ecological" studies. That is, the assignment of exposure status is based on local conditions as opposed to individual measures. Geographic or "ecological" studies lack sensitivity and can lead to erroneous results due to what is known as the "ecological fallacy." The "ecological fallacy" is a well known problem in epidemiologic studies which compare community disease rates with mean community levels of the exposure of interest. The communities may differ in many ways other than just the factor being studied. A difference in

community disease rates may be attributed to the exposure of interest when, in fact, it is actually due to one or more of the other factors.

Another major problem with this type of study when it is applied to a disease with a long latent period such as lung cancer is the effect of migration. In such studies, finding no effect of indoor radon on lung cancer risk is not good evidence that indeed there is no real effect. Studies of this type which do show a statistically significant effect are likely to underestimate the risk (Po80).

The greater the rate of migration, the more bias that is introduced into geographic studies. Using as large an area as practical for the geographic unit reduces the source of bias; however, when too large an area is used exposure misclassification is more likely. Knowledge of migration rates for the geographic unit can be used to estimate the effect of this factor.

In general, ecological studies are less likely to show a statistically significant effect of a geographically related exposure when one truly exists than case-control studies which use an individual measure of exposure. Therefore, it is not surprising that the case-control studies consistently show an association between indoor radon and lung cancer whereas the ecological studies are equivocal. Case-control studies can be subject to the same bias towards the null when inadequate measures of exposure are used, i.e. recent exposures as opposed to effective lifetime exposure.

STUDIES IN PROGRESS

The concern with the potential effects of radon daughter exposure from indoor radon on the general population and the inadequacy of the currently available data have emphasized the need for new research projects. While a review of the studies in progress cannot add to our present knowledge with regard to radon risk coefficients, it can give us an estimate of the potential for improving those coefficients on the basis of epidemiology. Studies in progress are summarized in Appendix D. These studies are generally funded by state and federal agencies. Depending on how the studies are designed, the information derived from them has the potential to enhance the ability to make reasonable risk estimates or to validate the risk estimates derived from the underground miner data.

Several of the studies in progress have similar characteristics and, in contrast to previously published studies, the data may be ammenable to pooling by statistical methodology. This is an advantage derived from communication among investigators in the field and direction from some funding agencies with regard to study design.

The results of most of these studies should be available within the next four to five years. Until that time, however, risk estimates for presentation to the general public must be based on the risk coefficients derived from occupational exposure studies with appropriate adjustment for the factors which affect the dosimetry.

Since studies of uranium miners have established a causative role of radon daughter exposure for lung cancer, the major benefit which can be derived from these studies is a better understanding of the quantitative

risk coefficients. Therefore, it is essential that careful assessment be made of the exposures of all study subjects.

STATISTICAL POWER OF STUDIES IN PROGRESS

In order to assess the potential of studies in progress with regard to improving the current risk coefficients, it is necessary to examine their statistical power (i.e. the probability of finding a statistically significant effect if, in fact, one exists).

The a priori determination of sensitivity or statistical power of an epidemiologic study is an important consideration in study design. Several of the studies in progress involve relatively small case and control numbers (<500) due to the relative rarity of lung cancer and the constraints of geographic area. It is useful to know in advance if these studies have the potential to show a statistically significant effect of indoor radon exposure when one truly exists. This a priori determination of statistical power should not be confused with the determination of statistical significance of a completed study. Studies which do not have great statistical power (<0.80) may still show a statistically significant effect.

All but two of the investigations in progress are case-control studies. The simplest form of this type of epidemiologic study compares the fraction of cases exposed to the factor of interest to the fraction of controls exposed using a dichotomous exposure classification. The statistical power calculation requires estimates of the relative risk and the fraction of the control population exposed. For indoor radon the relative risk can be estimated from the relative risk coefficients derived from the

underground miner studies and the mean radon daughter exposures for the "exposed" and "unexposed" classification. The fraction of controls exposed can be estimated on the basis of indoor radon concentration distributions measured on a random basis.

In order to make a generic estimate of statistical power for case-control studies, the following assumptions are made and are illustrated in Table 3:

a. The distribution of residential radon concentrations in the populations under study is represented by the random measurements made by Dr. B. Cohen, University of Pittsburgh Radon Project, as reported by J. Stolwijk (Sto87), and shown in the first two columns of Table 3.

b. The designation of "exposed" vs "unexposed" is based on either a 2 pCi ℓ^{-1} (columns 3 and 4) or 4 pCi ℓ^{-1} (columns 5 and 6) cutoff. Since it is unlikely that many individuals remain in the same residence for a lifetime, a weighted mean radon concentration was calculated for the "exposed" population based on 15 years of residence in the high radon concentration residence and 35 years of residence at the average radon concentration for the "unexposed" population.

c. The excess lifetime relative risk from exposure to radon daughters is 1% to 4% per WLM lifetime exposure.

The weighted mean lifetime residential radon concentration for "exposed" individuals with a 2 pCi ℓ^{-1} cutoff is 3.4 pCi ℓ^{-1}. The weighted mean concentration for the measurements greater than 2 pCi ℓ^{-1} is 9.1 pCi ℓ^{-1}. Therefore, the weighted mean lifetime concentration for the exposed population, assuming 15 years residence at the mean concentration

Table 3. Distribution of Indoor Radon Concentrations in U.S. Population Adjusted for 4 pCi ℓ^{-1} and 2 pCi ℓ^{-1} Exposure Cutoff Points

Original Data		2 pCi ℓ^{-1} Cutoff		4 pCi ℓ^{-1} Cutoff	
Frac. Pop.	Rn Conc. pCi ℓ^{-1}	Frac. Pop.	Rn Conc. pCi ℓ^{-1}	Frac. Pop.	Rn Conc. pCi ℓ^{-1}
0.05	0.1	0.05	0.1	0.05	0.1
0.10	0.3	0.10	0.3	0.10	0.3
0.10	0.5	0.10	0.5	0.10	0.5
0.20	0.8	0.20	0.8	0.20	0.8
0.20	1.4	0.20	1.4	0.20	1.4
0.20	3.2	0.10	1.8*	0.20	3.2
0.10	6.2	0.10	3.2	0.05	3.6*
		0.10	6.2	0.05	6.2
0.03	15.0	0.03	15.0	0.03	15.0
0.0125	32.0	0.0125	32.0	0.0125	32.0
0.005	48.0	0.005	48.0	0.005	48.0
0.0025	100.0	0.0025	100.0	0.0025	100.0
Mean = 3.1		Mean unexp. = 0.9		Mean unexp. = 1.5	
		Wtd. mean exp. = 3.4**		Wtd. mean exp. = 5.8**	
		Frac. exp. = 0.25		Fract. exp. = 0.10	

* Partitioned on the basis of a log-normal plot of the data.

** Assuming 15 years exposure at concentrations greater than the cutoff and 35 years exposure at mean concentrations for unexposed.

greater than the 2 pCi ℓ^{-1} cutoff and 35 years residence at the mean concentration lower than the 2 pCi ℓ^{-1} cutoff is as follows:

$$[(15y)\ (9.1\ pCi\ \ell^{-1}) + (35)\ (0.9\ pCi\ \ell^{-1})] / [50y] = 3.4\ pCi\ \ell^{-1}$$

For a 4 pCi ℓ^{-1} cutoff the mean lifetime residential radon concentration is 5.8 pCi ℓ^{-1}. The mean radon concentrations for "unexposed" individuals with a 2 pCi ℓ^{-1} cutoff is 0.9 pCi ℓ^{-1}, with a 4 pCi ℓ^{-1} cutoff, 1.5 pCi ℓ^{-1}. The percent of population exposed with a 2 pCi ℓ^{-1} cutoff is 25%, and for a 4 pCi ℓ^{-1} cutoff, 10%.

The estimated relative risks with a specified risk coefficient and exposure cutoff points are shown in Table 4.

The number of cases required (assuming an equal number of controls) for a given level of statistical significance (α) and power ($1-\beta$) can be calculated from the following equation (Sc74).

$$N = (Z_\alpha \sqrt{2u(1-u)} + Z_\beta \sqrt{f(1-f) + p_3q_3)^2}/(f-p_3)^2$$

where:

f = fraction exposed among controls

R = relative risk

p_3 = probability of exposure among cases

$q_3 = 1-p_3$

$u = 0.5f\ 1+R/(1+f(R-1))$

$p_3 = fR/(1+f(R-1))$

α = 0.05 (one sided)

β = 0.10 or 0.20

Z_α = standard normal deviate = 1.645 for α = 0.05 (one-sided)

Z_β = standard normal deviate = 1.28 or 0.824 for β = 0.10 and β = 0.20

Table 4. Estimated Relative Risk for Various Cutoff Concentrations and Risk Coefficients

Relative Risk Coefficient (%/WLM)	Exposure Cutoff (pCi ℓ^{-1})	Estimated Relative Risk
1	2	1.24
2	2	1.48
3	2	1.72
4	2	1.96
1	4	1.42
2	4	1.84
3	4	2.26
4	4	2.68

Sample Calculation:

Lifetime excess exposure at 2 pCi ℓ^{-1} cutoff:

$$(3.4 \text{ pCi } \ell^{-1} - 0.9 \text{ pCi } \ell^{-1}) = 2.5 \text{ pCi } \ell^{-1}$$

$$\frac{(2.5 \text{ pCi } \ell^{-1})(0.5)(8760 \text{ hr/a})(0.75)(50\text{a})}{(100 \text{ pCi } \ell^{-1}\text{-WL})(170 \text{ hr/a})} = 24 \text{ WLM}$$

Relative risk:

$$R = 1 + (0.01)(24) = 1.24$$

$$\text{Equilibrium factor} = \frac{\text{WL}}{[\frac{\text{pCi } \ell^{-1}}{100}]} = 0.5 \quad \text{(See Appendix A)}$$

Fraction of time spent indoors = 0.75

The calculated numbers of cases required for a given statistical power are shown in Table 5.

These calculations represent the simplest, ideal condition with well defined exposure and no confounding variables. This is not generally the case in real epidemiologic investigations. Smoking or other factors potentially associated with both lung cancer and indoor radon concentrations would reduce the theoretical power of the study as would uncertainty in exposure. In addition, the assumptions regarding mean exposure for "exposed" and "unexposed" are arbitrary and may not be a true reflection of exposure distribution for individual studies. Therefore, the estimated numbers of cases required represent a lower limit.

Several of the proposed studies will use more than one control per case, increasing the statistical power. Most of the studies planned or in progress will have more than 300 cases. Therefore, they have a fair chance of showing an association between lung cancer and indoor radon concentrations if the random measurements taken by Cohen and used in this analysis are representative of the areas in which the studies take place and if the current relative risk coefficients (USEPA86) are realistic. For areas where exposures are higher, the statistical power could be greater.

The statistical power of each of the studies in progress depends on the conditions in the geographic areas, migration patterns and the extent of stratification into appropriate subgroups and must be calculated on an individual basis as several of the researchers have done. The generic calculation gives a crude indication of the potential of these studies in general to produce statistically significant results.

Table 5. Calculated Number of Cases Required for p = 0.05 Level of Statistical Significance and Statistical Power 0.80 or 0.90

Exposure Cutoff (pCi ℓ^{-1})	Relative Risk Coefficient (%/WLM)	R	f	p_3	N (1-β)=0.90	N (1-β)=0.80
2	1	1.24	0.25	0.29	1900	1400
2	2	1.48	0.25	0.33	550	400
2	3	1.72	0.25	0.36	280	200
2	4	1.96	0.25	0.40	180	130
4	1	1.42	0.10	0.14	1400	980
4	2	1.84	0.10	0.17	410	290
4	3	2.26	0.10	0.23	210	150
4	4	2.68	0.10	0.23	140	100

R = estimated relative risk

f = fraction of controls exposed

p_3 = fraction of cases exposed

N = number of cases required assuming equal numbers of controls

Several of the studies in progress have sufficient similarities to allow for eventual pooling of the data which may result in greater statistical power and the potential for some quantitative determination of exposure-response. The studies already published do not provide sufficient basis for such an analysis but do suggest a positive association between indoor radon and lung cancer. Therefore, the main contribution of the studies in progress will be to quantify the exposure-response relationship if pooling of the data from several of the studies can be accomplished. Most do not have enough cases to allow for such refined analyses on an individual basis.

RISK MODELS

The data from studies of lung cancer in underground miners have been used to develop various risk models. At the present time these models are the basis for the projected risk to the general population from exposure to radon daughters. As noted in the section on dosimetry, the risk coefficients derived from these models may need adjustment to account for differences between miners and members of the general population as well as differences between the mine atmosphere and residential environments. However, the basic forms of the models are applicable to either situation. The risk models are summarized in this report simply to add to its usefulness. No analysis or discussion of the relative merits or deficiencies of each type of model is included.

Three basic types of models have been used to predict the risk of radon induced lung cancer in the presence of other risk factors: absolute, additive, and multiplicative or proportionate hazards models.

Absolute risk model

$$\lambda_{rx}(t) = \lambda_x(t) + \beta W$$

where:

$\lambda_{rx}(t)$ = lung cancer risk at age t with specific risk factors x and radon, r.

$\lambda_x(t)$ = age specific lung cancer risk with no excess radon daughter exposure

β = risk coefficient for radon daughter exposure

W = cumulative radon daughter exposure

The absolute risk model assumes the risk of lung cancer from radon daughter exposure is independent of both the baseline cancer risk and all other risk factors.

Additive risk model

$$\lambda_{rx}(t) = \lambda_o(t)\ (1 + \beta W + \gamma X)$$

where:

$\lambda_o(t)$ = baseline age specific lung cancer risk with no excess radon daughter exposure or exposure to other risk factors

X = risk factors other than radon daughter exposure such as smoking

Y = risk coefficients for other risk factors

The additive risk model assumes that the radon daughter induced lung cancer risk is dependent on the baseline or age dependent lung cancer risk but independent of all other risk factors.

Proportionate hazards model

The proportionate hazards model predicts the risk of indoor radon as a function of the baseline risk and all other lung cancer risk factors.

$$\lambda_{rx}(t) = \lambda_o(t)\, e^{(\beta W + \gamma X)}$$

This equation represents the general form of the proportionate hazards model. The exponential or log-linear form is commonly used in epidemiology. However, the exponential function can be replaced by any other function such that the risk function is equal to 1 when all exposures or all risk coefficients are zero. The linear multiplicative model is the form of the proportionate hazards model most commonly used in radon risk estimation.

$$\lambda_{rx}(t) = \lambda_o(t)\,(1 + \beta W)\,(1 + \gamma X)$$

The proportionate hazards models, including the multiplicative risk model, take into account interaction between radon daughter exposure and other risk factors.

The most commonly used models for projecting the impact of indoor radon on public health are applications of these basic forms. Some examples are as follows.

BEIR III (BEIR80)

The BEIR III risk estimates are based on an age dependent absolute risk model. That is, the risk coefficient is a function of the age at diagnosis for lung cancer: 10 per million person-years-WLM for ages 35-49, 20 per million person-years-WLM for ages 50-65, and 50 per million person-years-WLM for ages over 65. The term person-years refers to the population and period at risk following exposure. No interaction with smoking or other risk factors is assumed for these risk coefficients. BEIR III is equivocal, stating that if the lung cancer risk after radiation is consistent with a multiplicative effect of radiation on smoking induced lung cancer, then the excess risk for smokers would be increased by about 50% and decreased by a factor of six for nonsmokers. BEIR III states that a purely multiplicative relationship between lung cancer risks for smoking and radiation is unlikely.

NCRP 78 (NCRP84)

The basic risk model used in NCRP 78 is a modification of the absolute risk model

$$A(t|t_o) = RC\ P(t|t_o)\ e^{-k(t-to)}$$

where:

$A(t|t_o)$ = attributable annual tumor rate at age t from one WLM exposure at time t_o

RC = absolute risk coefficient

$P(t|t_o)$ = probability that an individual who survives to age t_o will be alive at age t.

k = rate of risk expression due to cell death, repair or other mechanism

An absolute risk coefficient of 10 per million person-years per WLM was used in the NCRP 73 risk calculations.

This model does not take into account any interaction with other risk factors such as smoking, but does correct for survival and latent period. When used to calculate risk from chronic exposure the model takes into account a five year latent period. In contrast to the ICRP50, BEIR III and EPA models, the NCRP78 model accounts for reduction in risk over time, due to cell death or repair, with a 20 year half-time. In their analysis of the U.S. miner data, Hornung and Meinhardt (Ho87) found a decrease in risk per WLM with time outside the mine. Thomas and McNeill (Th85) reported an initial increase in relative risk coefficient vs. time since first exposure, followed by a decrease.

EPA (EPA85)

$$\lambda_{rx}(t) = \lambda_x(t)\ (1 + \beta W)$$

This is a simple linear multiplicative risk model. The relative risk coefficient is assumed to be between 1% and 4% per WLM.

ICRP 50 (ICRP87)

ICRP 50 gives a proportionate hazards model (linear multiplicative) to express risk of lung cancer from chronic exposure to radon daughters. The multiplicative risk model can be represented as follows:

$$\lambda Sr(t) = \lambda_o(t)\ (1 + S(t))\ (1 \pm \bar{r}\ E\ (t-T))$$

where:

$\lambda Sr\ (t)$ = the risk of lung cancer with radon exposure and smoking status at age t

$\lambda_o(t)$ = the baseline lung cancer risk at age t

$S(t)$ = the risk factor for smoking at age t

$\bar{r}$ = the mean relative risk coefficient for exposure to radon daughters

E = the mean annual exposure to radon daughters

T = latent period for expression of lung cancer following exposure

The estimated relative risk coefficients for radon daughter exposure are 0.019/WLM for exposure to radon daughters up to age 20, and 0.0064/WLM for exposures at ages greater than 20. These coefficients were derived from uranium miner risk coefficients adjusted for various factors such as breathing rate and the presence of other carcinogenic factors in the mine environment.

BEIR IV

The BEIR IV (NAS 88) model is a proportionate hazards (multiplicative) model with an adjustment for age at risk and time since exposure (TSE).

$$\lambda_{rx}(t) = \lambda_x(t)[1 + 0.025\gamma(t)(W_1 + 0.5\ W_2)]$$

(The symbols have been changd to be consistent with those used for previously defined models in this report.)

$\lambda_{rx}(t)$ = lung cancer mortality rate from all causes

$\lambda_x(t)$ = age specific background lung cancer mortality rate (all causes except radon)

$\gamma(t)$ = age specific adjustment to radon risk coefficient

$\gamma(t) = 1.2$ for $t < 55$ years

$\gamma(t) = 1.0$ for $t = 55 - 64$ years

$\gamma(t) = 0.4$ for $t > 64$ years

W_1 = cumulative exposure incurred between 5 and 15 years before age t

W_2 = cumulative exposure incurred 15 years or more before age t

This model weights exposures received more than 15 years in the past by a factor of 0.5 to account for the decrease in risk per WLM observed in miners with time out of the mine or time since first exposure (Ho87, Th85). The authors of the BEIR IV report avoided speculation regarding the biological reasons for the decrease citing a need for further clinical and laboratory investigations.

The age specific risk coefficient takes into account the observed decrease in excess relative risk with age at which the risk is evaluated.

Table 6 shows a comparison of estimated lifetime risk of lung cancer from indoor radon exposure at the presumed U.S. average (1 pCi ℓ^{-1}) and the EPA guideline (4 pCi ℓ^{-1}) calculated on the basis of each of the models. The risk calculations are shown in Appendix E.

Several models have been developed on the basis of the U.S. miner data. Whittemore and McMillan (Wh83) concluded that a multiplicative linear model fit the data better than an additive model and that combining the additive and multiplicative models did not improve the fit of the data. Hornung and Meinhardt (Ho87) used an exponential proportionate hazards model and a power function model. The power function model appeared to provide the best fit to the data.

In both cases only the U.S. miner data was used. A large fraction of this cohort of miners is still living. There is some suggestion that with

Table 6. Comparison of Estimated Lifetime Excess Lung Cancer Risk Due to Indoor Radon Exposure

Mean Indoor Radon Concentration	Smoking Status	Lifetime Excess Risk (%)				
		MODEL				
		BEIR III	NCRP	ICRP	EPA	BEIR IV
1 pCi ℓ^{-1}	Never Smoked	1	0.2	0.1	0.1-0.3	0.1
	Ex-smoker	1	0.2	0.2	0.2-0.5	0.3
	Chronic Smoker (1 pack/day)	1	0.2	0.4	0.4-1	1
4 pCi ℓ^{-1}	Never Smoked	4	0.7	0.3	0.3-1	0.5
	Ex-smoker	4	0.7	0.7	0.7-2	1
	Chronic Smoker	4	0.7	2	2-5	5

increased follow-up, the data will show closer correspondence to an additive risk model (Ar87b).

The principal cause of lung cancer in the general population is cigarette smoking and it is generally the major factor taken into consideration when the risks due to indoor radon are projected. Tobacco smoke is traditionally treated as a single variable. However, tobacco smoke contains a variety of known or suspected carcinogens including Po-210 (PHS82). It is likely that some components have a multiplicative interaction with radon daughter exposure and others such as the Po-210 an additive relationship. Therefore, it may be assumed that the interaction of tobacco smoke with radon daughters is a complex function, neither strictly additive nor strictly multiplicative. A model that is intermediate between additive and multiplicative might better represent the true condition.

Whittemore and McMillan (Wh83) compared a mixture model with the linear multiplicative risk model and found that it was not a significant improvement when the U.S. miner data were examined. However, this may have been a result of too short a follow-up period in this cohort. Some other miner studies with longer follow-up show a risk relationship best represented by the additive model.

The indoor radon epidemiologic data published to date is inadequate to test the fit of these models to non-occupational exposures. Therefore, at this time, the risk model which best fits the miner data may have to be used to project risk of non-occupational exposure.

CONCLUSIONS

A review of the dosimetric models and the existing epidemiologic studies with regard to lung cancer and indoor radon exposure leads to the following conclusions:

Dosimetric analyses that take into account differences between underground miners and members of the general public, in terms of lung morphometry, breathing patterns and environmental aerosol characteristics, indicate that the dose per unit exposure to radon daughters may be marginally higher for nonoccupational exposures than for miners. Therefore, there is no apparent rationale for redefining the Working Level (WL) for indoor radon exposure simply on the basis of the reduced volume of air inhaled per unit time.

The uncertainty in applying risk estimates derived from studies of underground miners to the general public may be reduced by determining the fraction of the time persons inhale through the nose vs. the mouth, the physical characteristics of residential aerosols which would influence the unattached fraction, and the relationship between lung cancer risk and age at exposure.

The results of epidemiologic studies dealing with indoor radon provide persuasive evidence of an association between lung cancer and residential radon exposure. However, these data are not sufficient to allow derivation of quantitative risk estimates specific for

indoor radon or validation of risk estimates derived from underground miner data.

Epidemiologic research in progress may provide a basis for revision or validation of current risk models and coefficients. This is feasible only if the individual investigations employ designs which allow for pooling of data to obtain greater statistical power than that possible for any single study.

REFERENCES

Ar87a Archer, V. E. Association of lung cancer mortality with precambrian granite. Arch. Env. Health 42:87-91; 1987.

Ar87b Archer, V. E. University of Utah, Personal Communication, 1987.

Ax79 Axelson, O.; Edling, C.; Kling, H. Lung cancer and residency: A case-referrent study on the possible impact of exposure to radon and its daughters in dwellings. Scand. J. Work Environ. Health 5:10-15; 1979.

Be82 Bean, J. A.; Isacson, D.; Hohns, R. M. A.; Kohler, J. Drinking water and cancer incidences in Iowa: II. Radioactivity in drinking water. Am. J. Epidemiol. 116:924-932; 1982.

Ca87 Castren, O. Dealing with radon in dwellings. In: Proceedings of Second International Specialty Conference on Indoor Radon. New Jersey. Air Pollution Control Association; 1987.

Co87a Cohen, B. L. University of Pittsburgh. Paper presented at the 32nd Annual Health Physics Society Meeting, Salt Lake City, UT, July 9, 1987.

Co87 Cohen, B. S. Deposition of ultrafine particles in the human tracheobronchial tree. In: "Radon and its decay products." Hopke, P., ed.; Proceedings of the American Chemical Society; 1987.

Da86 Damber, L. Lung cancer in males: An epidemiologic study in northern Sweden with special regard to smoking and occupation. Umea University Medical Dissertations. New Series No. 167:113-125; 1986.

Do85 Dousset, M.; Jammet, H. Comparison de la mortalite par cancer dans le Limousin et le Poitou-Charentes. Radioprotection 20:61-67; 1985.

Ed82 Edling, C.; Comba, P.; Axelson, O.; Flodin, U. Effects of low-dose rate radiation — A correlation study. Scand. J. Work Environ. Health 8, Suppl. 1:59-64; 1982.

Ed84 Edling, C.; Kling, H.; Axelson, O. Radon in homes — a possible cause of lung cancer. Scand. J. Work Environ. Health 10:25-34; 1984.

Fl81 Fleischer, R. L. A possible association between lung cancer and phosphate mining and processing. Health Phys. 41:171-175; 1981.

Fl86 Fleischer, R. L. A possible association between lung cancer and a geological outcrop. Health Phys. 50:823-827; 1986.

Fo85 Forastiere, F.; Valesini, S.; Arco, M.; Magliola, M. E.; Michelozzi, P.; Tasco, C. Lung cancer and natural radiation in an Italian province. Sci. Total Environ. 45:519-526; 1985.

Ga72 Gastineau, R. M.; Walsh, P. J.; Underwood, N. Thickness of bronchial epithelium with relation to exposure to radon. Health Phys. 23:857; 1972.

Ga85 Gamage, R. B.; Kaye, S. V. Indoor Air and Human Health. Oak Ridge, TN:Lewis Publishing; 1985.

Go49 Cormley, P. G.; Kennedy, M. Diffusion from a stream flowing through a cylindrical tube. Proc. Irish Acad. Section A. 52:163; 1949.

Ha72 Harley, N. H.; Pasternack, B. S. Environmental radon daughter alpha dose factors in a five lobed human lung. Health Phys. 42:771-782; 1972.

Ha84 Harley, N. H. Comparing Radon Daughter Dose: Environmental Versus Underground Exposure. Radiation Prot. Dos. 7:371-375; 1984.

Ha86 Harley, N. H.; Cohen, B. S. Updating radon daughter bronchial dosimetry. In: "Radon and its decay products." Hopke, P., ed., Proceedings of the American Chemical Society, pp.419-429; 1986.

He83 Hess, C. T.; Weifenbach, C. V.; Norton, S. A. Environmental radon and cancer correlations in Maine. Health Phys. 45:339-348; 1983.

Hi87 Hieber, L.; Pansel, G.; Roos, H.; Fenn, S.; Fromke, E.; Kellerer, A. M. Absence of a dose-rate effect in the transformation of C3H 10T½ cells by α-rays. Institut für Medizinische Strahlenkunde; Universität Würzburg, Versbacher Strasse 5, D-8700 Würzburg, West Germany; 1987.

Ho79 Hofmann, W.; Steinhausler, F.; Pohl, E. Dose calculations for the respiratory track from inhaled natural radioactive nuclides as a function of age-I. Health Phys. 37:517-532; 1979.

Ho85 Hofmann, W.; Katz, R.; Zhang, C. Lung cancer incidence in a Chinese high background area — epidemiological results and theoretical interpretation. Sci. Total Environ. 45:527-534; 1985.

Ho86 Hofmann, W.; Katz, R.; Zhang, C. Lung cancer risk at low doses of alpha particles. Health Phys. 51:457-468; 1986.

Ho87 Hornung, R. W.; Meinhardt, T. J. Quantitative risk assessment of lung cancer in U.S. uranium miners. Health Phys. 52:417-430; 1987.

ICRP77 International Commission on Radiological Protection. Recommendations of the ICRP; Report No. 26; Oxford, England:Pergamon Press; 1977.

ICRP81 International Commission on Radiological Protection. Limits for Inhalation of Radon Daughters by Workers; Report No. 32; Oxford, England:Pergamon Press, 1981.

ICRP87 International Commission on Radiological Protection. Lung cancer risk from indoor exposures to radon daughters. New York:Pergamon Press; 1987.

In75 Ingham, D. B. Diffusion of aerosols from a stream flowing through a cylindrical tube. Aerosol Sci. 6:125; 1975.

Ja80 Jacobi, W.; Eisfeld, K. Dose to tissues and effective dose equivalent by inhalation of radon 222 and radon 220 and their short lived daughters. GSF-Report-S-626; Munich, Neuherberg, West Germany; 1980.

Ja84 James, A. C. Dosimetric Assessment of Risk From Exposure to Radioactivity in Mine Air. Occupational Radiation Safety in Mining; Stocker, H., ed., Canadian Nuclear Association, 111 Elizabeth Street, Toronto, Ontario, Canada, pp. 415-427; 1984.

Ja86 James, A. C. A reconsideration of cells at risk and other key factors in radon daughter dosimetry. In: "Radon and its decay products." Hopke, P., ed , Proceedings of the American Chemical Society, pp. 400-418; 1986.

Ja87 James, A. C. Lung dosimetry for radon and thoron daughters: A review and reassessment with emphasis on domestic exposure. In: Nazaroff, W. W. and Nero, A. V., eds.; "Radon and Its Progeny in Indoor Air;" New York:Wiley Interscience; 1987.

Kn83 Knutson, E. O.; George, A. C. Koh, B. R. Radon daughter plateau II, Prediction model. Health Phys. 45:445-452; 1983.

La85 Lanctot, E. M. Radon in the domestic environment and its relationship to cancer: An epidemiologic study. Master's Thesis, State University of New York at Stony Brook. Maine Geological Survey, Dept. of Conservation Publication 85-88; 1985.

La82 Lanes, S. F. Lung cancer and environmental radon exposures: A case-control study. Doctoral Dissertation, University of Pittsburgh; 1982.

Le87 Lees, R. E. M.; Steele, R.; Roberts, J. H. A case-control study of lung cancer relative to domestic radon exposure. Int. J. Epid. 16:7-12; 1987.

Le83 Letourneau, E. G.; Mao, Y.; McGreggor, R. G.; Semenciw, R.; Smith, M. H.; Wigle, D. T. Lung cancer mortality and indoor radon concentrations in 18 Canadian cities. In: Epidemiology Applied to Health Physics. Proceedings of the Sixteenth Midyear Topical Meeting of the Health Physics Society, Albuquerque, NM; 1983.

Ll79 Lloyd, E. D.; Gemmell, M. A.; Henning, C. B.; Gemmell, D. S.; Zabransky, J. B. Transformation of mammalian cells by alpha particles. Int. J. Radiat. Biol. 36.:467-478; 1979.

Ma72 Martin, D.; Jacobi, W. Diffusion deposition of small sized particles in the bronchial tree. Health Phys. 23:23-29; 1972.

NAS80 National Academy of Sciences, Committee on the Biological Effects of Ionizing Radiations. The effects on populations of exposure to low levels of ionizing radiation. Washington DC:National Academy Press; 1980.

NAS88 National Academy of Sciences, Committee on the Biological Effects of Ionizing Radiations. Health risks of radon and other internally deposited alpha emitters. Washington DC:National Academy Press; 1988.

NCRP84 National Council on Radiation Protection and Measurements. NCRP Report No. 78: Evaluation of occupational and environmental exposures to radon and radon daughters in the United States. Bethesda, MD:NCRP; 1984.

Ne86 Nero, A. V.; Schwehor M. B.; Nazaroff, W. W.; Revzan, K. L. Distribution of Airborn Radon-222 Concentrations in U. S. Homes, Science 234:992-997; 1986.

OBr86 O'Brien, T. R.; Decoufle, P.; Rhodes, P. R. Selected cancer mortality in Florida counties where radium water levels exceed the EPA limit. Report to Florida Department of Health and Rehabilitative Services; 1986.

OECD83 Organization for Economic Cooperation and Development. Dosimetry aspects of exposure to radon and thoron daughter products. Report by a Group of Experts; OECD, 2 rue Andre Pascal, 75775 Paris, Cedex 16, France; 1983.

Ou83 Ouimette, D.; Ferguson, S. W.; Zoglo, D.; Murphey, S.; Alley, S.; Bohler, S. An epidemiologic study of selected malignant neoplasms in Mesa County, Colorado, 1970-1979. Final Report. Denver CO:Colorado Department of Health; 1983.

Pa85 Phalen, R. F.; Oldham, M. J.; Beaucage, C. B.; Crocker, T. T.; Mortensen, J. D. Postnatal enlargement of human tracheobronchial airways and implication for particle deposition. Anat. Rec. 212:368; 1985.

Pe84 Pershagen, G.; Damber, L.; Falk, R. Exposure to radon in dwellings and lung cancer: A pilot study. In: Proceedings of the Third International Conference on Indoor Air Quality and Climate, Vol. 2. Stockholm, Sweeden, 73-78; 1984.

Po80 Pollsar, L. The effect of migration on comparison of disease rates in geographic studies in the United States. Am. J. Epidemiol. 111:175-182; 1980.

Ro83 Robertson, J. B.; Koehler, A.; George, J.; Little, J. B. Oncogenic transformation of mouse BALB/3T3 cells by Pu-238 alpha particles. Radiat. Res. 96:261-274; 1983.

Ro86 Rothman, K. J. Modern Epidemiology. Boston: Little, Brown and Company; 1986.

Sc74 Schlesselman, J. J. Sample size requirements in cohort and case-control studies of disease. Am. J. Epidemiol. 99:381-384; 1974.

Sc82 Schlesselman, J. J. Case-control studies: Design, conduct, analysis. Second printing. New York:Oxford University Press; 1982.

Si84 Siegler, R. G.; Mason T. J.; Stemhagen, A.; Hoover, R.; Schoenberg, J. B.; Gridley, G.; Virgo, P. W.; Altman, R.; Fraumeni, J. F. Jr. Dietary carotene and vitamin A and risk of lung cancer among white men in New Jersey. J.N.C.I. 73:1429-1435; 1984.

Si83 Simpson, S. G.; Comstock, G. W. Lung cancer and housing characteristics. Arch. Environ. Health 38:248-251; 1983.

Str86 Stranden, E. Radon in Norwegian dwellings and the feasibility of epidemiologic studies. Radiat. Environ. Biophys. 25:37-42; 1986.

Str87 Stranden, E. Radon-222 in Norwegian dwellings. In: Hopke, P. K., ed. Radon and Its Decay Products: Occurrence, properties, and health effects. ACS Symposium Series 331:70-893; 1987.

Sto87 Stolwijk, J. A. J. Yale University, Testimony before Subcommittee on Environmental Protection, Senate Committee on Environment and Public Works, April 24, 1987.

Sv87 Svensson, C.; Eklung, G.; Pershagen, G. Indoor exposures to radon from the ground and bronchial cancer in women. Intl. Arch. Occup. Environ. Health 59:123-131; 1987.

Th85 Thomas, D. C.; McNeill, KK. G.; Dougherty, C. Estimates of lifetime lung cancer risks resulting from Rn progeny exposure. Health Phys. 49:825-846; 1985.

USEPA78 U.S. Environmental Protection Agency. Indoor radon exposure due to Radium-226 in Florida Phosphate Lands. EPA 520/4-78-013; 1978.

USEPA86 U.S. Environmental Protection Agency. A Citizens Guide to Radon. OPA-86-004; 1986.

USPHS82 U.S. Public Health Service. The health consequences of smoking. Cancer: A report of the Surgeon General. Rockville MD:USHPS; 1982.

Ve82 Vena, J. E. Air pollution as a risk factor in lung cancer. Am. J. Epidemiol. 116:42-56; 1982.

Wa86 Walter, S. D.; Meigs, J. W.; Heston, J. F. The relationship of cancer incidence to terrestrial radiation and population density in Connecticut 1935-1974. Am. J. Epidemiol. 123:1-14; 1986.

We63 Weibel, E. R. Morphometry of the Human Lung. Orlando, FL:Academic Press; 1963.

We83 Weinstein, I. B.; Horowitz, A.; Jeffery A. and Ivanovic, V. Cellular Events in Multistage Carcinogenesis, In Genes and Proteins in Oncogeneses (I. B. Weisstein and H. J. Vogel, eds). Acadmic Press: 99-110; 1983.

Wh83 Whittemore, A. S.; McMillan, A. Lung cancer mortality among U.S. uranium miners: A reappraisal. J. Natl. Cancer Inst. 71:489-499; 1983.

Wy83 Wynder, E. L.; Goodman, M. T. Smoking and lung cancer: Some unresolved issues. Epidemiologic Reviews 5:177-207; 1983.

Wy77 Wynder, E. L.; Stellman, S. D. Comparative epidemiology of tobacco-related cancers. Cancer Res. 37:4608-4622; 1977.

Ye80 Yeh, H. C.; Schum, G. M. Models of human lung airways and their application to inhaled particle deposition. Bull. Math. Bio. 42:461; 1980.

APPENDIX A

SPECIAL QUANTITIES AND UNITS

The concentration of radon gas in air is expressed in terms of radioactivity per unit volume. The most common quantities are pCi ℓ^{-1} and Bq m^{-3} where,

$$1 \text{ pCi } \ell^{-1} = 37 \text{ Bq} \cdot m^{-3}$$

When radon gas decays it initiates the appearance and eventual decay of the short-lived daughters, ^{218}Po, ^{214}Bi, ^{214}Pb and ^{214}Po. The health risk is directly associated with radon daughters that remain suspended in air and eventually inhaled.

Normally, the concentration of daughters is not expressed in terms of radioactivity per volume of air. This departure is based on the premise that once daughters are deposited in the respiratory system they remain there until the decay sequence of short-lived daughters is completed. The concept of potential alpha energy was developed to accommodate the principle. It is a measure of the total kinetic energy released by alpha particles for any mixture of radon daughters in air that proceeds through the entire serial decay sequence down to ^{210}Pb. Potential alpha energy is expressed in units of J m^{-3} or MeV ℓ^{-1}. A working level, WL, is defined as

$$WL = 1.3 \times 10^5 \text{ MeV } \ell^{-1} = 2.1 \times 10^{-5} \text{ J } m^{-3}$$

These seemingly peculiar numbers are obtained from the situation where all of the short-lived daughters are in radioactive equilibrium at 100 pCi ℓ^{-1}.

The concept of potential alpha energy does not require that the daughters have equal concentrations. Any mixture that yields 1.3×10^5 MeV ℓ^{-1} is equal to 1 WL. The concentration of radon gas does not provide a priori information on the concentration of potential alpha energy and vice versa. Independent measurements are required. However, it is frequently convenient to generalize or estimate one from the other. For this purpose the equilibrium factor (EF) is defined as the ratio of the potential alpha energy actually present to the value that would be present if the daughters were in radioactive equilibrium with the existing concentration of radon gas. For example

$$EF = \frac{WL}{\frac{Rn(pCi\ \ell^{-1})}{100}}$$

The potential alpha energy concentration of any mixture of radon daughters can also be expressed in terms of the equilibrium equivalent concentration (EEC). The EEC of a mixture of radon daughters in air is that activity concentration of ^{222}Rn in radioactive equilibrium with its short-lived daughters which has the same potential alpha energy concentration as the actual mixture.

The EEC can be expressed in terms of the equilibrium factor

$$EEC = EF \times C_{Rn}$$

where C_{Rn} is the activity concentration of radon gas.

The amount of alpha energy deposited in the lung is related to the potential alpha energy concentration and the duration of time that a person is

exposed to this concentration. This can be expressed as J m^{-3} h or Bq m^{-3} h when EEC is used to express the concentration of radon daughters.

A special quantity, the working level month (WLM), was defined for expressing occupational exposure to radon daughters. A working level month is equivalent to exposure at 1 working level for 170 hours (NCRP84). Although this was based on working schedules for miners it applies without modification to environmental or indoor exposures:

$$WLM = \frac{WL \times hr}{170}$$

The WLM should not be confused with a calendar month since exposure to 1 WL for 170 h is the same as 10 WL for 17 h or 0.2 WL for 850 h. Relationships to other quantities are as follows:

$$1 \text{ WLM} = 170 \text{ WL h}$$

$$1 \text{ WLM} = 3.5 \times 10^{-3} \text{ J m}^{-3} \text{ h}$$

$$1 \text{ WLM} = 6.3 \times 10^{5} \text{ Bq m}^{-3} \text{ h}$$

APPENDIX B

SUMMARY OF PUBLISHED STUDIES WITH REGARD TO INDOOR RADON DAUGHTER EXPOSURE AND LUNG CANCER RISK

The published epidemiologic studies involving non-occupational exposure to radon daughters are summarized in this appendix. Most studies listed involved several different analyses of the data including separate analyses for males and females and various levels of adjustment for confounding variables. The results given in this table generally represent the analyses with the greatest degree of adjustment for those factors. The analysis with the greatest degree of adjustment for confounding variables was used as the basis for determining whether a study indicated an excess risk of lung cancer with radon daughter exposure. That determination is the judgement of the authors of this report. In some cases the researcher used a more conservative standard for concluding whether an excess risk was demonstrated. The researcher's conclusions are also stated in such cases.

Author: Axelson

Publication date: 1979

Country: Sweden

Type of study: Case-control

Cases: 37 lung cancer cases from rural population greater than 40 years old

Controls: 178 from death register three positions before and after each case.

Control or adjustment for confounding variables: none

Determination of radon daughter exposure:
Surrogate - type of housing
wood, no basement - 0
stone with basement - 2
all others - 1

Results:

Exposure category	Odds ratio	90% confidence limits
0 vs 1+2	1.8	(0.99,3.2)
0 vs 2	5.4	(1.5, 19)

Etiologic fraction = 29%
Significant exposure-response trend ($p<0.05$)

Excess risk indicated: yes

Estimated risk coefficient: not applicable

Reference:
Axelson, O., Edling, C., Kling, H. Lung cancer and residency: A case-referrent study on the possible impact of exposure to radon and its daughters in dwellings. Scand. J. Work Environ. Health 5: 10-15; 1979.

Author: Ouimette

Publication date: 1983

Country: USA (Mesa County, Colorado)

Type of study: Case-control

Cases: All lung cancer cases - Mesa County, 1970-1979 - 273

Controls: Colon, stomach and pancreatic cancers occurring during the same time period - 275 controls

Control or adjustment for confounding variables:
Uranium mining history, smoking, sex, vital status, years of residence in Mesa County, age at diagnosis

Determination of radon daughter exposure:
Ever lived in Type A home (home contaminated with mill tailings)

Results: Lung cancer cases no different from controls with respect to residence in Type A homes
Crude odds ratio = 0.98
Adjusted odds ratio = 1.23 ($p = 0.66$)

Excess risk indicated: no

Estimated risk coefficient: not applicable

Reference:
Ouimette, D., Ferguson, S. W., Zoglo, D., Murphey, S., Alley, S., Bohler, S. An epidemiologic Study of Selected Malignant Neoplasms in Mesa County, Colorado, 1970-1979. Final Report; June 1983.

Author: Pershagen

Publication date: 1984

Country: Sweden

Type of study: Case-control (pilot studies)

Cases: Lung cancer cases among twins - 53
Lung cancer patients from northern Sweden - 30

Controls: Twins of lung cancer cases - 53
Unrelated controls from northern Sweden - 30

Control or adjustment for confounding variables: smoking

Determination of radon daughter exposure:
Lifetime residence histories obtained for cases and controls. Dwellings categorized by several factors: information on basement, building material, type of house, ventilation, year of construction. Radon level in each dwelling estimated on the basis of results from nationwide measurements.

Results: No difference in radon exposure for cases and controls in twin study for either smokers or non-smokers.
For the study of lung cancer in northern Sweden, cases who smoked showed significantly higher radon exposures than controls who smoked. No difference between non-smoking cases and controls.

Excess risk indicated: equivocal

Estimated risk coefficient: not applicable

Reference:
Pershagen, G., Damber, L., Falk, R. Exposure to radon in dwellings and lung cancer: A pilot study. In: Proceedings of the Third International Conference on Indoor Air Quality and Climate, Vol. 2. Stockholm, Sweden, 73-78; 1984.

Author: Edling

Publication date: 1984, 1986

Country: Sweden

Type of study: Case-control

Cases: Lung cancer deaths meeting specified criteria - 23 (22 controlled for smoking, 19 where actual radon measurement was used)

Controls: From death register - 202 (178 controlled for smoking, 159 where actual radon measurement used)

Control or adjustment for confounding variables: smoking, age, sex

Determination of radon daughter exposure:
Visual classification of house
0 - wood house without basement on normal ground
2 - wood house with basement on alum shale ground
stone, brick or plaster house with basement on any ground
1 - all others
Categorization by actual radon measurement - cellulose nitrate film

Results:
Adjusted for smoking - actual radon measurement

Exposure cat.	Odds ratio	(90% CL)	Mean Measured conc.	
0 vs 1+2	2.7	(1.1,6.4)	0	0.11 WL
0 vs 2	5.1	(1.4,18.5)	1	0.15 WL
0 vs 1	2.3	(0.9,5.9)	2	0.46 WL
			1+2	0.25 WL

Adjusted for smoking - visual calssification

0 vs 1+2	1.8	(0.9,3.9)
0 vs 2	3.5	(1.3,9.2)
0 vs 1	1.2	(0.5,3.0)

Significant exposure-response trend
Smoking mulltiplicative with radon

Excess risk indicated: yes

Estimated risk coefficient: 5 - 7/1E6 person-yrs-WLM for non-smokers

Reference:

Edling, C., Kling, H., Axelson, O. Radon in homes - a possible cause of lung cancer. Scand. J. Work Environ. Health 10: 25-34, 1984.

Edling, C., Wingren, G., Axelson, O. Quantification of lung cancer risk from radon daughter exposure in dwellings - an epidemiological approach. Env. Int. 12:55-60; 1986.

Author: Damber

Publication date: 1986

Country: Sweden

Type of study: Case-control (pilot)

Cases: Male lung cancer patients, 1972 - 1977, from the three northernmost counties - 604 cases

Controls: Deceased controls drawn from the National Registry matched for sex, year of death, age, and municipality; for cases born after 1900, a living control selected, matched for sex, year of birth and municipality

Control or adjustment for confounding variables:
Smoking, occupation

Determination of radon daughter exposure:
Surrogate - years of living in non-wooden house

Results:
No radon effect on lung cancer risk from smoking seen, implying no multiplicative effect
No significant difference in odds ratios after adjusting for smoking only

Results of analysis for persons without occupational risk after adjusting for smoking

Model I - Cases and matched deceased controls

Years in non-wooden houses	OR (95% CI)
1-20	1.36 (0.83,2.25)
>20	1.53 (0.75,3.24)

Model II - Cases born after 1900 and both living and deceased controls

1-20	1.46 (0.91,2.34)
>20	2.01 (1.01,4.03)

Excess risk indicated: yes (marginally significant for one analysis)

Estimated risk coefficient: not applicable

Reference:

Damber, L.: Lung cancer in males: An epidemiological study in northern Sweden with special regard to smoking and occupation. Umea University Medical Dissertations. New Series No. 167: 113-125; 1986.

Author: Lees

Publication date: 1987

Country: Canada (Port Hope, Ontario)

Type of study: Case-control

Cases: Lung cancer cases living in Port Hope 1969 - 1979, living in Port Hope at least 7 years prior to diagnosis - 27 cases

Controls: Two controls for each case; one deceased and one living for deceased cases, two living controls for living cases, matched on sex and date of birth - 49 controls

Control or adjustment for confounding variables: smoking, duration of residence in Port Hope

Determination of radon daughter exposure:
Prior radon or radon daughter measurement; estimated background radon daughter exposure subtracted, cumulative radon daughter exposure calculated for each subject

Results:
Conditional logistic regression analysis controlled for smoking:
OR = 2.36 (p = 0.057, one-sided) for exposed vs unexposed (CWLM - bkg = 0)
Not controlled for smoking:
OR = 1.55 (p = 0.19, one sided)
Radon daughter exposure treated as continuous variable with smoking controlled in analysis - positive correlation (p = 0.014)

Excess risk indicated: yes (Lees, et al considered the results inconclusive)

Estimated risk coefficient: not applicable

Reference:
Lees, R. E. M., Steele, R., Roberts, J. H. A case-control study of lung cancer relative to domestic radon exposure. Int. J. Epid. 16: 7-12; 1987.

Author: Svensson

Publication date: 1987

Country: Sweden (Stockholm)

Type of study: Case-control

Cases: Female unspecified epithelial lung cancers, principally small cell anaplastic and large cell, diagnosed between 1972 - 1980, 292 cases

Controls: Population based controls matched by year of birth and alive at the time of diagnosis of the case - 584

Control or adjustment for confounding variables: none

Determination of radon daughter exposure:
Radon + high radon geological type ground, ground level dwelling
Radon - above ground dwelling
10% of sample measured - all homes designated Radon +, and a random sample of 110 homes designated Radon -

Results:
For both matched and unmatched analyses RR = 2.2 (p = 0.01)
95% Confidence limits (1.2,4.0)

Excess risk indicated: yes

Estimated risk coefficient: not applicable

Reference:
Svensson, C., Eklung, G., Pershagen, G. Indoor exposure to radon from the ground and bronchial cancer in women. Int. Arch. Occup. Environ. Health 59: 123-131; 1987.

Author: Bean

Publication date: 1982

Country: USA (Iowa)

Type of study: Ecological

Exposed: High Ra-226 concentration in water, 2 categories

Unexposed: Low Ra-226 concentration in water

Method: Age adjusted cancer rates determined for 22 small municipalities (1000 - 10000) with wells >500 ft deep as sole public water supply. Counties divided into 3 groups according to Ra-226 concentration in water. Cancer rates compared for each group

Control or adjustment for confounding variables:
Smoking patterns for municipalities, median income, percent of manufacturing workers, percent of agricultural workers, fluoride levels in water.

Determination of radon daughter concentration:
Surrogate - Ra-226 concentration in water
(No correlation has been found between radium in water and radon in indoor air.)

Results:
Significant relationship between Ra-226 concentration in water and male lung cancer ($p = 0.028$)
Exposure-response trend noted

Excess risk indicated: yes

Estimated risk coefficient: not applicable

Reference:
Bean, J. A., Isacson, D., Hohne, R. M. A., Kohler, J. Drinking water and cancer incidence in Iowa: II Radioactivity in drinking water. Am. J. Epidemiol. 116:924-32; 1982.

Author: Dousset

Publication date: 1985

Country: France

Type of study: Ecological

Exposed: Limousin region - high gamma and radon

Unexposed: Poitou-Charentes - low gamma and radon

Control or adjustment for confounding variables: tobacco consumption the same for the two regions studied

Determination of radon daughter exposure:
Surrogate - geographic location (background radiation)

Results:
Lung cancer rates for males and females no different
High background - Male 52 E-5/a; female 6.8 E-5/a
Low background - Male 53.8 E-5/a; female 6.8 E-5/a

Excess risk indicated: no

Estimated risk coefficient: not applicable

Reference:
Dousset, M., Jammet, H. Comparaison de la mortalite par cancer dans le Limousin et le Poitou-Charentes. Radioprotection 20:61-67; 1985.

Author: Forastiere

Publication date: 1985

Country: Italy (Viterbo Province)

Type of study: Ecological

Exposed: High background area (volcanic soils)

Unexposed: Low background area (non-volconic soil)

Method:
Comparison of lung cancer mortality rates for 1969 - 1978 for population 35 - 74 years old

Control or adjustment for confounding variables:
age, degree of degree of urbanization, cigarette sales

Determination of radon daughter exposure:
Surrogate - volcanic content of soils, background radioactivity

Results:
Risk ratio males - 1.22 (p = 0.22)
Risk ratio females - 1.24 (p = 0.37)
Risk ratio total - 1.20 (p = 0.22))

Excess risk indicated: equivocal

Estimated risk coefficient: not applicable

Reference:
Forastiere, F., Valesini, S., Arco, M., Magliola, M. E., Michelozzi, P., Tasco, C. Lung cancer and natural radiation in an Italian Province. Sci. Total Environ. 45: 519-526; 1985.

Author: Hoffman

Publication date: 1985, 1986

Country: China, Austria

Type of study: Ecological

Exposed: China - High background area - 0.38 WLM/a
includes both radon and thoron daughters
Austria - Badgastein - 0.4 WLM/a

Unexposed:
China - Low background area - 0.16 WLM/a
includes both radon and thoron daughters
Austria - Salzburg - 0.2 WLM/a

Control for factors other than radon: For China, smoking habits and sex ratios comparable for both populations

Determination of radon daughter concentration:
Actual measurements of radon and thoron concentration

Results:
No difference in lung cancer rates between exposed and unexposed for both Austria and China

Excess risk indicated: no

Estimated risk coefficient: not applicable

Reference:
Hofmann, W., Katz, R., Zhang, C. Lung cancer incidence in a Chinese high background area - epidemiological results and theoretical interpretation. Sci. Total Environ. 45: 527-534; 1985.

Hofmann, W., Katz, R., Zhang, C. Lung cancer risk at low doses of alpha particles. Health Physics 51:457-468; 1986.

Author: Archer

Publication date: 1987

Country: USA (Reading Prong)

Type of study: Ecological

Exposed: 16 counties in NY, NJ, and PA associated with Reading Prong
Reading Prong (RP) counties = 7
Fringe counties (F) = 9

Unexposed: Counties adjacent to fringe counties = 17

Method: Lung cancer rates for whites compared for the three groups of counties

Control or adjustment for confounding variables:
none, (urban-rural, socioeconomic factors considered but not in analysis)

Determination of radon daughter exposure:
Surrogate - association with Reading Prong

Results:
Significant increase in lung cancer rates in RP and F counties

	Rate/100,000 (99% CL)
RP	31.32 (30.52,32.12)
F	27.49 (26.80,28.08)
C	23.91 (23.37,24.45)

Exposure-response effect observed
Population growth highest in RP counties indicating greatest degree of migration

Excess risk indicated: yes

Estimated risk coefficient: not applicable

Reference:
Archer, V.E.: Association of lung cancer mortality with precambrian granite. Arch. Env. Health 42: 87-91; 1987.

Author: Fleischer

Publication date: 1981

Country: USA

Type of study: Ecological

Method:

Comparison of counties with high lung cancer risk with geographic location

1. Counties in top decile of lung cancer rate - statistically significant difference from national average
2. Counties where 95% confidence interval on the lung cancer rate does not overlap 95% confidence interval for national rate
3. Counties with high lung cancer rates but overlapping confidence intervals

Determination of radon daughter exposure:

Surrogate - Geographic location (counties with phosphate mines, deposits or processing plants)

Control or adjustment for confounding variables: population

Results:

Comparisons of observed coincidences between phosphate counties and highest and significantly high lung cancer counties with expected coincidences showed obs/exp >1 ($p<0.01$) for males and females. When adjusted for population, effect was seen for all males ($p = 0.01 - 0.08$) and females in the most highly populated areas ($p<0.015$)

Excess risk indicated: yes

Estimated risk coefficient: not applicable

Reference:

Fleischer, R.L.: A possible association between lung cancer and phosphate mining and processing. Health Physics 41: 171-175; 1981.

Author: Edling

Publication date: 1982

Country: Sweden

Type of study: Ecological

Number of locations: 24 counties

Control or adjustment for confounding variables: none

Determination of radon daughter exposure:
Surrogate - background gamma radiation

Results:
Excess risk shown for lung cancer
Males r = 0.46 (p = 0.012)
Females r = 0.55 (p = 0.003)

Excess risk indicated: yes

Estimated risk coefficient: not applicable

Reference:
Edling,C., Comba, P., Axelson, O., Flodin, U. Effects of low-dose radiation - A correlation study. Scand. J. Work Environ. Health 8; suppl 1: 59-64; 1982.

Author: Hess

Publication date: 1983

Country: USA (Maine)

Type of study: Ecological

Number of locations: 16 counties

Control for factors other than radon: none

Determination of radon daughter exposure:
Surrogate - Radon concentration in water

Results:
Males, $r = 0.46$ ($p<0.10$)
Females, $r = 0.65$ ($p<0.01$)
Average, $r = 0.56$ ($p<0.05$)

Excess risk indicated: yes

Estimated risk coefficient: not applicable

Reference:
Hess, C.T., Weifenbach, C. V., Norton, S. A. Environmental radon and cancer correlations in Maine. Health Physics 45: 339-348; 1983.

Author: Letourneau

Publication date: 1983

Country: Canada

Type of study: Ecological

Number of locations: 18 cities

Control or adjustment for confounding variables: smoking for 14 cities

Determination of radon daughter exposure:
Geometric mean of the measured radon daughter concentrations

Results:
No significant correlation between lung cancer rates and geometric mean radon daughter concentration
Multiple linear regression on smoking and radon daughter concentration showed no effect of radon

Excess risk indicated: no

Estimated risk coefficient: not applicable

Reference:
Letourneau, E.G., Mao, Y., McGreggor, R. G., Semenciw, R., Smith, M. H., Wigle, D. T. Lung cancer mortality and indoor radon concentrations in 18 Canadian cities. Proceedings of the Sixteenth Midyear Topical Meeting of the Health Physics Society, Epidemiology Applied to Health Physics. pp 470 - 483; 1983.

Author: Fleisher

Publication date: 1986

Country: USA (Reading Prong)

Type of study: Ecological

Method:

Comparison of high lung cancer risk counties with geographic location

Risk groups:

1. Counties in top decile of lung cancer rates - statistically significant difference from national rates
2. Counties where 95% confidence interval on lung cancer rate does not overlap 95% confidence interval for national rate
3. Counties with high lung cancer rate but with 95% confidence interval overlaping 95% confidence interval for national rate

Control or adjustment for confounding variables: none

Determination of radon daughter exposure:

Geographic location

1. >50% within Reading Prong - 3 counties
2. <50% within Reading Prong - 10 counties

Results:

Comparison of observed coincidences between Reading Prong counties and highest, significantly high and not significantly high lung cancer counties with expected coincidences showed obs/exp > 1 ($p = 0.1$) for coincidences between highest and significantly high lung cancer counties and >50% Reading Prong counties

Excess risk indicated: yes

Estimated risk coefficient: not applicable

Reference:

Fleischer, R.L. A possible association between lung cancer and a geological outcrop. Health Physics 50: 823-827; 1986.

Author: Walter

Publication date: 1986

Country: USA (Connecticut)

Type of study: Ecological

Number of locations: 169 towns

Control or adjustment for confounding variables: socioeconomic status, population density

Determination of radon daughter exposure: none
Background radiation was the exposure variable

Results:
No significant correlation between lung cancer rates and background radiation

Excess risk indicated: no

Estimated risk coefficient: not applicable

Reference:
Walter, S. D., Meigs, J. W., Heston, J. F. The relationship of cancer incidence to terrestrial radiation and population density in Connecticut 1935 - 1974. Am. J. Epidemiol. 123: 1-14; 1986.

Author: Stranden

Publication date: 1986, 1987

Country: Norway

Type of study: Ecological

Number of sites: 75 locations measured; 20 homes/location

Control or adjustment for confounding variables: smoking

Determination of radon daughter exposure:
Activated charcoal and TLD; two per home

Results:
Significant correlation (95% confidence level) found between lung cancer incidence and mean radon concentration in grouped locations categorized by radon concentration*

Excess risk indicated: yes

Estimated risk coefficient:
Excess relative risk: 0.001 - 0.003/Bq-m-3 for radon
0.002 - 0.006/Bq-m-3 for progeny**
0.003 - 0.009/WLM***

Reference:
Stranden, E.: Radon-222 in Norwegian Dwellings. Radon and Its Decay Products; Occurrence, Properties, and Health Effects. ACS sypmosium Series 331, Hopke, P.K. ed. p 70 - 83; 1987.
Stranden, E.: Radon in Norwegian dwellings and the feasibility of epidemiologic studies. Radiat. Environ. Biophys. 25: 37-42; 1986.

* It is unclear whether the data was analyzed individually by location or whether locations were grouped by mean radon concentration and grouped data compared to lung cancer risk.

** Paper states radon progeny risk factor as 0.002 - 0.06
It was assumed that the 0.06 was a typographical error that should have been 0.006.

*** (0.002/Bq m-3)(3.7 E3 Bq m-3/WL) = 7.4/WL
(1 WL)(8760 hr/a/170 hr/mo)(0.8) = 40 WLM/WL a
((7.4/WL)/(40 WLM/WL a))(60 a) = 0.003/WLM

Author: Castren

Publication date: 1987

Country: Finland

Type of study: Descriptive

Method: Comparison of geographical distribution of lung cancer and elevated radon concentrations

Control or adjustment for confounding variables: none

Determination of radon daughter exposure: alpha track detectors in homes

Results: No observed resemblance between high lung cancer rates and high radon concentrations for males; some indication of resemblance in distribution for rural women

Excess risk indicated: no

Estimated risk coefficient: not applicable

Reference:

Castren, O. Dealing with radon in dwellings. Second International Specialty Conference on Indoor Radon. Air Pollution Control Association. New Jersey, April, 1987.

Author: Simpson

Publication date: 1983

Country: USA (Maryland)

Type of study: Cohort

Control or adjustment for confounding variables:
age, sex, many other variables; all housing variables studied except the one of interest

Determination of radon daughter exposure:
Surrogate - housing characteristics (basement construction, building material of walls , heat source, cooking fuels

Results: No difference in lung cancer rates with housing characteristics

Excess risk indicated: no

Estimated risk coefficient: not applicable

Reference:
Simpson, S. G., Comstock, G. W. Lung cancer and housing characteristics. Arch. Environ. Health 38:248-251; 1983.

APPENDIX C

SUMMARY OF UNPUBLISHED STUDIES WITH REGARD TO INDOOR RADON EXPOSURE AND LUNG CANCER RISK

The studies summarized in Appendix C are completed but as yet unpublished. One of the studies is the subject of a paper in press (Stockwell, American Journal of Epidemiology). Results of the other studies were reported in Masters or PhD theses, as oral presentations at meetings, as a special report or were obtained by personal communication with the researcher. As with the summaries of the published studies, the results shown are generally those for the analyses with the greatest degree of adjustment or control for confounding.

C 2

Author: Cohen

Country: USA

Type of study: Ecological

Method:
Correlation between lung cancer mortality rates and average radon exposure in various counties in the U. S. (310 counties)

Results:
Weak negative correlation observed.

Excess risk demonstrated: no

Estimated risk coefficient: not applicable

Reference:
Cohen, B. L. University of Pittsburgh. Personal communication: October, 1986, September, 1987.

Author: Lanes

Country: USA (Pennsylvania)

Type of study: Case-control

Cases: Lung cancers from 1/1/61 to 12/31/79 in Cannonsburg and Houston Boroughs - 50 cases

Controls: Sequential artheriosclerotic heart disease deaths from death records - 48

Control or adjustment for confounding variables: Socio-economic status, smoking (by assumption that all lung cancer cases were smokers), no stratification by sex, no adjustment for age

Determination of radon daughter exposure:
Track etch detectors (Terradex) summer and winter

Results:
Mean concentration in homes of cases was compared to mean concentration in homes of controls

No significant difference between case and control homes for geometric mean radon concentration

Borderline significant difference between case and control homes for arithmetic mean ($p = 0.09$, summer measurement; $p = 0.13$ for winter measurement)

Excess risk indicated: equivocal

Estimated risk cofficient: not applicable

Reference:
Lanes, S. F.: Lung cancer and environmental radon exposures: A case control study. Doctoral Dissertation, University of Pittsburgh; 1982.

Author: Stockwell

Country: USA (Florida)

Type of study: Case-control

Cases: All cases of lung cancer among Florida residents from 1981 - 1983 - 25,398 cases

Controls: Individuals with cancer of colon or rectum - approximately 22,000

Control or adjustment for confounding variables:
Smoking status considered in the analysis

Determination of radon daughter exposure:
Surrogate: residence in central Florida where phosphate deposits are located

Results:
Two-fold increase in lung cancer risk among non-smoking males living in study area.
Slight, but not significant, increase in risk among smokers.
No significant elevation in risk among women.
Residents of Tampa, not a high phosphate area, also showed increased risk of lung cancer.

Excess risk indicated: yes

Estimated risk coefficient: not applicable

Reference:
Stockwell, H. University of South Florida, Tampa, FL. personal communication. September, 1987. (paper in press)

Author: Stockwell

Country: USA (Florida)

Type of study: Case-control

Cases: All cases of carcinoma of the lung first diagnosed between 1981 and 1983 among residents of 53 Florida counties - 25,266 cases

Controls: All cases of colon and rectal cancers among residents of the same counties during the same time period

Control or adjustment for confounding variables: age, sex, race and tobacco use

Determination of radon daughter exposure:
Residence in county classified as having elevated radon levels based on statewide radon mapping study
3 counties - 15% or more of measured homes above 4 pCi/l
15 other counties with elevated radon levels
35 counties with no evidence of elevation in indoor radon potential

Results:
Males: significant elevation in odds ratio for highest three counties (All cell types: white, OR = 1.3, 95% CI (1.1,1.6); non-white, OR = 2.7, 95% CI (1.4,5.2)
Females: no significant increase in lung cancer risk
Odds ratios adjusted for age, sex, race and tobacco use:
Three highest counties: OR = 1.25, 95% CI (1.09,1.43)
Remaining 15 counties: OR = 0.88 95% CI (0.84,0.92)

Excess risk indicated: yes (among males only)

Estimated risk coefficient: not applicable

Reference:
Stockwell, H. paper presented at the Fourth International Symposium on The Natural Radiation Environment in Lisbon Portugal, December, 1987.

Author: Lanctot

Country: USA (Maine)

Type of study: Case-control pilot study

Cases: Lung cancer cases in Maine at least 10 years using water from privately owned drilled well - 35

Controls: Other cancers - 118 self-selected
Non cancer patients - 174 self-selected
All controls using water from privately owned drilled well

Control or adjustment for confounding variables:
Analysis for smoking, sex, age, residence history, education, occupation

Determination of radon daughter concentration:
Alpha track placed in kitchen - 2 month exposure

Results:
Significant excess risk of lung cancer for men under the age of 65 with radon concentration greater than 3 pCi/L in home

Excess risk indicated: yes

Estimated risk coefficient: not applicable

Reference:
Lanctot, E.M.: Radon in the domestic environment and its relationship to cancer: An epidemiologic study. Masters Thesis, State University of New York at Stony Brook. Maine Geological Survey, Department of Conservation Publication 85-88; 1985.

Author: Austin

Country: USA (Uravan, Colorado)

Type of study: Cohort

Method: Lung cancer rate for women living in Uravan, CO for at least one year were compared to expected rate (U.S. population, age adjusted; Colorado, age adjusted)

Control or adjustment for confounding variables: none

Determination of radon daughter exposure:
Measurement of individual residences by alpha track
Mean = 0.02 WL

Results: 6 cancers observed vs 3 expected (Colorado cancer rate)
SIR = 2.0 95% confidence limits (0.73,4.36)
Compared to U. S. cancer rate:
SIR = 1.15 95% confidence limits (0.42,2.51)

38,000 person-years of follow-up

Excess risk indicated: yes, but not statistically significant and only when results are compared to Colorado cancer rate.
(Austin considers results inconclusive.)

Estimated risk coefficient: not applicable

Reference:
Austin, S., Fort Collins, CO, personal communication, September, 1987.

APPENDIX D

SUMMARY OF STUDIES IN PROGRESS WITH REGARD TO INDOOR RADON EXPOSURE AND LUNG CANCER RISK

The following summaries of studies in progress are based in most cases on personal interviews with the principal investigator or other researchers involved as well as written study protocols. For three studies (Stebbings, Stockwell, Stockwell), the information was obtained from telephone communication.

The procedures described are those planned as of the date of the interview and may be changed before or during the studies.

D 2

Country: Sweden

Principal investigator: Pershagan

Type: Case-Control
Females

Cases: Females admitted to hospital with suspect lung or bronchus malignancy

Controls: Control born on the same day determined from population registry

Estimated numbers: Cases - 200
Controls - 400

Control or adjustment for confounding variables: Diet (Vitamins A and C)
Passive smoking, active smoking

Determination of radon daughter exposure:

1. Questions asked about all residences lived in more than two years
   location, type of house, building year, type of heating system, type of ventilation, type of building materials
2. Radon exposure estimated from geological conditions and building characteristics
3. Measurement of radon gas by track etch - two week measurement
   "high risk" homes in Stockholm area
   random sample of "low risk" homes in Stockholm
4. Measurement of radon gas by track etch - one year - 1500 case and control homes

Expected date for preliminary results: 1987

Expected date for final results: 1988

Reference:

Pershagan, G. National Institute of Environmental Medicine, Stockholm, Sweden. Personal communication; May, 1987.

Country: Canada (Winnipeg, Manitoba)

Principal investigator: LeTourneau, Health and Welfare Canada

Type: Case control
Male and female

Cases: Lung cancers diagnosed - living at time of interview
(no surrogate interviews)

Controls: No cancer, selected at random, matched for age, sex and occupation

Estimated numbers: Cases - 700 (200/yr)
Controls - 700

Control or adjustment for confounding variables:
Questionnaire requests information on marital status, ethnicity, education, education, employment, vitamin use, health history, smoking, passive smoking, use of hair dye, income, use of oral contraceptives and hormones

Determination of radon daughter exposure:
Radon exposure to be determined for all current and previous residences using alpha track detectors, soil sampling and grab sampling

Expected date for preliminary results: none

Expected date for final results: 1990

Reference:
Letourneau, E. Health and welfare Canada, Ottawa, Ontario, Canada. Personal communication; June, 1987.

D 4

Country: Hungary (Miskolc)

Principal investigators: Takacs and Paripas; Regional Health Department, Miskolc, Hungary

Type: Ecological
Indoor radon concentrations compared for two towns, one with high lung cancer (5 E-4/a) and one with low lung cancer rate (2 E-4/a)

Estimated numbers: not known

Control or adjustment for confounding variables: no information on smoking

Determination of radon daughter exposure:
Radon measurements made in approximately 100 residences in each town using alpha track detectors
Thoron measurements made (estimate from total alpha minus radon)
External gamma measurements made using TLDs

Preliminary results:
No significant difference in radon concentrations between the two towns
Gamma exposure approximately 20% higher in high lung cancer rate town
Thoron concentration significantly higher in high lung cancer rate town

Final results: Study is continuing; no specific date for final results

Reference:
Takacs, S., Regional health department, Miskolc, Hungary. Personal communication; August, 1987.

Country: England (Cornwall and Devon)

Principal investigators: Doll, Darby; Imperial Cancer Research Fund
NRPB

Type: Case-control

Cases: Patients under 75 years of age admitted to hospital with presumptive diagnosis of lung cancer

Controls: Matched sample of patients admitted to same hospital with presumptive diagnosis of conditions unrelated to smoking
Matched sample of healthy individuals randomly selected from Family Practitioner Committee lists for Devon and Cornwall

Estimated numbers: Cases - 500 - 1000
Controls - 1000 - 2000

Control or adjustment for confounding variables:
Smoking, occupation, sex, age
Use of presumptive diagnosis and later rejection of cases with other confirmed diagnosis provides control group free of interview bias

Determination of radon daughter exposure:
Measurement of atmospheric radon in random sample of homes stratified by area and length of time in which individuals inhabited them

Expected date for preliminary results: unknown (interviews to be completed in two years)

Expected date for preliminary results: unknown

Reference:
James, A. National Radioligical Protection Board. Personal communication; April, 1987.
Darby, S. C. Personal communication; April, 1987.
Muirhead, C. R. Personal communication; April, 1987.

Country: Norway

Principal investigator: Stranden, Norwegian Statens Institutt for Stralenhygiene in collaboration with:
NPRB, United Kingdom
Norwegian Cancer Registry

Type: Correlation

Method: Lung cancer incidence by municipality as determined from Cancer Registry data compared to mean radon concentration in dwellings

Control or adjustment for confounding variables: smoking

Determination of radon daughter exposure:
Stratified random sample of dwellings in each municipality; number to be proportional to population except in two largest cities.
(Sample stratified by type of housing) - 10,000 dwellings
NRPB dosemeters in each dwelling for six months in main bedroom

Expected date for preliminary results: End of 1988

Expected date for final results: unknown

Reference:
Stranden, E. Norwegian Statens Institutt for Stralenhygiene, Oslo, Norway. Personal communication; May, 1987.

Country: Finland (Uusimaa, Kymi)

Principal investigators: Castren, Ruosteenoja
Finnish Centre for Radiation and Nuclear Safety
Finnish Cancer Registry

Type: Case-control

Cases: Male lung cancer cases diagnosed 1980 - 1985 in study area

Controls: Population based - random sample of men living in study area, stratified by age, from Finnish Population Register Center

Estimated numbers: Cases - 300
Controls - 1500

Control or adjustment for confounding variables: smoking, rural residents only used

Determination of radon exposures:
Radon daughter level measured in all long-term residences from 1950 - 1980
Alpha track film in living room for two months

Expected date for preliminary results: unspecified

Expected date for final results: December, 1987

Reference:
Castren, O. Finish Centre for Radiation and Nuclear Safety, Helsinki, Finland. Personal communication; May, 1987.

Country: USA (Pennsylvania)

Principal investigator: Stebbings, Argonne National Lab

Type: Case-control

Cases: Female lung cancer cases - women born in state and dying as resident of state, case series defined by lung cancer cell type

Controls: undetermined

Estimated numbers: 2,000 cases

Control or adjustment for confounding variables: Smoking

Determination of radon daughter exposure:
Alpha track measurement in major living areas

Expected date for preliminary results: none given

Expected date for final results: none given

Reference:
Stebbings, J. Argonne National Laboratory. Personal communication; July, 1987.

D 9

Country: USA (Missouri)

Principal investigator: Brownson, Missouri Dept. Health

Type: Case-control (population-based)

Cases: Non-smoking female incident lung cancer cases determined from Missouri cancer registry

Controls: Random sample of non-smoking female Missouri population, frequency matched to overall case series by age, race and smoking status.

Estimated numbers: Cases - approximately 280
Controls - approximately 560

Control or adjustment for confounding variables:
All cases and controls non-smoking
Questionnaire will obtain information with regard to residential history, passive smoking, family history of cancer, nonmalignant respiratory disease, hormonal factors and menstrual history, use of space heating and cooking, dietary history, occupational exposures and history
Data will be analyzed by family history of lung cancer and by lung cancer cell type

Determination of radon daughterexposure:
Radon measurement made by alpha track in homes of each case and control occupied during the past thirty years. Two detectors per home to be left in place for one year

Expected date for preliminary results: 1988 - 1990

Expected date for final results: 1990

Reference:
Brownson, R. Missouri Department of Health, Columbia, Mo. Personal communication, June, 1987.

Country: USA (Maine, New Hampshire)

Principal investigator: Rand, Maine Medical Center

Type: Case-control
male and female

Cases: Incident cases of lung cancer contacted soon after diagnosis, pathology report required, must have lived in area for 5 years, must be able to measure 80% of past exposure (5 - 35 years in the past)

Controls: Population based from drivers licenses under age 65, Health Care Financing records over age 65; frequency matched for age and sex - same criteria as for cases

Estimated numbers: 500 female cases and controls
500 male cases and controls

Control or adjustment for confounding variables: smoking, occupational exposures, house construction and health

Determination of radon daugter exposure:
Alpha track detectors will be placed in living room and bedroom of all residences cases and controls lived in during the period 5 - 35 years prior to diagnosis - only cases and controls for whom 80% of the prior exposure can be determined will be included in the study

Expected date for preliminary results: unknown

Expected date for final results: unknown

Reference:
Rand, P., Lacombe, E. Maine Medical Center, Portland, ME.
Personal communication; June, 1987.

Country: USA (Maine) - Pilot study

Researcher: Bogdan, Maine Department of Human Services

Type: Case-control
males and females

Cases: Lung cancer cases living or recently deceased served by a privately-owned drilled well for at least ten years

Controls: Individuals with other cancers
Individuals with no cancer

Estimated numbers: Cases - 100
Controls - 150, 250

Control or adjustment for confounding variables: smoking, occupational exposures; medical history
Questions asked about house construction, water use, occupancy habits

Determination of radon daughter exposure:
Terradex Track Etch dosimeters on refrigerator in kitchen
Radon in water

Expected date for preliminary results: Preliminary results reported in MS thesis, E. M. Lanctot (see Appendix C, Unpublished studies)

Expected date for final results: 1987

References:

Lanctot, M. Maine Geological Survey, Augusta, ME. Personal communication; September, 1987.

Rand, P., Lacombe, E. Maine Medical Center, Portland, ME. Personal communication; June, 1987.

Country: USA (New Jersey)

Principal investigator: Klotz, New Jersey Department of Health

Type: Case-control
Females only

Cases: Primary and histologically confirmed cancers, females, 8/82 - 9/83

Controls: Stratified by age, race
Interviewed cases under age 65 - controls selected from drivers license files
Cases interviewed over age 65 - controls from HCFA files
Next of kin interviewed cases - controls from death certificates matched by age and date of death

Estimated numbers: Cases - 994
Controls - 995

Control or adjustment for confounding variables: smoking, diet

Determination of radon daughter exposure:
Radon measurement in residence of longest duration over 10 - 30 years prior to diagnosis (greater than 10 years residence)
Charcoal canisters in basement and master bedroom (4 days) 10/86 - 4/87, repeat Fall 87 - Winter 88
Alpha track (Terradex) 2 or 3 per house, 1 year

Expected date for preliminary results: none

Expected date for final results: Fall 1988

Reference:
Klotz, J., Schoenberg, J. New Jersey Department of Health, Trenton, NJ. Personal communication; June, 1987.

Country: USA

Principal investigator: Cohen

Type: Ecological

Method: Lung cancer incidence by county compared to mean measured indoor radon concentrations

Control or adjustment for confounding variables: unknown

Determination of radon daughter exposure:
Charcoal canister

Expected date for preliminary results: ongoing study, results reported periodically

Expected date for final results: none given

Reference:
Cohen, B. University of Pittsburgh, Pittsburgh, PA. Personal communication; October, 1987.

Country: USA - Florida

Principal investigator: Stockwell, University of South Florida

Type: Pilot study - Case-control

Cases: Females with lung cancer

Controls: Females, randomly selected, matched for age, race and general geographic area

Estimated numbers: Cases - 80
Controls - 80

Control or adjustment for confounding variables:
Smoking, diet, occupation controlled in analysis

Determination of radon daughter exposure:
Alpha track detectors (3 months) in homes lived in 10 years or longer

Expected date for preliminary results: none

Expected date for final results: Dec. 1987

Reference:
Stockwell, H. University of South Florida, Tampa, Florida. Personal communication; September, 1987.

Country: USA - Florida

Principal investigator: Stockwell

Type: Case-control

Cases: Non-smoking women living in Florida 10 years or longer, newly diagnosed lung cancer

Controls: Non-smoking women randomly selected, matched for age, race, geographic location, living in Florida at least 10 years

Estimated numbers: Cases - 300
Controls - 600

Control or adjustment for confounding variables:
Control in analysis for effects of factors such as passive smoking, occupation, diet, family history

Determination of radon daughter exposure:
Alpha track detectors in home for one year. Current home if lived in 10 or more years; up to 4 previous Florida homes, lived in at least 5 years

Expected date for preliminary results: none given

Expected date for final results: 1992 or 1993

Reference:
Stockwell, H. University of South Florida, Tampa, Florida. Personal communication; September, 1987.

APPENDIX E

COMPUTATIONS OF LIFETIME LUNG CANCER RISKS ATTRIBUTABLE TO INDOOR RADON

Estimates of lifetime lung cancer risk due to indoor radon exposure were computed using models developed by:

- The National Academy of Sciences Committee on the Biological Effects of Ionization Radiation, BEIR III (NAS80) and BEIR IV (NAS88)
- The National Council on Radiation Protection and Measurements, NCRP78 (NCRP84)
- The International Commission on Radiation Protection, ICRP50 (ICRP87)
- The U.S. Environmental Protection Agency, (USEPA86)

Exposure to indoor radon was calculated for mean annual indoor radon concentrations of 1.0 pCi ℓ^{-1}, the presumed U.S. average concentration (Ne86), and 4.0 pCi ℓ^{-1}, the EPA guideline where some remedial action is recommended (USEPA86). The fraction of time spent indoors was assumed to be 75%, with a mean outdoor concentration of 0.2 pCi ℓ^{-1}, and an equilibrium factor of 0.5 for both indoors and outdoors.

The annual exposure at 1.0 pCi ℓ^{-1} (18.5 Bq m^3 EEC) is:

$$\frac{[(1.0\ \text{pCi}\ \ell^{-1})(0.75) + (0.2\ \text{pCi}\ \ell^{-1})(0.25)][0.5][8760\ \text{h}\ a^{-1}]}{[100\ \text{pCi}\ \ell^{-1}\text{WL}^{-1}]\ [170\ \text{WL h WLM}^{-1}]}$$

$$= 0.21\ \text{WLM}\ a^{-1}\ (1.3\text{x}10^{5}\ \text{Bq h m}^{-3})$$

The annual exposure at 4.0 pCi ℓ^{-1} (74 Bq/m^3 EEC) is:

$$\frac{[(4.0\ \text{pCi}\ \ell^{-1})(0.75) + (0.2)(0.25)]\ [0.5]\ [8760\ \text{h}\ a^{-1}]}{[100\ \text{pCi}\ \ell^{-1}\text{WL}^{-1}]\ [170\ \text{WL h WLM}^{-1}]}$$

$$= 0.79\ \text{WLM}\ a^{-1}\ (5.0\text{x}10^{5}\ \text{Bq h m}^{-3})$$

BEIR

The BEIR III risk coefficients are:

$10\text{x}10^{-6}$ WLM^{-1} a^{-1}	ages 35-49
$20\text{x}10^{-6}$ WLM^{-1} a^{-1}	ages 50-65
$50\text{x}10^{-6}$ WLM^{-1} a^{-1}	ages 65-75

Assuming a minimum 5 year latent period and a mean lifespan of 75 years the excess lifetime risk can be calculated.

The average number of years of exposure for the age group 35-49 is 42 years. Taking into account a latent period of 5 years, the mean effective exposure time is 37 years. Therefore, the mean effective cummulative exposure at 1 pCi ℓ^{-1} and 4 pCi ℓ^{-1} indoors is

$$(37a) \times (0.21\ \text{WLM}\ a^{-1}) = 7.8\ \text{WLM}$$

$$(37a) \times (0.79\ \text{WLM}\ a^{-1}) = 29\ \text{WLM}$$

Repeating this for the 50-65 age group:

$$(52.5a)\ (0.21\ WLM\ a^{-1}) = 11.03\ WLM$$
$$(52.5a)\ (0.79\ WLM\ a^{-1}) = 41.48\ WLM$$

and the 66-75 age group:

$$(65.5a)\ (0.21\ WLM\ a^{-1}) = 13.76\ WLM$$
$$(65.5a)\ (0.79\ WLM\ a^{-1}) = 51.75\ WLM$$

The lifetime excess lung cancer risks were obtained by multiplying the risk coefficients by the number of years at risk and the mean effective cummulative exposure. The number of years at risk is the total number of years in the age range to which the risk coefficient applies up to age 75. At 1 pCi ℓ^{-1}:

$$(10\times10^{-6}\ a^{-1}\ WLM^{-1})\ (15\ a)\ (7.77\ WLM) = 1.2\times10^{-3}$$
$$(20\times10^{-6}\ a^{-1}\ WLM^{-1})\ (16\ a)\ (11.03\ WLM) = 3.5\times10^{-3}$$
$$(50\times10^{-6}\ a^{-1}\ WLM^{-1})\ (10\ a)\ (13.76\ WLM) = 6.9\times10^{-3}$$
$$\text{Total} \quad 1.2\times10^{-2}$$

At 4 pCi ℓ^{-1}

$$(10\times10^{-6}\ a^{-1}\ WLM^{-1})\ (15\ a)\ (29.23\ WLM) = 4.4\times10^{-3}$$
$$(20\times10^{-6}\ a^{-1}\ WLM^{-1})\ (16\ a)\ (41.48\ WLM) = 1.3\times10^{-2}$$
$$(50\times10^{-6}\ a^{-1}\ WLM^{-1})\ (10\ a)\ (51.75\ WLM) = 2.6\times10^{-2}$$
$$\text{Total} \quad 4.4\times10^{-2}$$

NCRP

From NCRP78, Table 10.2, the lifetime excess lung cancer risk for a lifetime exposure of 1.0 WLM a^{-1} is 9.1×10^{-3}

Thus, for 1 pCi ℓ^{-1}, the lifetime risk is:

$$(0.21 \text{ WLM } a^{-1}) (9.1 \times 10^{-3} \text{ a WLM}^{-1}) = 1.9 \times 10^{-3}$$

For 4.0 pCi ℓ^{-1} the lifetime risk is:

$$(0.79 \text{ WLM } a^{-1}) (9.1 \times 10^{-3} \text{ a WLM}^{-1}) = 7.2 \times 10^{-3}$$

ICRP

The model used by the ICRP is a proportionate hazards model with a relative excess risk coefficient dependent on age at exposure. The lifetime risk is:

0.019 WLM^{-1}	for ages 0-20a
0.0064 WLM^{-1}	for ages >20a

The average relative excess risk coefficient adjusted for age at exposure, assuming a lifespan of 75 years, is 0.0098 WLM^{-1}.

The ICRP model takes into account the effect of premature death due to indoor radon exposure. However, the relative excess risk coefficient remains constant for annual exposures less than 3 WLM.

Proportionate hazards vs. relative risk models can be applied to populations using the "observed" lung cancer risk corrected for the population mean radon risk component:

$$\bar{R} = R_o + \bar{r}\,\bar{E}\,R_o$$

where: $\bar{R}$ = the observed lung cancer risk

$\bar{r}$ = mean relative risk coefficient for radon daughter exposure

$\bar{E}$ = mean lifetime radon daughter exposure

R_o = baseline (no radon daughter exposure) lung cancer risk.

$$R_o = \frac{\bar{R}}{1 + \bar{r}\,\bar{E}}$$

The ICRP uses a baseline lifetime lung cancer risk of 0.6% for nonsmokers without radon exposure. This was derived by subtracting 10% from the calculated nonsmoker lifetime lung cancer risk to account for the radon daughter contribution.

The excess lung cancer risk from radon daughter exposure at an average indoor radon concentration of 1.0 pCi ℓ^{-1} (0.21 WLM a^{-1}) would be:

$$(0.21\ \text{WLM}\ a^{-1})\ (70a)\ (0.006)\ (0.0098\ \text{WLM}^{-1}) = 0.00086$$

For heavy smokers (>2 packs/day) the lung cancer mortality is 15 to 25 times that for nonsmokers (USPHS82). However, due to premature death from other smoking related diseases, the ratio of the lung cancer risk due to radon for smokers versus nonsmokers is not a linear function. For annual indoor radon daughter exposures less than an EEC of 10^6 Bq h m^{-3} (1.6 WLM) the ratio

of lifetime lung cancer risk due to radon for one pack/day smokers vs. nonsmokers is approximately 5 (ICRP87). For heavy smokers (>1 pack/day) that ratio is unlikely to exceed 7.

For people who have stopped smoking for at least 15 years, the mortality rate for lung cancer is about twice that for nonsmokers (USPHS82).

Therefore, for smokers the lifetime lung cancer risk attributable to radon daughters at a mean indoor radon concentration of 1.0 pCi ℓ^{-1} is:

$$(5)\ (0.00086) = 0.0043$$

For ex-smokers at 1.0 pCi ℓ^{-1}

$$(2)\ (0.00086) = 0.0017$$

At an average indoor radon concentration of 4.0 pCi ℓ^{-1} the lifetime excess lung cancer risk for a nonsmoker is:

$$(0.79\ \text{WLM}\ a^{-1})\ (70a)\ (0.006)\ (0.0098\ \text{WLM}^{-1}) = 0.0033$$

For a smoker at 4 pCi ℓ^{-1}:

$$(0.0033)\ (5) = 0.016$$

For an ex-smoker at 4 pCi ℓ^{-1}:

$$(0.0033)\ (2) = 0.0065$$

EPA

The EPA uses a relative risk model with risk coefficients of 0.01 WLM^{-1} to 0.04 WLM^{-1}. For the relative risk coefficient of 0.01 WLM^{-1} the baseline lung cancer risk, used for the ICRP risk calculation, 0.6%, is appropriate since the ICRP relative risk coefficient is nearly the same.

For an assumed relative risk coefficient of 0.04 WLM^{-1}, the baseline lung cancer risk must be adjusted to account for the greater contribution of indoor radon at mean concentration levels to the observed lung cancer rate.

$$R_o = \frac{\bar{R}}{1 + r\bar{E}}$$

$$\bar{R} = R_o (1 + rE)$$

Assuming the relative risk coefficient is 0.0098 WLM^{-1} (ICRP87)

$$\bar{R} = 0.6\% \left[1 + (0.0098\ WLM^{-1})\ (14.7\ WLM)\right]$$

$$\bar{R} = 0.69\%$$

Assuming the relative risk coefficient is 0.04 WLM^{-1}

$$R_o = \frac{0.69}{1 + (0.04)\ (14.7)} = 0.43$$

Assuming a lifespan of 75 years and a latent period of 5 years, at a mean indoor radon daughter concentration of 1.0 pCi/ℓ the lifetime lung cancer risks are as follows:

Nonsmoker

$$(0.01\ WLM^{-1})\ (0.006)\ (0.21\ WLM\ a^{-1})\ (70a) = 0.0009$$

$$(0.04\ WLM^{-1})\ (0.0043)\ (0.21\ WLM\ a^{-1})\ (70a) = 0.0025$$

Using the increased baseline risks for ex-smokers and chronic smokers described in the section regarding the ICRP model, the lifetime attributable lung cancer risk for ex-smokers is:

$$(0.01\ WLM^{-1})\ (2)\ (0.006)\ (0.21\ WLM\ a^{-1})\ (70a) = 0.0018$$

$$(0.04\ WLM^{-1})\ (2)\ (0.0043)\ (0.21\ WLM\ a^{-1})\ (70a) = 0.0051$$

For chronic smokers:

$$(0.01\ WLM^{-1})\ (5)\ (0.006)\ (0.21\ WLM\ a^{-1})\ (70a) = 0.0044$$

$$(0.04\ WLM^{-1})\ (5)\ (0.0043)\ (0.21\ WLM\ a^{-1})\ (70a) = 0.013$$

At a mean indoor radon daughter concentration of 4 pCi ℓ^{-1} the following lifetime risks are calculated:

Nonsmoker:

$$(0.01\ WLM^{-1})\ (0.006)\ (0.79\ WLM\ a^{-1})\ (70a) = 0.0033$$

$$(0.04\ WLM^{-1})\ (0.0043)\ (0.79\ WLM\ a^{-1})\ (70a) = 0.0095$$

Ex-smoker:

$$(0.01\ WLM^{-1})\ (2)\ (0.006)\ (0.79\ WLM\ a^{-1})\ (70a) = 0.0066$$

$$(0.04\ WLM^{-1})\ (2)\ (0.0043)\ (0.79\ WLM\ a^{-1})\ (70a) = 0.019$$

Chronic Smoker:

$$(0.01\ WLM^{-1})\ (5)\ (0.006)\ (0.79\ WLM\ a^{-1})\ (70a) = 0.017$$

$$(0.04\ WLM^{-1})\ (5)\ (0.0043)\ (0.79\ WLM\ a^{-1})\ (70a) = 0.048$$

The EPA (USEPA86) based their risk estimates on a mean population lung cancer risk. This risk is heavily weighted by smoking related lung cancers. Approximately 85% of lung cancers occur in smokers (USPHS86). Therefore, while this method is appropriate for estimating the effect of indoor radon exposure on the entire population, the resulting estimates should not be interpreted as representing individual risks. Smoking experience is the overwhelming factor in determining an individual's lung cancer risk. Other conditions such as diet, occupational exposures, air pollution and genetic make-up may be also critical factors in lung cancer risk for some individuals. Therefore, the projected excess lung cancer risk for an individual is subject to considerable uncertainty.

EPA also adjusts the radon daughter exposure to account for the difference in breathing rates between occupationally exposed individuals, principally miners, and individuals exposed at home or in sedentary occupations. The calculations included in this Appendix and shown in Table 6 use WLM without adjustment.

BEIR IV

The excess lung cancer risks due to indoor radon exposure were estimated from the risk ratios given in Table 2-4 of the BEIR IV Report (NAS88). The lifetime baseline lung cancer risks for smokers and nonsmokers were assumed to be the mean of those for males and females. The baseline risk for ex-smokers was assumed to be twice that for nonsmokers.

In order to be consistent with the calculation of the risk estimates based on the EPA model, the baseline risks were adjusted for average radon exposure. (BEIR IV estimates do not include this adjustment since it was considered to be insignificant compared to other uncertainties inherent in the analysis.)

Estimated lifetime risk of lung cancer from BEIR IV (NAS88).

Males	
Smokers	0.123
Nonsmokers	0.0112
Females	
Smokers	0.058
Nonsmokers	0.0060

The lifetime risks were adjusted for mean radon daughter exposure by dividing by a factor of 1.18, the estimated lifetime risk ratio for exposure to 0.2 WLM/yr. The estimated mean baseline lifetime risks for a mixed population, 50% male and 50% female, reduced to account for average radon daughter exposure are 0.077 for smokers and 0.0073 for nonsmokers.

The risk ratios, R_e/R_o, (lifetime lung cancer risk for exposed vs. lifetime lung cancer risk for unexposed) estimated in BEIR IV (NAS88) are as follows:

	0.2 WLM/year	0.8 WLM/year
Smokers		
Males	1.16	1.62
Females	1.18	1.69
Mean	1.17	1.66
Nonsmokers		
Males	1.19	1.73
Females	1.18	1.73
Mean	1.19	1.73

Therefore, the excess lifetime risk at 0.2 WLM/year (1 pCi ℓ^{-1}) is as follows:

Smokers

(0.17) (0.077) = 0.013

Nonsmokers

(0.19) (0.0073) = 0.0014

Ex-smokers

(0.19) (0.0073) (2) = 0.0028

at 0.8 WLM/yr (4 pCi ℓ^{-1}):

Smokers

(0.66) (0.077) = 0.051

Nonsmokers

(0.73) (0.0073) = 0.0053

Ex-smokers

(0.73) (0.0072) (2) = 0.011

The BEIR IV risk estimates are based on a multiplicative model. The authors of BEIR VI (NAS88) found evidence in Colorado miner data to support a submultiplicative interaction between smoking and radon daughter exposure but the analysis was not sufficiently persuasive to abandon the more conservative multiplicative model.

END

DATE

FILMED

7-26-88

NTIS